

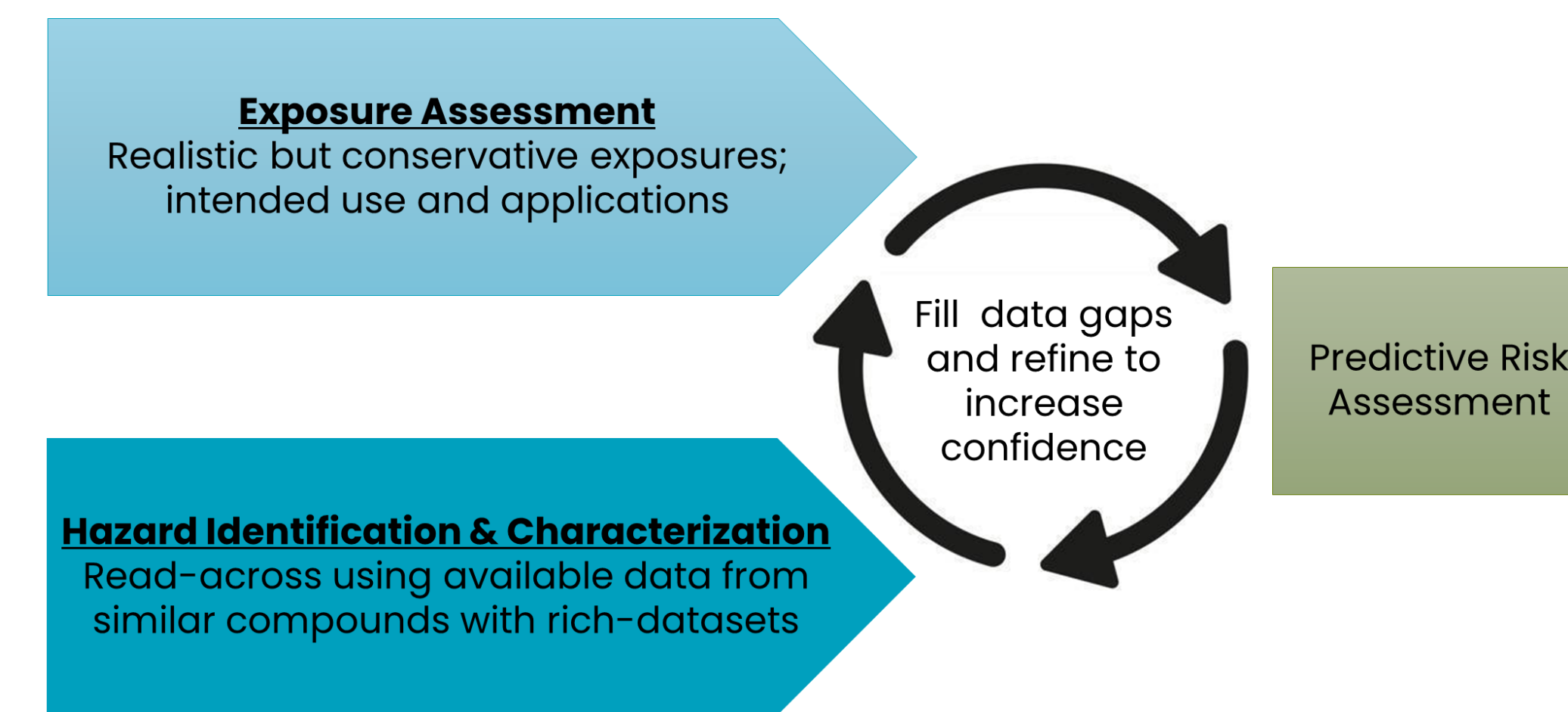
A Framework for Predictive Risk Assessment of Non-genotoxic Agrochemicals using Read-across to Reduce Vertebrate Testing

Amber Goetz¹, Natalia Ryan¹, Elaine Freeman², Muna Nahar², Christian Picard², David Dreier¹, Gina Hilton³, Richard A. Currie⁴, Tharacad Ramanarayanan¹
¹Syngenta Crop Protection LLC, Greensboro, NC; ²Exponent Inc., Washington, DC, WA; ³PETA Science Consortium International, e.V., Germany; ⁴ Syngenta Crop Protection, Bracknell, United Kingdom

Motivation



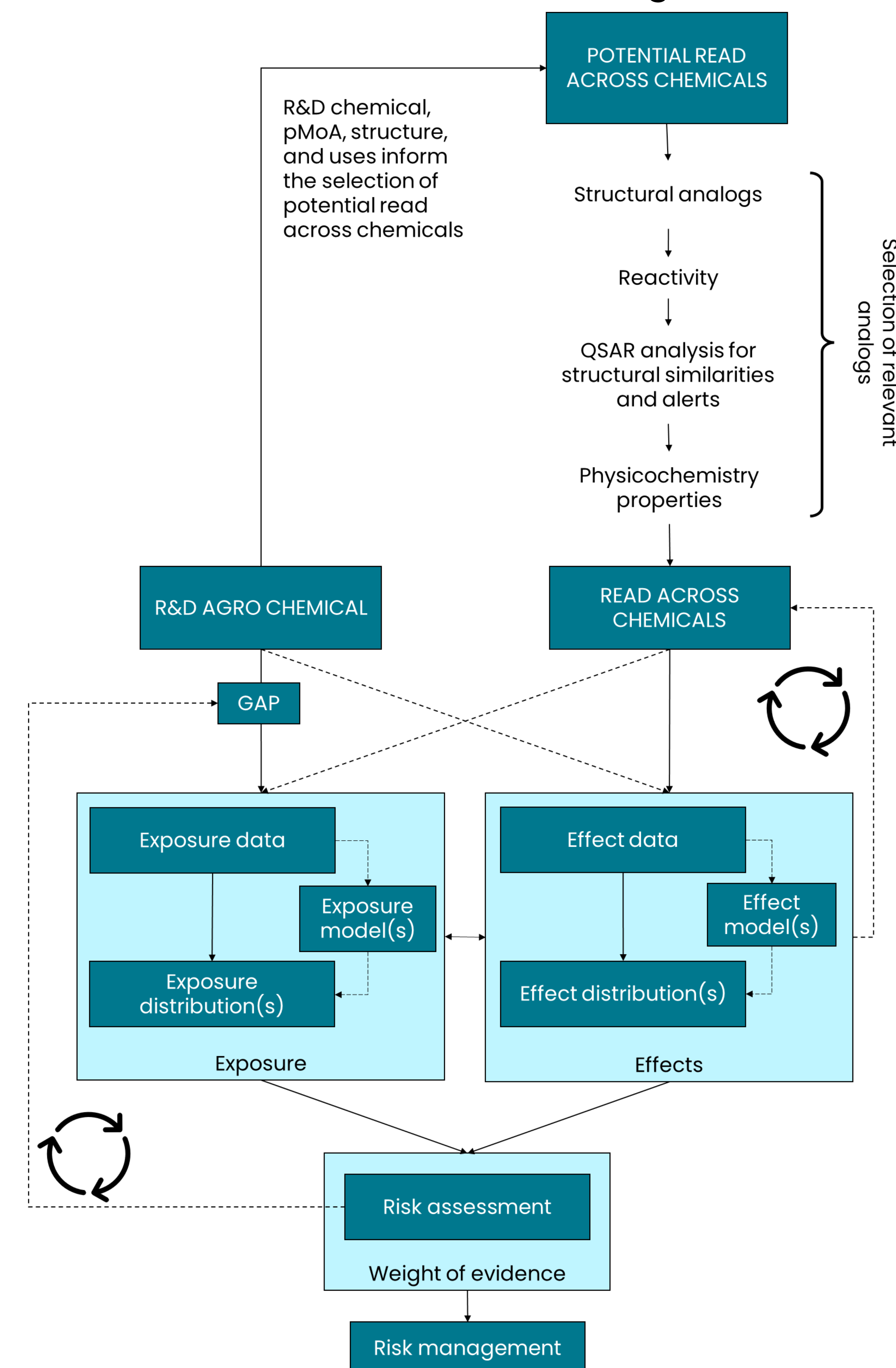
An Alternative Approach to Traditional Risk Assessments Using Read-Across



The Framework Purpose of Use

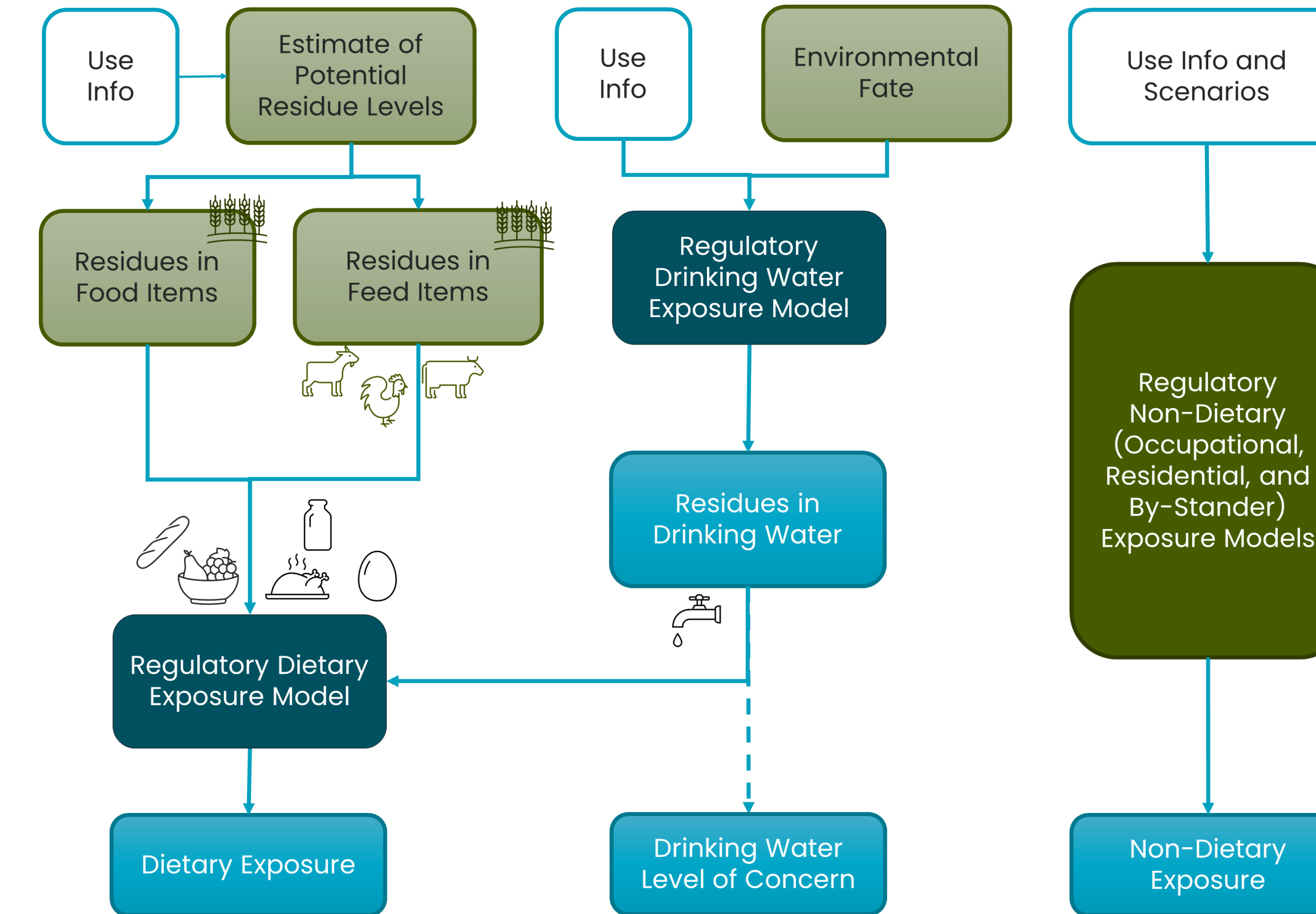
- Identify and obtain realistic, but conservative, anticipated exposures from the intended use and application of the agrochemical using standard regulatory approaches;
- Use existing toxicity data within the same mode of action to determine endpoints for risk assessment, decreasing reliance on vertebrate studies;
- Combine exposure data with the hazard endpoints to forecast risk; and
- Organize the findings of the predictive risk assessment.

Decision Tree to Evaluate New Active Ingredients using Read-Across and Weight of Evidence

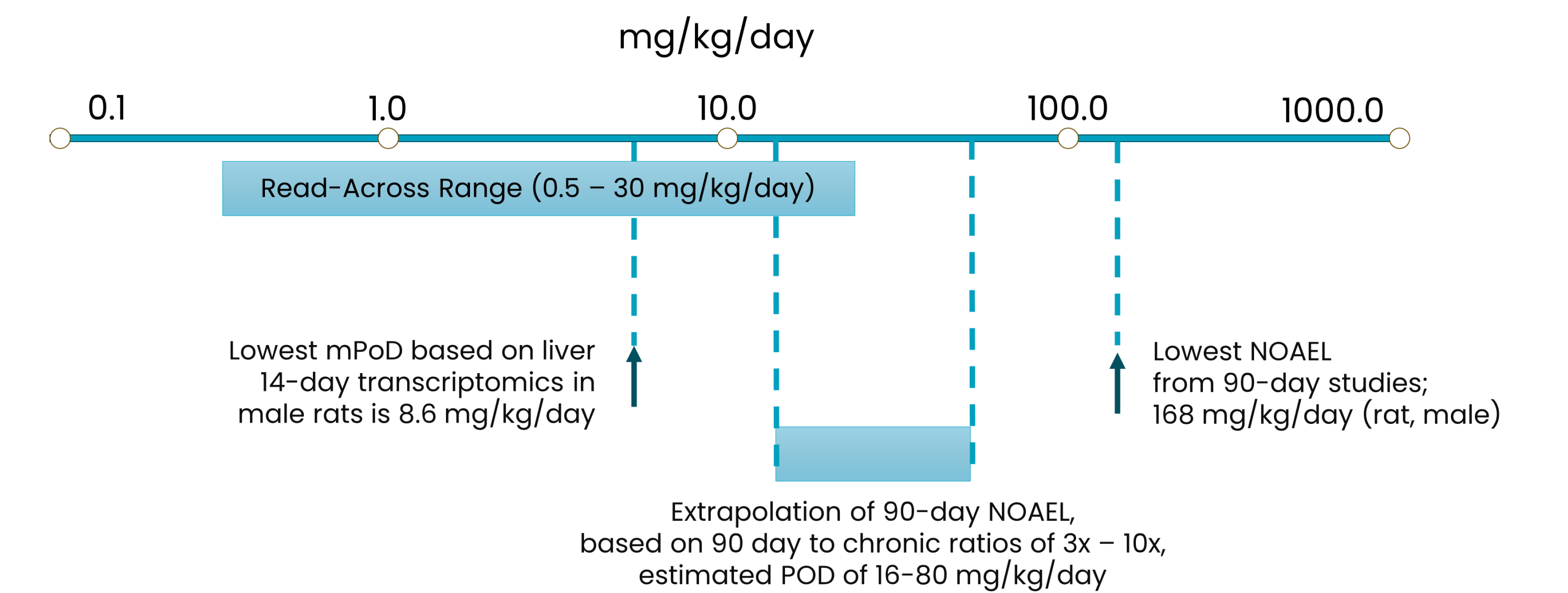


Exposure Assessment

* Agrochemical Exposure Assessment is presented here as an example for Specific Use-Based Exposure Assessment *

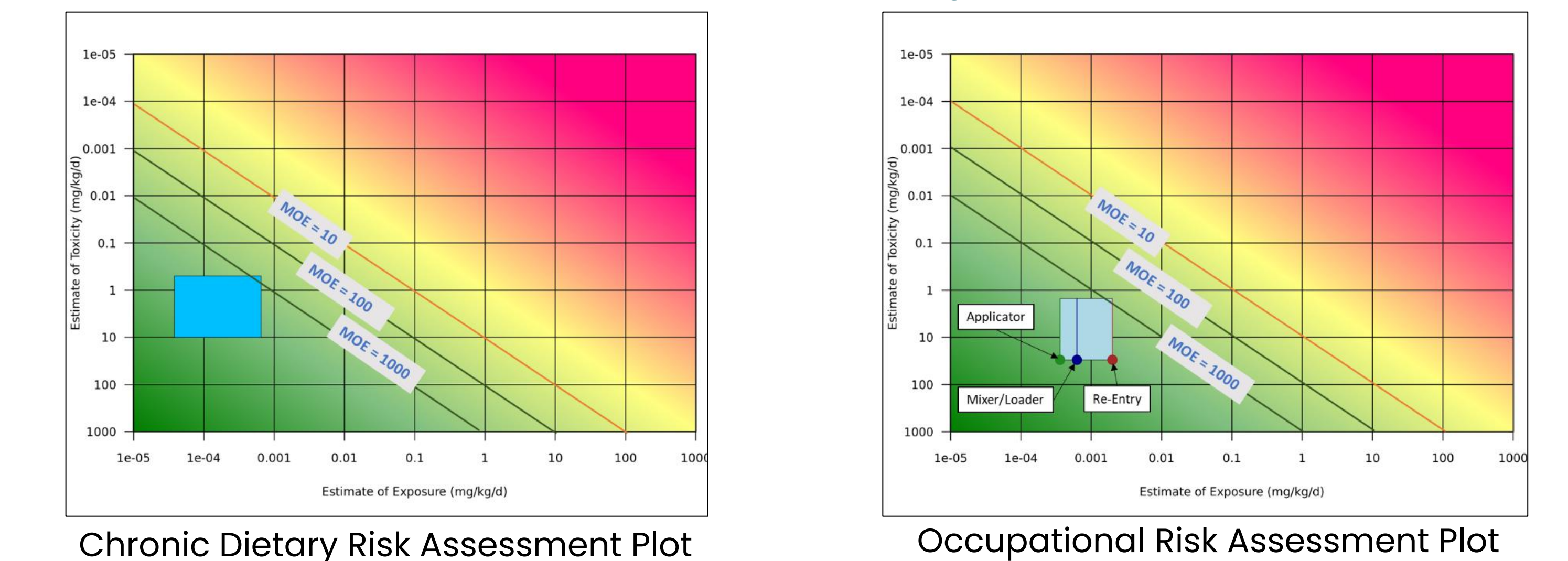


ACCcase Inhibitor Case Exemplar: Estimate of Chronic POD

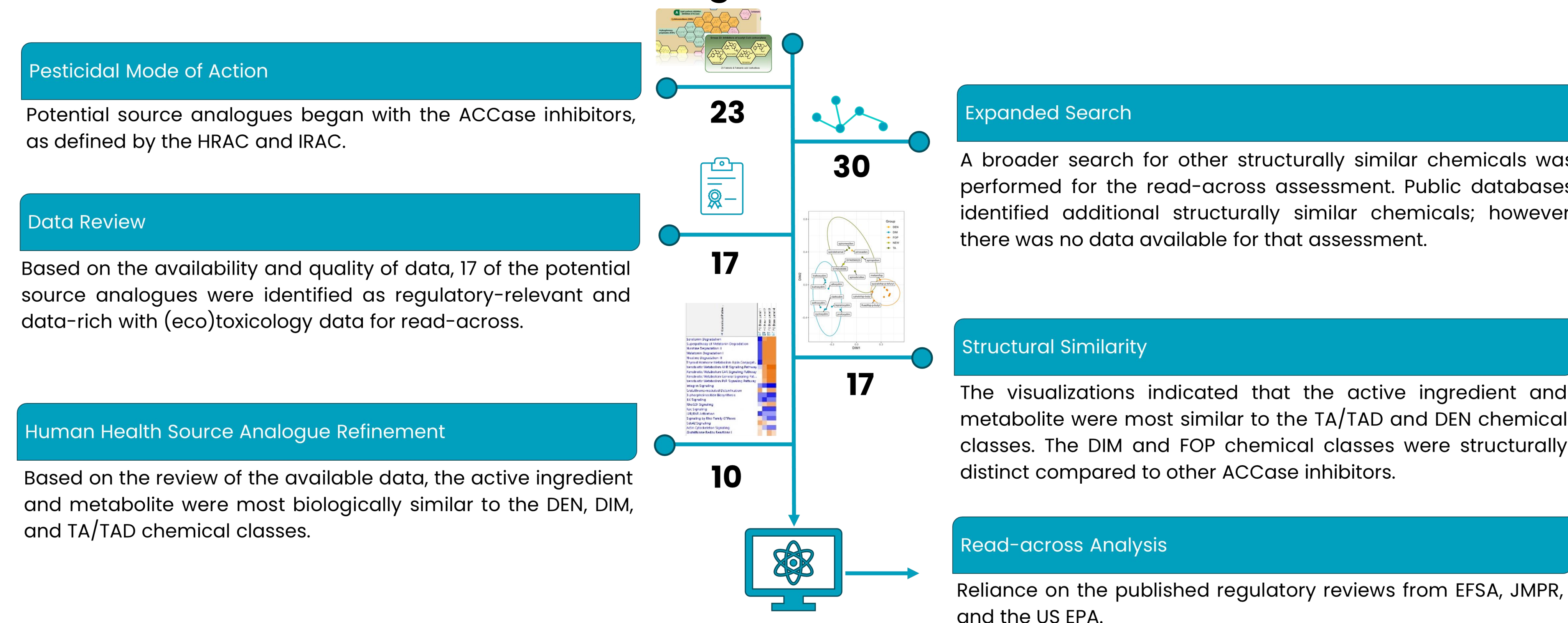


Risk21 Plots Based Solely on Read-Across and Proposed Use

<https://risk21.org/>



ACCcase Inhibitor Case Exemplar: Selection of Source Analogues for Read-Across Assessment



Summary

- If the new ACCcase is the same or less toxic than the most toxic existing ACCcase, chronic dietary risk assessment will pass with nearly 1000X MOE
- Structural similarity, mode of action assessment, and transcriptomic analysis were used to support selection of read-across analogues.
- Occupational (dermal, inhalation, incidental oral) scenarios have resulted in similarly favorable predictive risk assessments.
- Given sufficient lines of evidence to support read-across and chemical groupings, a human health-protective risk assessment can be conducted without chemical-specific vertebrate testing/data.

References

Currie R.A., Abbott J., Dreier D.A., Lu H. et al. Developing prototypes of a Modernized Approach to Assess Crop Protection Chemical Safety. ALTEX 41(1), 119-130.
 Dreier D.A., Picard C., Kabler K., Ryan N. et al. Developing a modern approach to assess ecological risk from pesticides without unnecessary vertebrate animal testing. Environmental Chemistry 21 (2024) EN23105

