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

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## Motivation



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



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# An Alternative Approach to Traditional Risk Assessments Using Read-Across

**Exposure Assessment** Realistic but conservative exposures; intended use and application

dentification & Characteriz ead-across using available data fror milar compounds with rich-datas

### **Exposure Assessment**

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



# **ACCase Inhibitor Case Exemplar:** Selection of Source Analogues for Read-Across Assessment

### esticidal Mode of Action

Potential source analogues began with the ACCase inhibitors, as defined by the HRAC and IRAC.

#### Data Review

Based on the availability and quality of data, 17 of the potential source analogues were identified as regulatory-relevant and data-rich with (eco)toxicology data for read-across.

#### luman Health Source Analogue Refinement

Based on the review of the available data, the active ingredient and metabolite were most biologically similar to the DEN, DIM, and TA/TAD chemical classes.





#### panded Search

A broader search for other structurally similar chemicals was performed for the read-across assessment. Public databases identified additional structurally similar chemicals; however there was no data available for that assessment.

#### Structural Similarity

The visualizations indicated that the active ingredient and metabolite were most similar to the TA/TAD and DEN chemical classes. The DIM and FOP chemical classes were structurally distinct compared to other ACCase inhibitors.

#### Read-across Analysis

Reliance on the published regulatory reviews from EFSA, JMPR, and the US EPA.

#### References

- regulatory approaches;





Chronic Dietary Risk Assessment Plot

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





### The Framework Purpose of Use

 Identify and obtain realistic, but conservative, anticipated exposures from the intended use and application of the agrochemical using standard

• 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.

### Occupational Risk Assessment Plot

### Summary

If the new ACCase is the same or less toxic than the most toxic existing ACCase, 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.



