

Key learnings from OECD IATA case studies on carcinogenicity assessment of agrochemicals

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Background

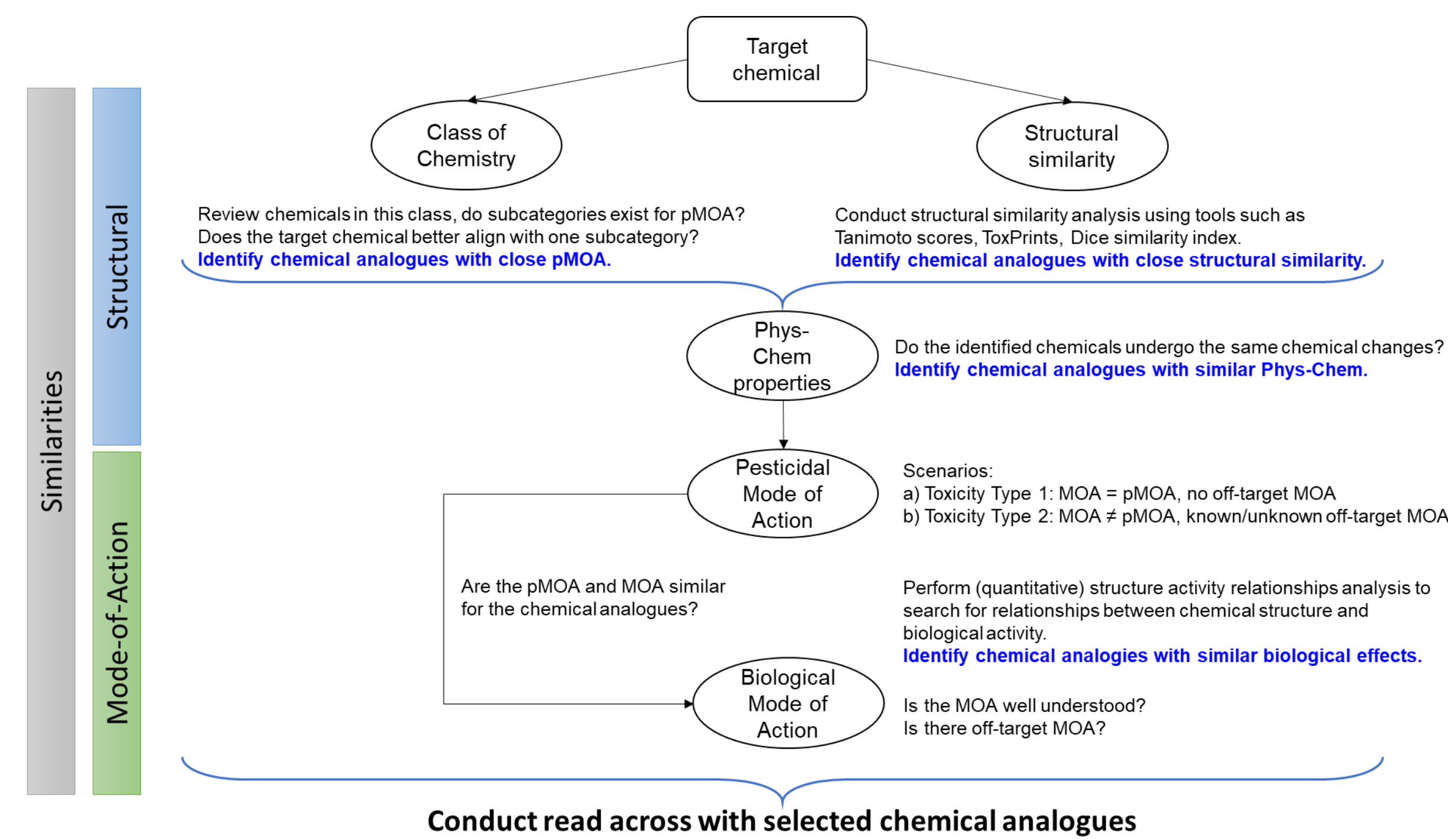
The Organisation for Economic Co-operation and Development (OECD) is an international standards-making body that collaborates with multiple stakeholders to establish evidence-based guidance.

OECD launched the IATA Case Studies Project with the intention of building experience through case studies that demonstrate their use to fulfill regulatory needs for product safety assessment.

OECD IATA Case Study Project

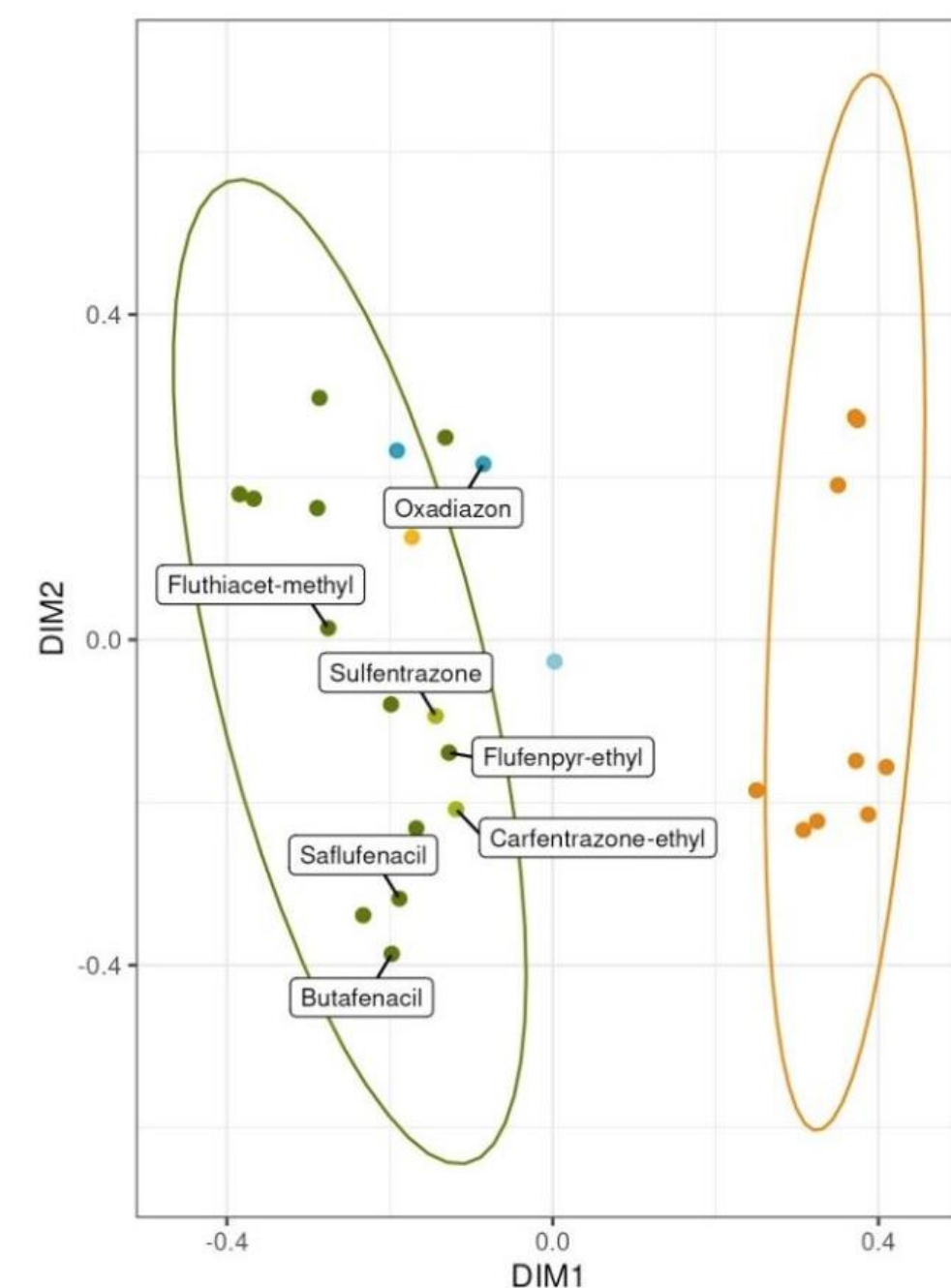


Read-across used in Weight of Evidence assessment



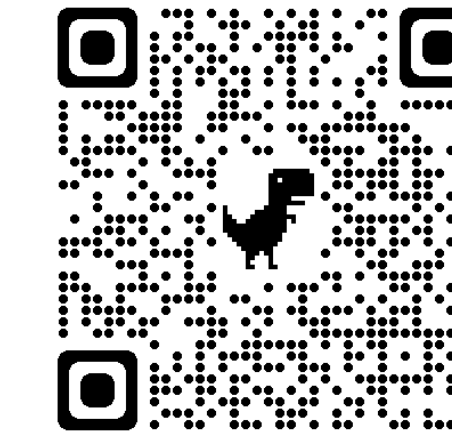
Structural Similarity

- Group
- Diphenyl ethers
- N-Phenyl-imides
- N-Phenyl-oxadiazolones
- N-Phenyl-triazolinones
- Other
- Phenylpyrazoles

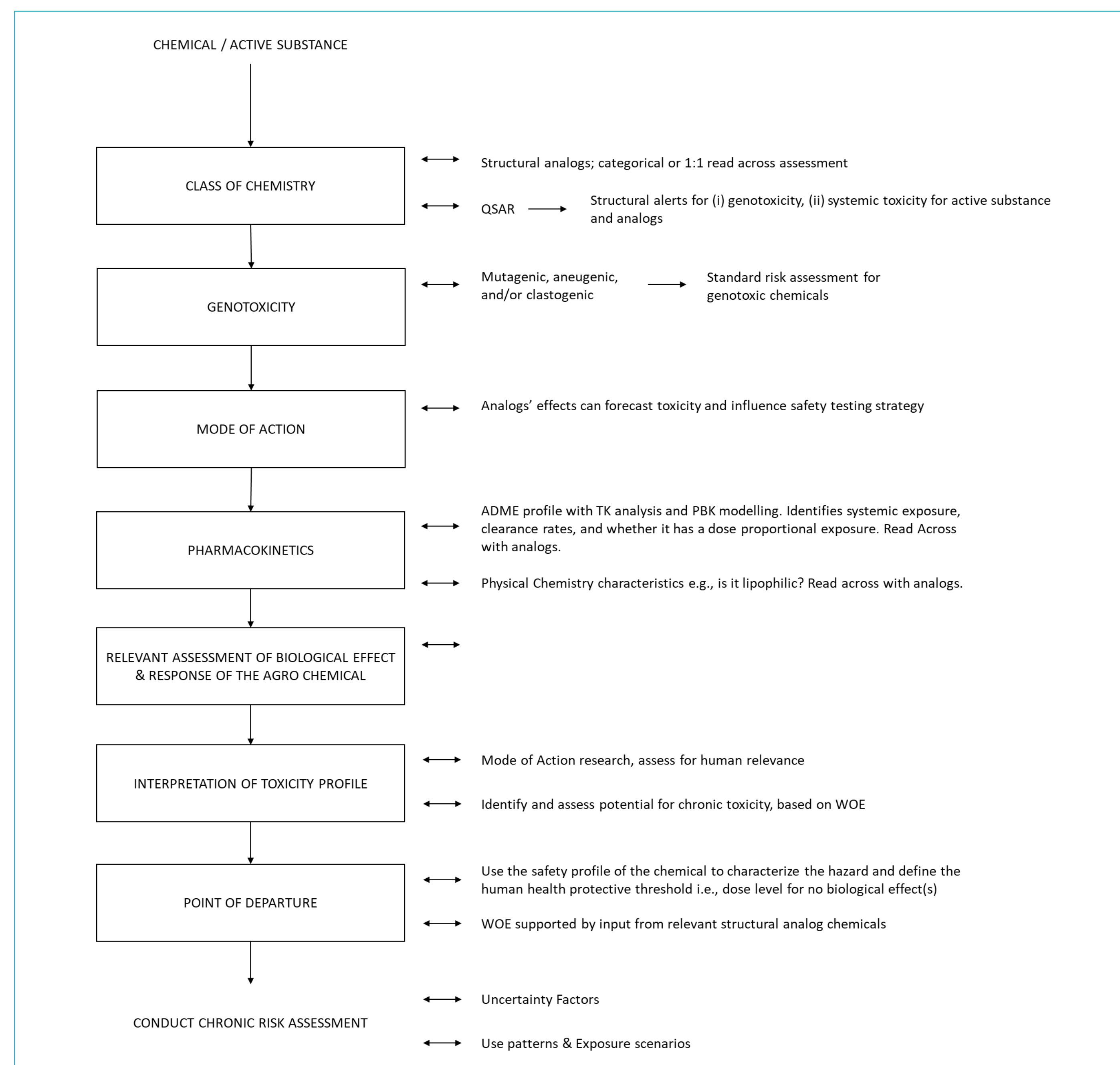


Information to include in the IATA case study

- 1. Introduction**
- 2. Purpose** (e.g., Purpose of use, target chemical, endpoint(s), Exposure)
- 3. Hypothesis for performing IATA**
- 4. Approaches used** (e.g., AOP, read-across, defined approach)
- 5. Data/Information gathering Application of IATA** (e.g., summary of data, uncertainty, strategy for integration)



A weight of evidence to estimate point of departure for chronic risk



ACKNOWLEDGMENTS

The authors would like to acknowledge the regulators and workshop participants for their time, effort, and helpful review comments of the case studies.

REFERENCES

Hilton, G.M., Adcock, C., Akerman, G., Baldassari, J., Battalora, M., Casey, W., Clippinger, A.J., et al. (2022). Rethinking chronic toxicity and carcinogenicity assessment for agrochemicals project (ReCAAP): framework to support a weight of evidence safety assessment without long-term rodent bioassays. *Regul. Toxicol. Pharmacol.* 131, 1-9. doi.org/10.1016/j.yrtph.2022.105160



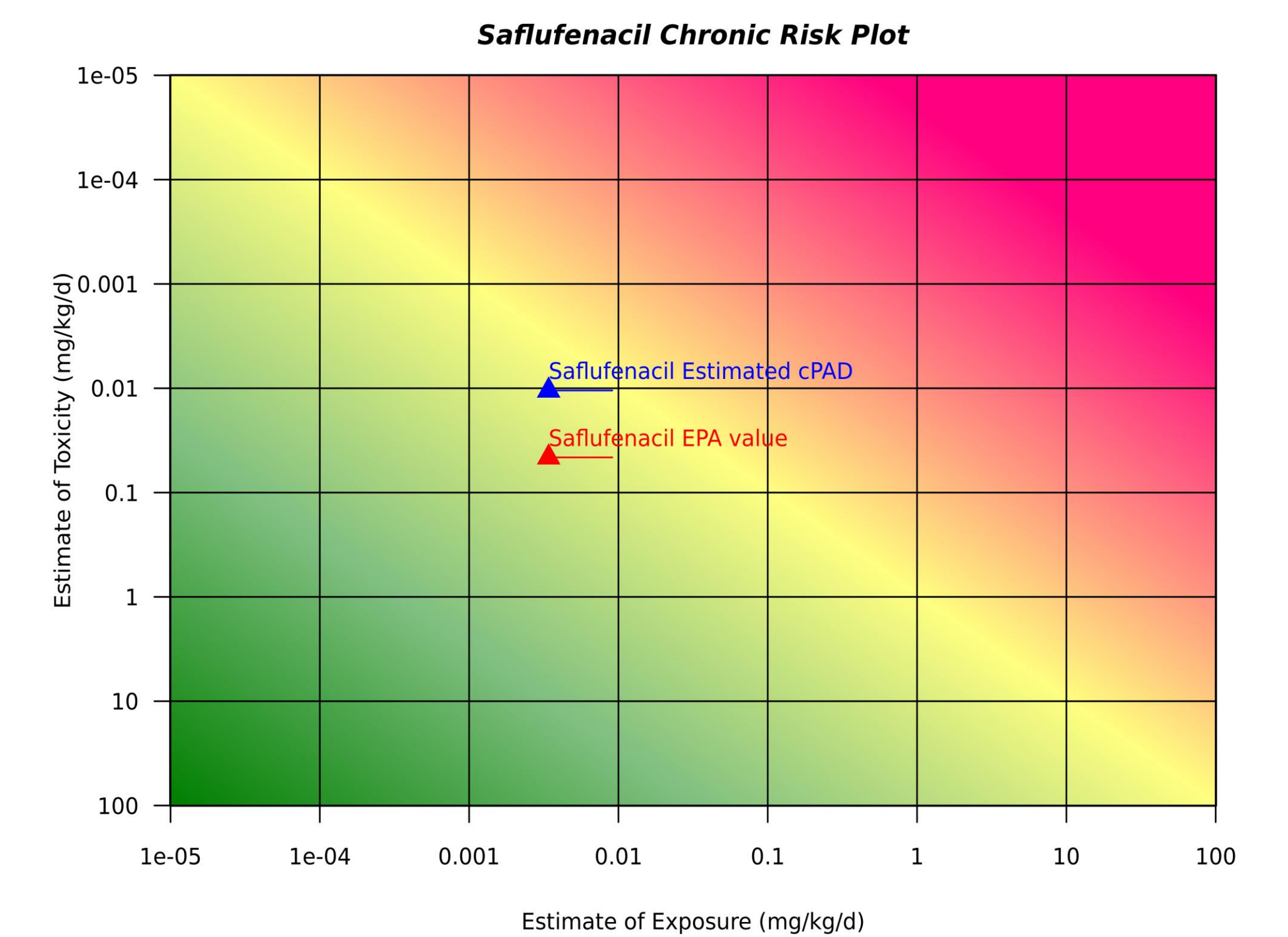
Key learnings

- Following the submission of an IATA case study to the OECD, expert reviewers from international regulatory authorities and other stakeholders provided feedback:
 - Inclusion and Exclusion Criteria for Read-across
 - More Detailed explanation for toxicological modes of action
 - Discussion of why the lowest dose level was not selected
 - Difference in country perspectives as to the adequacy of data and usefulness of the approach
- Out of the comments came the following key learnings:
 - Adapt and expand the existing OECD guidance on grouping and read across to reflect a fit-for-purpose agrochemical application of existing data.
 - Retrospective analyses illustrated that the IATA would result in health protective decisions.
 - Implementing such an IATA will require direct communication between the registrant and the regulatory agency that will be evaluating the submission.

Strongest aspects of the case study

Weight of Evidence assessment:

The WoE approach was reasonable and well thought out, as a framework. A WoE approach is used to estimate the POD without using rodent lifetime assays.



Further development & guidance

Mode of Action: Clearly report human relevance of the MOA. Provide case studies with quantitative and qualitative non-relevance to human exposures. Provide more molecular and cellular data to support the MoA and AOP.

Justification and rationales: The justifications presented in the different sections were considered sound. The justification of the inclusion of immunity and hormone data and its importance to genotoxicity was good; however, additional rationale and details would be beneficial in some areas.