Title: Application of molecular target homology-based approaches to predict species sensitivities to two pesticides, permethrin and propiconozole

Author: [*]Carlie A. LaLone, [*]Daniel L. Villeneuve, [†]Lyle D. Burgoon,[*]Christine L. Russom, [‡]Jason P. Berninger, [*]Joseph E. Tietge, [§]Henry Helgen, [*]Megan N. Severson, [¶]Jenna E. Cavallin, [*]Gerald T. Ankley

* US EPA Mid-Continent Ecology Division, Duluth, MN, USA

† US EPA, NCEA, Research Triangle Park, NC, USA.

§ Computer Sciences Corporation, Duluth, MN, USA.

¶ Oak Ridge Institute for Science and Education Fellow, Duluth, MN, USA.

Abstract:
In the U.S., registration of pesticide active ingredients requires a battery of intensive and costly in vivo toxicity tests which utilize large numbers of test animals. These tests use a limited array of model species from various aquatic and terrestrial taxa to represent all plants and animals potentially at risk. Predictive methods that systematically and quantitatively assess molecular target homology across species, i.e., at the molecular initiating event level of an adverse outcome pathway, show promise for identifying and ranking species most likely to respond to chemical perturbations of these protein targets. The advent and refinement of these strategies could lead to more focused and integrated approaches to testing and assessment, utilizing the most relevant species with mode of action (MOA) specific toxicity tests, thereby reducing cost and animal use. To further understand and demonstrate the capabilities of protein homology-based species sensitivity predictions, we conducted case studies with two pesticides with known MOAs: permethrin a common insecticide that targets voltage gated para-like sodium channels, and propioconozole a fungicide that inhibits sterol 14 alpha-demethylase (CYP51). Primary amino acid sequence and conserved functional domain analyses were conducted and non-target species were ranked according to their predicted relative sensitivity to the pesticides. We then compared the results of the homology analyses with empirical toxicity data as a means to demonstrate the appropriate domain(s) of applicability for such predictive methods. This presentation will describe these analyses, and additional progress made in the development of an automated web-tool for such protein-based assessments. *The contents of this abstract neither constitute nor reflect official US EPA policy.*

Contact information:
Carlie LaLone;
U.S. Environmental Protection Agency
6201 Congdon Blvd.
Duluth, MN, 55804
LaLone.Carlie@epa.gov

I prefer platform presentation

STICs Field	Entry
1 – Influence/profile	Not applicable
2 – Clearance tracking no.	Assigned automatically
3 – Principal Investigator / Project Officer	Carlie Lalone
4- Product title	Copy and paste from abstract
5 - Authors	See abstract all e-mail addresses in EPA domino system
6a- Product type	Presentations and technical summaries
6b-Product subtype	Abstract
6c – Records schedule	Not a senior official
7a – Impact statement	n/a
7b- Product description	Paste in abstract
8 – Bibliographic citation	SETAC North America 33rd Annual Meeting, 11-15 November, Long Beach, CA, USA.
9 - Access	Public
10 – Tracking and Planning Task	2.1.1 2.1.1: Adverse outcome pathway (AOP) discovery and definition
10 – Tracking and Planning Product	(3) Web-based tool for evaluating cross-species conservation of key molecular targets associated with molecular initiating events and/or key events represented in AOPs as a means for predicting the relative sensitivity or susceptibility of various species to adverse effects associated with exposure to chemicals acting through those AOPs.
11 – Copyright permission	No
12 - QA	not applicable
13 – Policy implications	No
14 - Keywords	pesticide species extrapolation dashboard adverse outcome pathway