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Abstract Title:
The utility of human ADME data for prioritizing the evaluation of pharmaceuticals in the environment.

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To proceed in the investigation of potential effects of pharmaceuticals in the environment, a cohesive data collection strategy is paramount. Given the lack of data for aquatic species, prioritization seems a logical starting point. Several methods have been put forward, for example using predicted persistence, bioaccumulation, and toxicity characteristics or sales data models. While these models are valid, critical prioritization strategies, they are not sufficiently comprehensive. Pharmaceuticals are biologically active, with specific physiological targets, suggesting that models built solely on physical-chemical properties and exposure potential cannot be adequate for prioritization. Given the nature of pharmaceuticals, the overall prioritization should include chronic effects and ADME (absorption, distribution, metabolism, excretion) parameters. The lack of available aquatic species data requires the development of an ADME-based prioritization model using read-across from the extensive mammalian knowledge-base. ADME data for 750 drugs were collected including: apparent volume of distribution, clearance rate, half life, protein binding, and therapeutic dose. For this initial prioritization, a probabilistic model was applied to data from each parameter, and subsequently divided into categories based on the each 10^{th} centile. Each centile group was given a corresponding score of 1 to 10 ($<10^{th}$ = 1, 10^{th} – 20^{th} centile = 2 … $<90^{th}$ centile =10). Higher scores were based on the likelihood of increased absorption and distribution, or decreased metabolism or elimination. Scores were tallied for each individual drug and summed across all parameters. The resulting prioritized list looks quite different (with some overlap) from lists created from previous prioritization exercises. The unique pharmacokinetic nature of this list provides a basis for the development of testable hypotheses. This ADME-based list has been used to identify potential additions to analyte list for environmental sample analysis. Internally, the prioritized list has been used to focus research decisions in the process of validating an ADME read-across model. As part of the cohesive strategy moving forward, ADME prioritization should be included as a tool within the overall prioritization strategy, with the highest testing priority given to drugs which rank highly using multiple prioritization schemes. *The contents of this abstract neither constitute nor reflect official US EPA policy.*

STICs Field	Entry
1 – Influence/profile	Not applicable
2 – Clearance tracking no.	Assigned automatically
3 – Principal Investigator / Project Officer	Gerald Ankley
4- Product title	Copy and paste from abstract
5 - Authors	See abstract
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	steroidogenesis fungicide toxicity fish

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