Exploiting enhanced non-testing approaches to meet the needs for sustainable chemistry

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Sustainable chemistry is the design and use of chemicals that minimize impacts to human health, ecosystems and the environment. To assess sustainability, chemicals must be evaluated not only for their toxicity to humans and other species, but also for environmental persistence and potential formation of toxic products as a result of biotic and abiotic transformations. Traditional approaches to evaluate these characteristics are resource intensive and normally lack biologically mechanistic information that might facilitate a "safety by design" approach. A more promising approach would exploit recent advances in high-throughput (HT) and high-content (HC) screening methods coupled with computational methods for data analysis and predictive modelling. The elements of a framework to assess sustainable chemistry could rely on integration of non-testing approaches such as (Q)SAR and read-across, coupled with prediction models derived from HT/HC methods anchored to biological pathways (eg., Adverse Outcome Pathways). Acceptance and use of such integrated approaches necessitates a level of validation that demonstrates scientific confidence for specific decision contexts. Here we illustrate a scientific confidence framework for Tox21 approaches underpinned by a mechanistic basis, and illustrate how this will drive the development of enhanced non-testing approaches. This framework also focuses development of prediction models that are hybrid yet local in terms of their chemistry in nature. Specific examples highlight how the extensive testing library within ToxCast was profiled with respect to its chemistry, resulting in new insights that direct strategic testing as well as formulate new predictive models specifically SARs. *This abstract does not necessarily reflect U.S. EPA policy.*