

Evolving the EPA Endocrine Disruptor Screening Program: The case for and against using high-throughput screening assays in EDSP Tier 1

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Testing has begun as part of the EPA Endocrine Disruptor Screening Program (EDSP) Tier 1 battery of 11 *in vitro* and *in vivo* tests. A recognized issue with the EDSP is that the current Tier 1 screening battery is highly resource intensive in terms of cost, time and animal usage for the large numbers of chemicals with unknown endocrine potential that need to be evaluated. The significant advances in both computational and molecular technologies have enabled a more rapid identification of markers for adverse outcome pathways since EPA began work on developing and implementing the EDSP. The EPA is proposing to evolve the EDSP by incorporating *in vitro* high-throughput screening (HTS) assays that can rapidly detect potential interactions of chemicals with the estrogen, androgen, thyroid hormone and steroidogenesis (EATS) pathways. In the near term, incorporating HTS assays will focus on developing a prioritized list of chemicals for evaluation in the current Tier 1 battery. (Prioritization would continue to take other factors into account, including exposure and use.) A longer term goal is to evolve the Tier 1 battery by fully incorporating HTS assays in order to increase reliance on nonanimal screens for which there is confidence in their ability to predict *in vivo* adverse effects. Although the overall approach is reasonable, it is highly provocative and debatable for a number of reasons. On the one hand, this proposal has the potential to greatly improve the speed, cost effectiveness, and mechanistic specificity of the EDSP using fewer animals, but on the other hand, there are concerns about reliability and relevance of the HTS assays and lack of full validation (e.g., transferability, between-laboratory evaluation) pharmacokinetics and metabolic capacity, etc. The roundtable speakers will present the case for and against using this approach and will allow time for open discussion with the audience. This abstract does not necessarily reflect US EPA policy.