Abstract Title: A Risk-based Prioritization Strategy for Thyroid Disruption

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Abstract:

The US Environmental Protection Agency (EPA) established the Endocrine Disruptor Screening Program (EDSP) to determine whether certain substances may have an effect in humans or wildlife that disrupt the estrogen, androgen or thyroid axes. The EDSP is now utilizing computational and high throughput screening (HTS) *in vitro* assays to more efficiently and rapidly assess chemicals for prioritization of endocrine disruption testing. Of the 11 Tier 1 assays, only three inform on potential thyroid disruption with limited endpoints and these are *in vivo* assays which are expensive and time-consuming. Recent comprehensive and systematic literature reviews of the thyroid pathway have identified a number of potential target sites that could serve as Molecular Initiating Events (MIEs) for potential thyroid disrupting chemicals. MIEs for thyroid disruption span the pathway starting with production and release of thyrotropin-releasing hormone (TRH) in the hypothalamus and going to transcriptional and cellular responses of thyroid receptor (TR) activation. Literature search results were combined with data from assays currently in EPA's ToxCast and the US Tox21 programs to: 1) support nominations for HTS assay development which would increase coverage of thyroid MIEs; and 2) generate a prioritized list of chemicals that in combination with exposure estimates, would yield a risk-based chemical prioritization leading to endocrine testing for thyroid disruption. The end goal is to develop computationally predictive models using results of HTS assays that inform on numerous MIEs in order to provide comprehensive coverage of relevant biological targets of the thyroid system.

This abstract does not necessarily represent US EPA policy.