Abstract for our Presentation at SOT Workshop: draft.

Title:
A Two-Tiered-Testing Decision Tree for Assays in the USEPA-EDSP Screening Battery: Using 15 years of experience to improve screening and testing for endocrine active chemicals.

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Abstract:

In 1996 the Food Quality Protection and Safe Drinking Water Acts instructed the USEPA to determine "…whether the pesticide chemical may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen or other endocrine effects;"*. In 1998 EDSTAC, an advisory committee to EPA, recommended that EPA develop a screening battery that included mammalian and non-mammalian in vivo and in vitro assays to detect chemicals for estrogen, androgen and thyroid activities (EAT). The battery was intended to detect chemicals that disrupted EAT pathways via the E and A nuclear receptors, steroid hormone synthesis and disruption on hypothalamic-pituitary-gonadal function via EAT modes of action. Over the last 15 years, since the release of the EDSTAC Final Report, EPA had been developing and validating the assays for screening and, as a result, a significant data base has been established for chemicals with known EDC activities. This database enables us to review assay performance and make recommendations about 1) Interpretation of assay results with unknowns, 2) Structuring the screening battery into a "Tiered-Testing Decision Tree" with two in vivo "Gatekeeper" assays and, 3) Specifically tailoring Tier 2 testing using the EDC information gained from Tier 1 screening.

This presentation will discuss development of the screening battery by EDSTAC, assay development and validation, how the battery detects different EAT modes of action, the strategy for detection of positives and negatives in a Tiered-Testing Decision Tree battery with "Gatekeeper" assays, why in vitro assays cannot serve as "Gatekeepers" and how the information from the screening battery can be used to enhance Tier 2 testing on a case-by-case basis. Additionally, due to challenges in interpreting Tier 1 data, and concern with the extensive animal use and cost of Tier 2, the potential value of incorporating a possible "Tier 1.5" screening strategy is proposed in lieu of moving directly to Tier 2 for chemicals with positive Tier 1 results. Tier 1.5 could be conducted following Tier 1 screening, and could utilize additional or refined in vitro or short-term in vivo assays to confirm equivocal Tier 1 screening results, or explore potential effects and modes of action in more detail prior to the selection and initiation of extensive Tier 2 testing. This presentation also will address; 1) some of the criticisms of the screening battery and reiterate how critical it is for laboratories executing the assays to strictly adhere to the published test guidelines for the screening assays; 2) describe an example of a logic tree using the Fish Short Term Reproduction Assay for discriminating endocrine from non-endocrine mediated toxicities in in vivo screening assays; and 3) How multigenerational test protocols could be enhanced on a case-by-case basis to detect effects of specific EDCs

* from: *FQPA - PUBLIC LAW 104–170*.

This is an abstract of a proposed presentation and does not reflect EPA policy.