



Update on EPA's Endocrine Disruptor Screening Program

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EDSP Implementation (List 1)

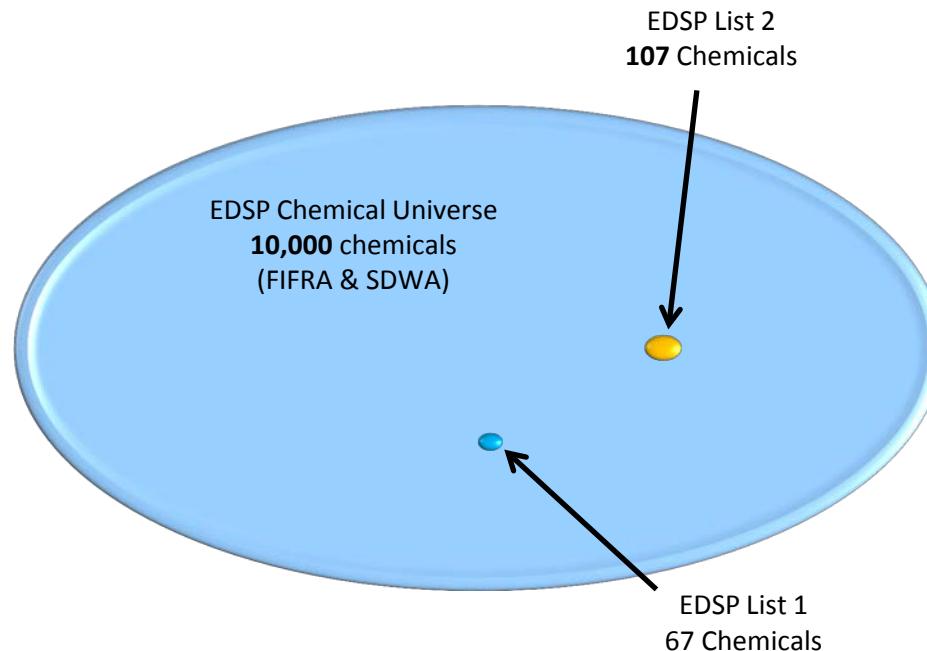
- EPA has reviewed ~500 studies required on EDSP List 1

- Initiated WOE evaluations of 52 chemicals for estrogen, androgen and thyroid (E, A & T) interactions
 - Agency currently reviewing Tier 1 data and other scientifically relevant information (OSRI)
 - Initial WOE evaluations of 52 chemicals anticipated in December 2014



EDSP Implementation (List 2)

- EPA issued revised EDSP List 2 with 107 chemical
- Selection based on registration review schedule of 41 pesticidal chemicals and 66 drinking water contaminants





Evolution of the EDSP

- Based on current pace it could take decades to screen all 10,000 chemicals for potential to interact with the endocrine system
- Recent advances in computational toxicology herald an important “evolutionary turning point” (Pivot) and an accelerated pace of screening and testing
- To address thousands of chemicals for potential to interact with the endocrine system, we must implement a more strategic approach to prioritize chemicals for targeted screening



Utility of Computational Toxicology

- Rapidly screen chemicals and use predictive models to evaluate thousands of chemicals for potential risk to human health and environment
- Increase capacity to prioritize, screen and predict chemical toxicity and exposure
- Overcome throughput limitations of traditional chemical toxicity testing, augmenting current data sources



Utility of Computational Toxicology

- Eventual replacement of some existing tests with non-animal alternatives
- Partner across EPA, with other federal agencies, state agencies, industry and non-governmental organizations to validate and apply tools
- Provide open access to data and adverse outcome pathways



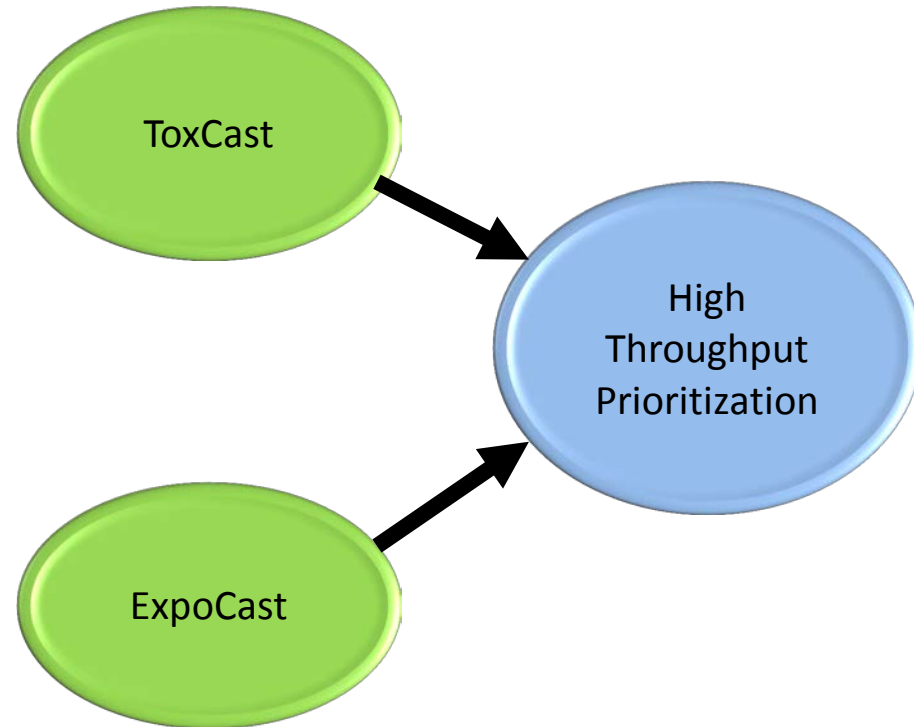
Screening and Prioritization

■ ToxCast

- Expanding use of CompTox (Phys-chem properties, QSARS, etc.) to support screening and prioritization
- Transparent and collaborative

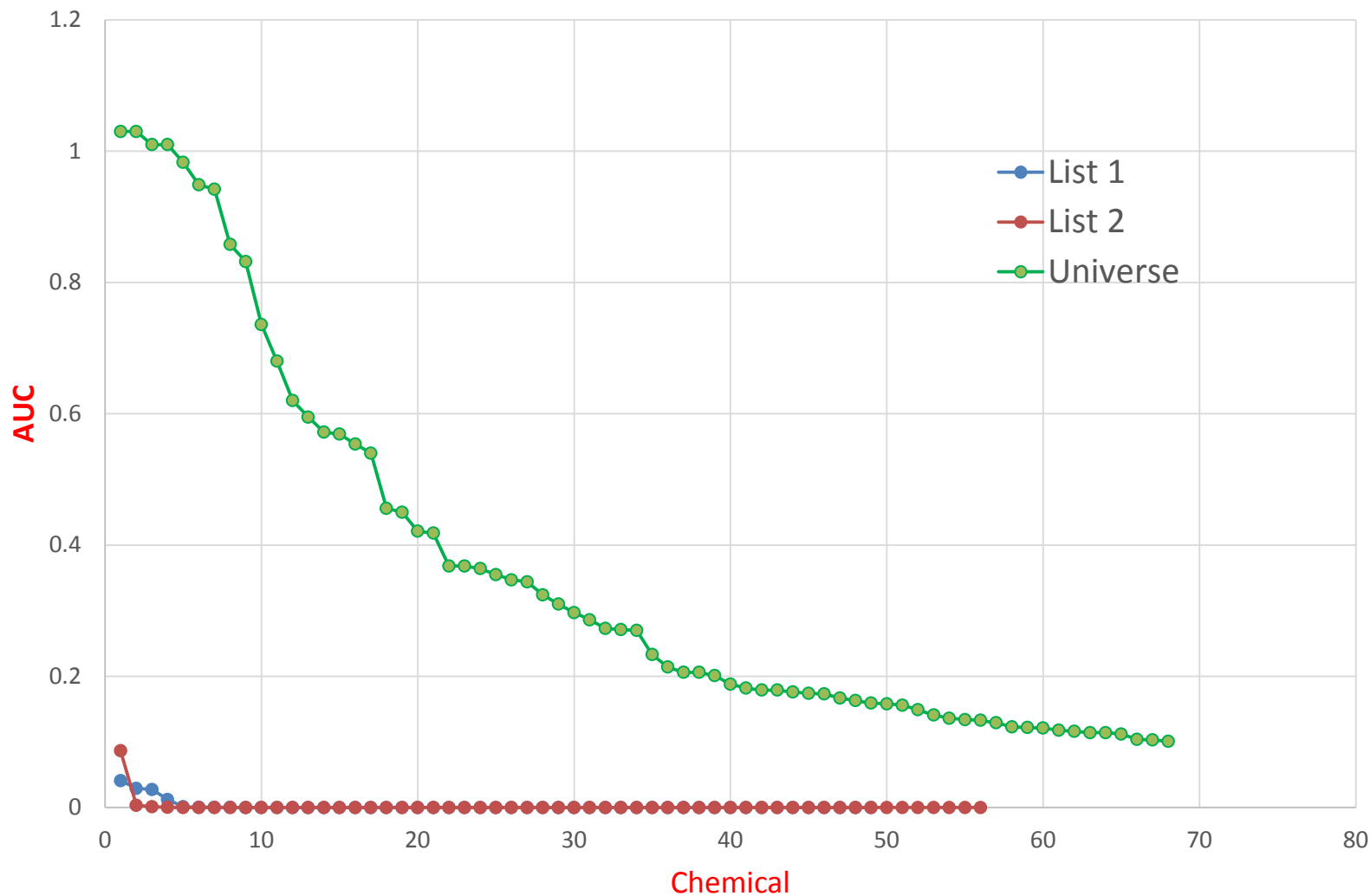
■ ExpoCast

- Rapid exposure estimation based on readily available chemical use and production data
- Use toxicokinetics to bridge *in vitro*, concentration-based ToxCast data to *in vivo*, dose-based Exposures from ExpoCast



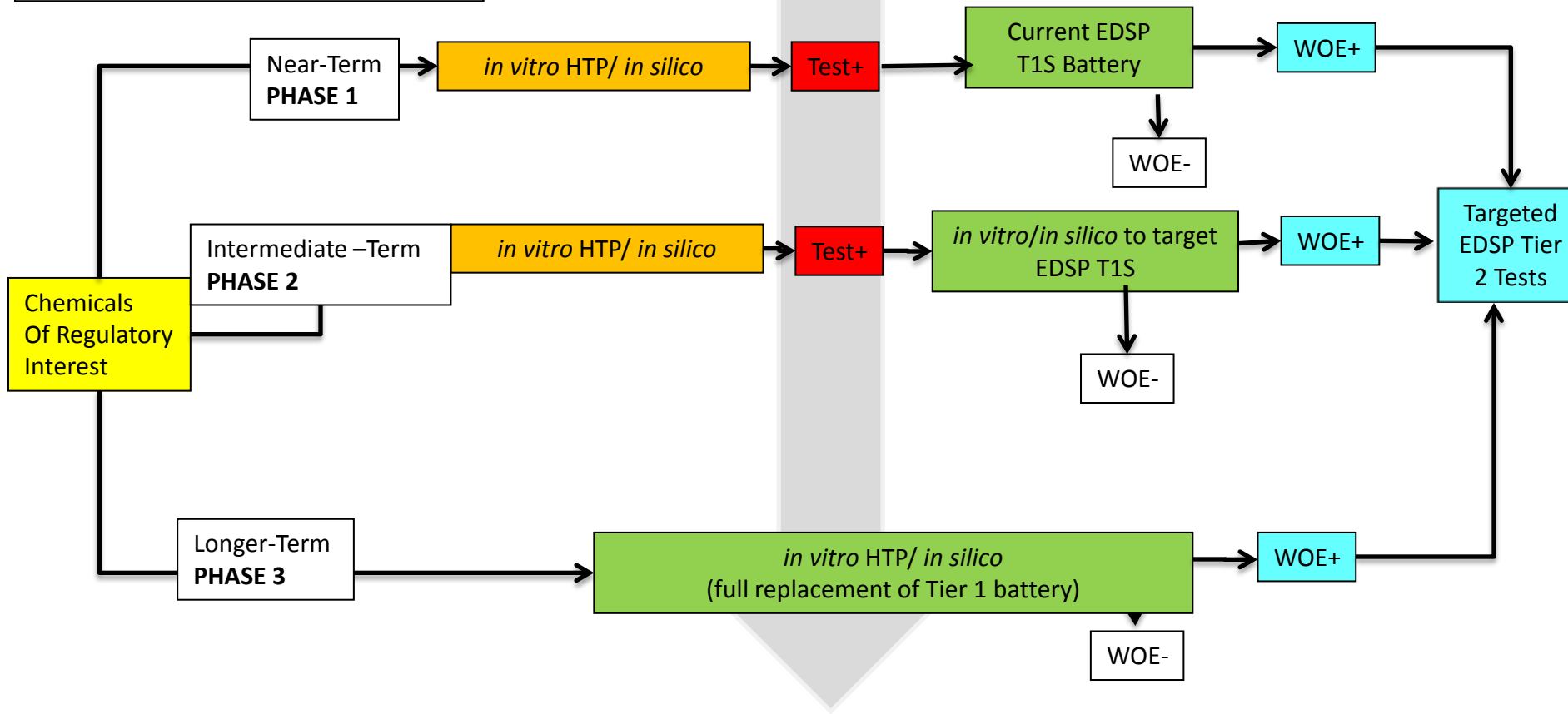


ToxCast Estrogen Activity



The universe of chemicals passes through each version of the HTP/*in silico* pipeline to evaluate chemicals in refined tests, for new pathways, to evaluate, improve, and validate methods.

EPA Research provides basis for improving the suite of assays and models to advance chemical prioritization and screening



Building Confidence: “Learn by Doing”
Phase 1: Incorporates HTP/*in silico* prioritization methods
Phase 2: Run subset of current T1S assays indicated by HTP and *in silico* predictions
Phase 3: Full replacement of EDSP T1S Battery





Current Status of EDSP

Prioritization and Screening

- 52 List 1 chemicals with complete Tier 1 datasets undergoing weight-of-evidence determination of EAT endocrine activity and possible Tier 2 testing
- 107 List 2 chemicals going through OMB review for Tier 1 screening
- EDSP Universe of chemicals being prioritized for EDSP screening using computational toxicology and other tools
- Scientific Advisory Panel peer reviews completed and planned:
 1. Exposure Prediction Models (July 29 - August 1, 2014)
 2. Integrated Bioactivity – Exposure Based Prioritization and Screening (December 2 - 5, 2014)
 3. Linking Endocrine Testing to Bioactivity-Exposure Based Prioritization and Screening (September 2015)



Current Status of EDSP Tier 2 Test Guidelines

- Ongoing Revisions
 - Medaka Extended One Generation Reproduction Test
 - Larval Amphibian Growth and Development Assay
- *Federal Register* (Sept – Oct 2014) – Availability of draft guidelines - 30 day public comment period
- Finalize Test Guideline Documents (Dec 2014 – Jan 2015)
- Standard Evaluation Procedures (Feb – Mar 2015)
- OECD WNT / Series 890 Test Guidelines (Apr – May 2015)