

US EPA ARCHIVE DOCUMENT

Update on the U.S. Endocrine Disruptor Screening Program (EDSP)

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EPA's Statutory Authority

- Federal Food, Drug, and Cosmetic Act (FFDCA)
 - Requires EPA to:
 - Develop a screening program using validated test systems and other scientifically relevant information, to identify chemicals that may have estrogenic effects in humans.
 - Test all pesticide chemicals
 - Authorizes EPA to obtain testing on:
 - Other endocrine effects, as designated by the EPA Administrator.
- Safe Drinking Water Act (SDWA) Amendments
 - Provides for testing of chemical substances that may be found in sources of drinking water, if a substantial human population may be exposed to the substance.

EDSP List 1 Timeline

- Issued approx 750 EDSP orders/DCIs requiring all Tier 1 screening assays for 67 chemicals:
 - chemicals were selected on the basis of exposure. (This is **not** a list of “likely” or “known” endocrine disruptors).
 - Orders were issued to the Registrants of 58 pesticide active ingredients.
 - Orders were also issued to manufacturers/importers of 9 high production volume / pesticide inert chemicals.
- Responses to Test Orders were due 90 days from receipt starting February 6th for individual responses and April 7th for consortia and ended in June and July 2010, respectively.
- Test data are due 24 months from issuance of Test Order.

List 1 Numbers

- Orders were issued for 67 chemicals
- The Agency will receive data for 53 chemicals.
 - 7 active ingredients voluntarily cancelled.
 - 7 inerts opted out of the pesticide market.
 - There will be approximately 500 EDSP List 1 Tier 1 studies submitted to the Agency.
 - Data began to arrive in the Agency late October 2011 and will continue to arrive through spring of 2013.

Submission of List 1 Data

- Formatted CD
 - Instructions on “How to submit information in response to a test order” are available at <http://www.epa.gov/pesticides/regulating/registering/submissions/>
- Paper submissions are acceptable
- MRIDs
- The Agency anticipates making full electronic submission capabilities available to support List 2.

Status of List 1

- The Agency will receive approximately 500 studies for 53 chemicals.
- As of April 12, 2012 the Agency has received 325 studies.
- These studies are either undergoing primary or secondary review.

Status of Other Activities

- Revised Weight-of-Evidence guidance document was posted to the docket on September 27, 2011.
- SEPs, DER templates and raw data spreadsheets have been posted to the EDSP website.
- EDSP21 Work Plan September 30, 2011

Proposed List 2

- **2010 Appropriations report directed EPA to issue a second list of no less than 100 chemicals.**
- **Proposed Second List (75 FR 70248)**
- **134 chemicals drawn from three sources:**
 - **Chemicals covered by National Primary Drinking Water Regulations**
 - **Contaminant Candidate List 3 (CCL3)**
 - **Pesticides on the registration review schedule for 2007 and 2008**

US EPA Proposed EDSP Tier 2 Tests

Mammalian Two-Generation Reproduction (rat)
(may be replaced by Extended F1-Generation)

Avian Two-Generation (Japanese quail)
[US lead, OECD validation program]

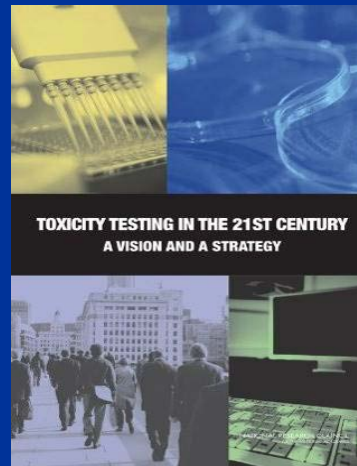
Larval Amphibian Growth and Development/ (Xenopus
Laevis) [US/Japan lead, OECD validation program]

Fish Multi-Generation (medaka)
[US/Japan lead, OECD validation program]

Mysid Multi-Generation
[US lead, OECD validation program]

EDSP in 21st Century

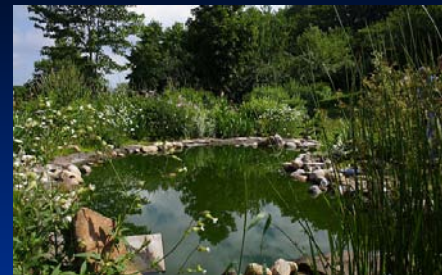
Hypothesis Driven, Targeted
Testing Strategy



Objective

- Maximize use of existing data.
- Targeted *in vivo* toxicity testing.
- Use a variety of tools in a tiered testing and assessment framework.
- Systematically and *incrementally* incorporate new tools, methodologies.
- Advance understanding of key events in toxicity pathways.

Application to Levels of Organization Based on Source to Outcome



Source

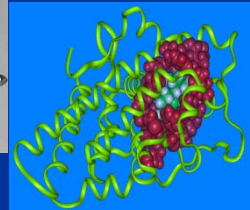


Community

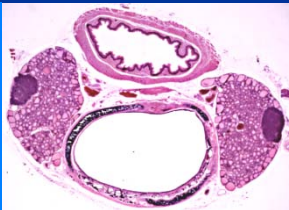
Environmental Contaminant



Exposure



Molecular Initiating Event



Cellular Effects



Individual

Population

Toxicity Pathway

Mode of Action

Adverse Outcome Pathway

Source to Outcome Pathway

EDSP21 Work Plan

Multi-level and Integrated approach to determine whether a chemical has the potential to interact with Endocrine, Androgen or Thyroid pathways.

Three Phases:

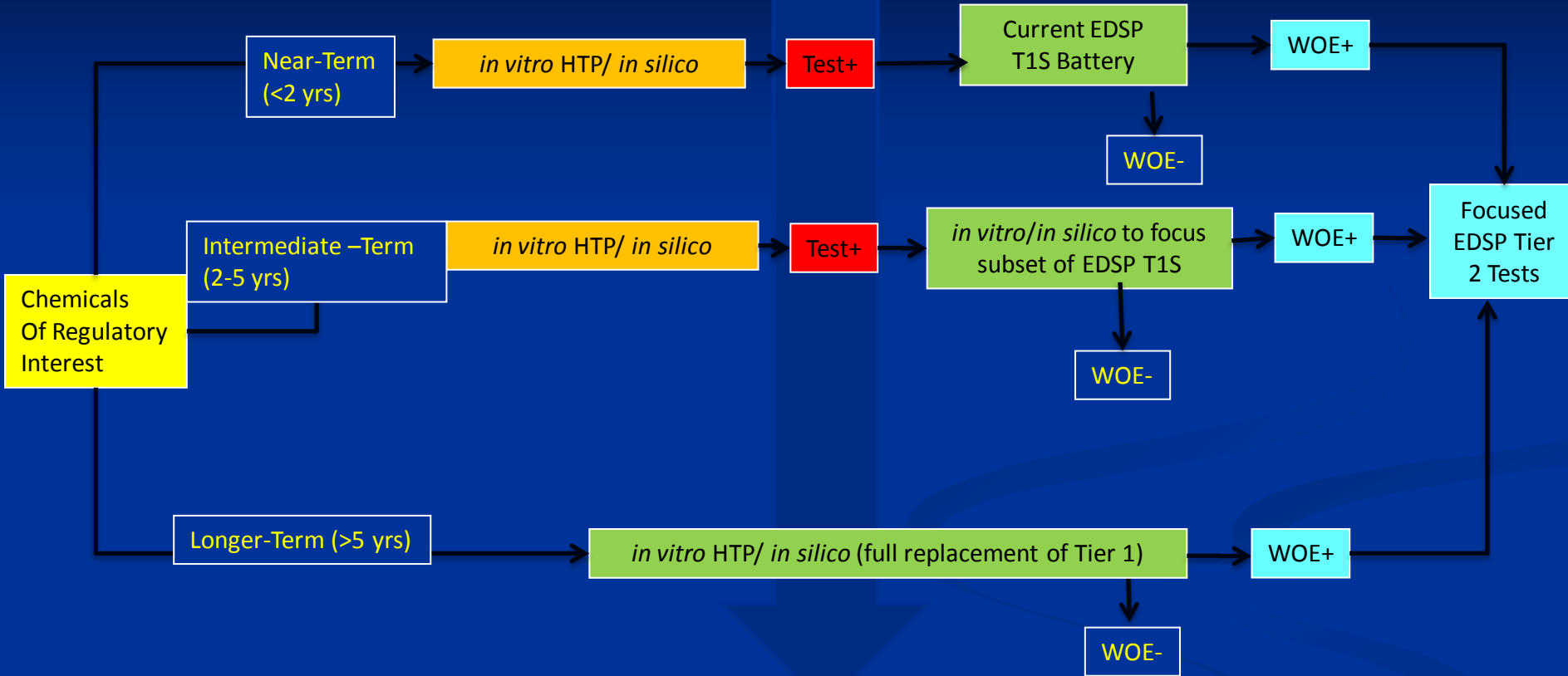
I. Prioritization - The near-term goal (<2 years)

II. Targeted Screening (Tier 1) - The intermediate-term goal (2-5 years)

III. Replacement – The long-term goal (>5 years)

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



Chemical Prioritization

Includes , registration review timeline, physico-chemical properties, exposure estimates, *in vitro* assays and computer models (QSAR, expert systems, systems biology models).

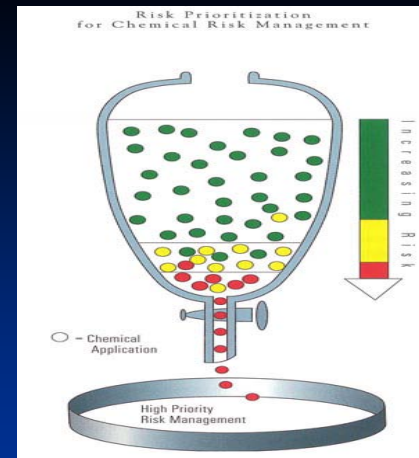
Screening Decisions

Near-Term: Incorporates HTP/*in silico* prioritization methods

Intermediate-Term: Run subset of current T1S assays indicated by HTP and *in silico* predictions

Longer-Term: Full replacement of EDSP T1S Battery

Chemical Prioritization



- Considerations of Multiple Data Streams:
 - Exposure
 - HTP assays for Estrogen, Androgen and Thyroid
 - Inherent chemical properties
 - Modeling predictions (e.g., QSAR, and expert systems)
 - Data from structural analogs (read across)
 - Toxicity pathway based and anchored by biological mechanistically based understanding

*Figure taken from 1996, *Chemical Manufacturers Association Product Risk Management Strategy Overview*

Key Considerations for Implementation of EDSP21

- Ensure Clarity of Programmatic Goal
- Define Application and Regulatory Decision Contexts
- Build Transparent Strategy with Sound Scientific Basis
- Determine Scientific Validity
- Ensure Peer Review and Public Outreach



For Additional Information

- General: www.epa.gov/endo
- Updated status of orders: www.epa.gov/scipoly/oscpendo/pubs/edsp_orders_status_012110.pdf
- EDSP Test Guidelines (OPPTS Guidelines - 890 series): www.epa.gov/oppts/pubs/frs/publications/Test_Guidelines/series890.htm
- Policy and Procedures: www.regulations.gov docket # EPA-HQ-OPPT-2007-1080
- Schedule of orders/DCI issuance: www.regulations.gov docket # EPA-HQ-OPP-2009-0634
- Final list of Chemicals for Initial Screening: www.regulations.gov docket # EPA-HQ-OPPT-2004-0109
- Information Collection Request under the Paper Reduction Act (PRA): www.regulations.gov docket # EPA-HQ-OPPT-2007-1081
- <http://www.epa.gov/endo/pubs/prioritysetting/list2facts.htm>
- <http://www.epa.gov/pesticides/regulating/registering/submissions/>
- http://www.epa.gov/endo/pubs/edsp21_work_plan_summary%20overview_final.pdf