

US EPA ARCHIVE DOCUMENT

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

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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 are due to the Agency beginning late October 2011 through August of 2012 (with the exception of catch up orders).

Submission of List 1 Data

- Formatted CD
 - Instructions on "How to submit information in response to a test order" are available at www.epa.gov/endo
- Paper submissions are acceptable
- MRIDs
- Agency is actively developing web based E-submissions.

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 are being posted to the EDSP website.

Next Steps for List 1 EDSP Orders

- DERs for the Tier 1 studies will not be considered as final or released until the Agency has completed their WoE analysis of the Tier 1 data and OSRI to determine which (if any) Tier 2 data are required.
- The Agency plans to begin to conduct WoE analyses in late FY 2012 to early 2013.

List 2

- 2010 Appropriations required EPA to issue a second list of no less than 100 chemicals.
- List 2 has 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

List 2 - cont'd

- Published proposed List 2 FRNs 11/17/10
 - Draft Policies and Procedures for SDWA Chemicals (75 FR 70558)
 - Second List of Chemicals (75 FR 70248)
 - ICR; Comment Request on Addendum for the Second List of Chemicals (75 FR 70568)
 - Supporting Materials - Draft Test Order Template, Draft Response Form for Individuals and Consortia, Process Flowchart

List 2- cont'd

- Next Steps for List 2 to have ICR in place to issue List 2 orders:
 - Provide response to comments and revise List 2 FRNs
 - Meet OMB terms of clearance

EDSP 21

Use of new High Throughput Screening Tools

EPA is working to develop and refine high throughput screening (HTS) tools to:

- Support prioritization of testing

- Build confidence in HTS tools to increase efficiency through prioritization for Tier 1 Screening.

Near term goal

- Prioritized list of chemicals for screening through EDSP Tier 1 Assay Battery

Longer term goal

- Enhance or replace current Tier 1 assays.

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>

Appendix

BACKGROUND INFO

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 Scope and Structure

- Two-Tiered Approach
 - Tier 1
 - *In vitro* and *in vivo* screens
 - Detect potential to interact with EAT hormone systems.
 - Tier 2
 - Multi-generation studies covering a broad range of taxa.
 - Provide data for dose response and risk assessment.

EDSP Tier 1 Screening Battery

In vitro

Estrogen Receptor (ER) Binding

Estrogen Receptor Transcriptional Activation Assay (ERTA)

Androgen Receptor (AR) Binding

Steroidogenesis

Aromatase

In vivo

Uterotrophic (rat)

Hershberger (rat)

Pubertal Female (rat)

Pubertal Male (rat)

Amphibian Metamorphosis Assay (frog)

Fish Short-Term Reproduction Assay

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]

Amphibian Growth/Reproduction (S. tropicalis)
[US/Japan lead, OECD validation program]

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

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

List 2 Chemicals

- EPA streamlined this list by excluding any chemical that fell into one or more of the following categories:
 - Biological agent and naturally-occurring chemicals (e.g., microbials, microbial toxins, inorganics, radionuclides).
 - Chemicals for which the manufacturer, importer or registrant cannot be clearly identified (e.g., disinfection byproducts or DBPs, microbes, microbial toxins, degradate compounds with more than one possible source etc.).
 - Chemicals already included on the first list to receive EDSP test orders except for inerts found in water that previously opted out of the pesticide market.
 - Chemicals that are hormones with confirmed endocrine effects.
 - Chemicals that are not likely to be biologically active or which are incompatible with testing assays for various reasons due to one or more of their physiochemical properties (e.g., gases, strongly acidic or basic, solubility, vapor pressure and molecular weight).
 - Pesticides that are scheduled for registration review after FY 2008.