Status of 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 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 hazard 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]

EDSP List 1 Timeline

- Issued 757 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.
- Progress reports are due 1 year after issuance.
- Test data are due 24 months from issuance of Test Order.
- Data are due to the Agency in late 2011 and early 2012.

Response Options

- Option 1 Generate data.
- Option 2 Submit or Cite Existing data .
- Option 3 Form / join a consortia / task force.
- Option 4 Claim not subject to the order/DCI.

Pesticides only

- Option 5 Voluntarily cancel the pesticide registration.
- Option 6 Reformulate the product(s) to exclude this chemical from the formulation.
- Option 7 Claim Formulators' Exemption.

Inerts only

- Option 8 Discontinue the manufacture / import of this chemical.
- Option 9 Do not / will not sell chemical for use in pesticides.

Citing Existing Data

The EDSP Policies and Procedures FRN published April 15, 2009 states:

- The Test Order provides the option of submitting or citing existing data along with a rationale as to how the data satisfy the order.

- "Existing data may include data that has already been generated using the assay(s) specified in the Order, or "**other scientifically relevant information (OSRI)**."

OSRI Science Review

- The Agency is responsible for the confirmation of the accuracy of the Test Order Recipient's OSRI rationale and supporting data.
- The Test Order Recipients may cite existing data from a journal article or Part 158 Guideline studies.
- The Test Order Recipient may request consideration of an alternate test protocol that will require science review.

OSRI Science Review - cont'd

Goal: consistent, transparent and defensible conclusions for "data rich" responses to the EDSP orders/DCIs. Including OSRI from public.

Challenges: the diversity of approaches to OSRI, as well as the volume and number of responses and short time frame (90 days).

Submissions evaluated on a chemical basis, rather than an individual response basis to:

- Confirm the claims made for OSRI.
- Make recommendations on Tier 1 test order requirements based on the OSRI rationale and cited existing data.

The Numbers

- Orders were issued for 67 chemicals
- OSRI was submitted for 47 chemicals
- For the remaining 20 chemicals
  - 7 will generate data for ALL eleven Tier 1 assays (5 active ingredients and 2 inerts).
  - 6 active ingredients voluntarily cancelled.
  - 7 inert ingredients either opted out of the pesticide market or claimed they were not subject to the order.

OSRI Responses

- As of December 10, 2010:
  - Of the 47 chemicals for which OSRI was submitted – 30 science review memos have been completed.
  - The remaining 17 science review memos are in draft.

Second List

- 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

Second List – cont'd

- 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 DP's, microbes, microbial toxins, degradate compounds with more than one possible source etc.).
  - Chemicals already included on the first list to receive EDSP test orders.
  - 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 molecular weight)
  - Pesticides that are scheduled for registration review after FY 2008.

Second List – cont'd

- List 2 is currently available for public comment FR November 17, 2010 [75 FR 70248-70254].
  - Comment period closes mid- January 2011.
  - Comment period on current ICR closes mid-January 2011.

Next Steps for EDSP Orders

- Continue completion/notification of Agency decisions regarding OSRI.
  - Make order recipient and Agency OSRI responses public.
- Continue to move forward on List 2.
- Draft SEP's and DER templates for T1 data review.
- Begin the review Tier 1 data.
- Conduct WOE for Tier 1 data and OSRI to determine which (if any) Tier 2 data are required.

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 Protocols (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