

US EPA ARCHIVE DOCUMENT

Status of the U.S. Endocrine Disruptor Screening Program (EDSP)

Richard Keigwin, OPP / PRD

Karen Whitby, OPP / IO

Session IX

PPDC April 2010

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 endocrine system
 - Tier 2
 - Tier 2 data called in only after review of Tier 1 data
 - 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 α (hER α) transcriptional activation

Androgen receptor (AR) binding

Steroidogenesis

Aromatase

In vivo

Uterotrophic (rat)

Hershberger (rat)

Pubertal female (rat)

Pubertal male (rat)

Amphibian metamorphosis (frog)

Fish short-term reproduction

US EPA EDSP Tier 2 Tests

Mammalian two-generation rat
(may be replaced by Extended F1-Generation)

Avian two-generation (Japanese quail)

Amphibian growth/reproduction (*S. tropicalis*)

Fish multigeneration (medaka)

Mysid multi-generation

EDSP Progress in 2009

- Issued the final list of 67 chemicals for initial screening April 15, 2009
 - 58 pesticides actives, and
 - 9 high production volume / pesticide inerts
 - chemicals were selected on the basis of exposure. (This is **not** a list of “likely” or “known” endocrine disruptors).
- EDSP Policies and Procedures for initial screening were published April 15, 2009
- Formal OMB review of the Information Collection Request (required under the Paper Reduction Act) was completed October 14, 2009.
- EDSP Tier 1 Screening Battery was published October 21, 2009.
- The Schedule of Issuance of the EDSP test orders/DCIs was published October 21, 2009.

EDSP Progress to date

- Issued 757 EDSP orders/DCIs requiring all Tier 1 screening assays
- Orders were issued to the Registrants of the pesticides and manufacturers/importers of the high production volume / pesticide inert chemicals (67 chemicals)
- Responses to Test Orders are due 90 days from receipt starting February 6th for individual responses and April 7th for consortia and ending 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.
- Orders are due 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 satisfies 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).”**”

Responses by Assay ---

(as of April 15 for 24 Pesticides)

Assay	Generate	Cite/OSRI
Amphibian	11	13
AR Binding	4	20
Aromatase	9	15
ER Binding	4	20
ER Transcriptional Act	5	19
Fish Repro Screen	11	13
Hershberger	10	14
Pubertal Female	5	19
Pubertal Male	4	20
Steroidogenesis	10	14
Uterotrophic	9	15

Order level Responses *As of 15 April

- Inerts - 524 orders/DCIs
 - Form / join a consortia / task force -1
 - Not subject to order -120
 - Discontinue manufacture / import -1
 - Do not/will not sell for use in pesticides -14
- Pesticide actives - 233 orders/DCIs
 - Form / join a consortia / task force - 88
 - Voluntarily cancel product -12
 - Formulators' Exemption – 32

Where to find this status orders/DCIs and responses?

www.epa.gov/endo

www.epa.gov/scipoly/oscp/endo/pubs/edsp_orders_status_012110.pdf

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 Recipient may cite existing data from a journal article or Part 158 Guideline studies.
- The Test Order Recipient may request the Agency to consider an alternate test protocol that will require science review.

OSRI Science Review - cont'd

Working to develop consistent, transparent and defensible conclusions for “data rich” responses to the EDSP orders/DCIs.

Challenges: the diversity of approaches to OSRI, as well as the volume and frequency of the order/DCI responses and short time frame (90 days). Including OSRI from public.

We are evaluating the submissions on a chemical basis, rather than an individual response basis to confirm the claims made for OSRI, and will make recommendations on Tier 1 test order requirements based on the OSRI rationale and cited existing data.

Next Steps for current EDSP Orders

- Continue receiving and processing responses
- Notification of Agency Decisions regarding responses
- Make order recipient and Agency responses public
- Review Tier 1 assays that are conducted
- Notification of Agency Decisions regarding Tier 1 assays

2010 Appropriations Language

...requires EPA to issue orders for a second list of no less than 100 chemicals by October 30, 2010 and

- Includes water contaminants
- Issue 25 orders (substances) per year for these chemicals
- The goal is to begin issuing orders in late 2010.
- These data would be due to the Agency in late 2012-2013.

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