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 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

<table>
<thead>
<tr>
<th><strong>In vitro</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Estrogen receptor (ER) binding</td>
</tr>
<tr>
<td>Estrogen receptor α (hERα) transcriptional activation</td>
</tr>
<tr>
<td>Androgen receptor (AR) binding</td>
</tr>
<tr>
<td>Steroidogenesis</td>
</tr>
<tr>
<td>Aromatase</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>In vivo</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Uterotrophic (rat)</td>
</tr>
<tr>
<td>Hershberger (rat)</td>
</tr>
<tr>
<td>Pubertal female (rat)</td>
</tr>
<tr>
<td>Pubertal male (rat)</td>
</tr>
<tr>
<td>Amphibian metamorphosis (frog)</td>
</tr>
<tr>
<td>Fish short-term reproduction</td>
</tr>
<tr>
<td>US EPA EDSP Tier 2 Tests</td>
</tr>
<tr>
<td>--------------------------</td>
</tr>
<tr>
<td><strong>Mammalian two-generation rat</strong> (may be replaced by Extended F1-Generation)</td>
</tr>
<tr>
<td><strong>Avian two-generation</strong> (Japanese quail)</td>
</tr>
<tr>
<td><strong>Amphibian growth/reproduction</strong> (S. tropicalis)</td>
</tr>
<tr>
<td><strong>Fish multigeneration</strong> (medaka)</td>
</tr>
<tr>
<td><strong>Mysid multi-generation</strong></td>
</tr>
</tbody>
</table>
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 theRegistrants 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)

<table>
<thead>
<tr>
<th>Assay</th>
<th>Generate</th>
<th>Cite/OSRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amphibian</td>
<td>11</td>
<td>13</td>
</tr>
<tr>
<td>AR Binding</td>
<td>4</td>
<td>20</td>
</tr>
<tr>
<td>Aromatase</td>
<td>9</td>
<td>15</td>
</tr>
<tr>
<td>ER Binding</td>
<td>4</td>
<td>20</td>
</tr>
<tr>
<td>ER Transcriptional Act</td>
<td>5</td>
<td>19</td>
</tr>
<tr>
<td>Fish Repro Screen</td>
<td>11</td>
<td>13</td>
</tr>
<tr>
<td>Hershberger</td>
<td>10</td>
<td>14</td>
</tr>
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<td>Uterotrophic</td>
<td>9</td>
<td>15</td>
</tr>
</tbody>
</table>
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
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:  
- EDSP Test Protocols (OPPTS Guidelines - 890 series):  
- 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):  