

Update on EDSP Activities

CPDA Spring Meeting

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Initial T1 EDSP Test Orders

- Approximately 750 test orders will be issued for 67 chemicals (58 pesticide active ingredients and 9 HPV inerts) between October 29, 2009 and February 25, 2010.
- Basis for chemical selection was potential for exposure via multiple pathways. (FRN Vol. 74 No. 71 April 15, 2009)
- This is not a list of "known" or "likely" endocrine disruptors.

Initial T1 EDSP Test Orders

- The first 90 day (initial) responses were due to the Agency February 6, 2010.
- The last (150 day for consortia) response is due July 29, 2010.
- The T1 data is due to the Agency 24 months after issuance of the test order.
- The Policies and Procedures for the initial screening of chemicals under EDSP is described in FRN Vol. 74 No. 71 April 15, 2009

Tier 1 Assays

- The T1 battery is comprised of 11 assays.
 - Amphibian Metamorphosis Assay
 - Androgen Receptor Binding Assay
 - Aromatase (Human Recombinant) Assay
 - Estrogen Receptor Binding
 - Estrogen Receptor Transcriptional Activation Assay
 - Fish Short-term Reproduction
 - Hershberger
 - Female Pubertal
 - Male Pubertal
 - Steriodogenesis
 - Uterotrophic

EDSP T1 Test Orders

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.""
- "Other scientifically relevant information may either be functionally equivalent to information obtained from the Tier 1 assays ...or may include data that provide information on a potential consequence or effect that could be due to effects on the estrogen, androgen, or thyroid systems."
- OSRI can include data from studies other than Tier 1 assays (e.g., studies conducted to satisfy part 158 or part 161 data requirements, data conducted to address an identified issue, or data found in the scientific literature).
- Any member of the public can submit OSRI, in addition to the T1 Test Order Recipient.

PART 2

Recipient's Initial Response: (Please refer to the Order/DCI for more information about response options, as well as detailed instructions on how to comply with the Order/DCI.)

2.1. I will generate new data or am citing/submitting existing data.

For each assay, check the appropriate box in the following table and follow the Order/DCI instructions to attach the data and/or required documentation.

- A. I will generate new data.
 B. I am citing existing data and/or other scientifically relevant information.
 C. I am submitting existing data and/or other scientifically relevant information.
 D. I am entering (or offering to enter) into an agreement to form a Consortium/Task Force to respond to the Order/DCI. The Consortium/Task Force must provide a separate initial response within 150 calendar days from issuance of the Order/DCI (see Initial Response Form for Consortium/Task Force at <http://www.epa.gov/endo/>.)

Assays:	A	B	C	D	Required documentation is attached.
2.1.1. Amphibian Metamorphosis (Frog)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="checkbox"/>
2.1.2. Androgen Receptor Binding (Rat Prostate)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="checkbox"/>
2.1.3. Aromatase (Human Recombinant)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="checkbox"/>
2.1.4. Estrogen Receptor Binding	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="checkbox"/>
2.1.5. Estrogen Receptor Transcriptional Activation (Human Cell Line (HeLa-9903))	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="checkbox"/>
2.1.6. Fish Short-term Reproduction	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="checkbox"/>
2.1.7. Hershberger (Rat)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="checkbox"/>
2.1.8. Female Pubertal (Rat)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="checkbox"/>
2.1.9. Male Pubertal (Rat)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="checkbox"/>
2.1.10. Steroidogenesis (Human Cell Line – H295R)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="checkbox"/>
2.1.11. Uterotrophic (Rat)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="checkbox"/>

2.2. I am citing and/or submitting other scientifically relevant information that I believe can be used to satisfy all of the Order/DCI. Required documentation is attached.

2.3. I am not subject to the Order/DCI. Required documentation is attached.

These Response Options Apply Only to Registered Pesticides:

2.4. I intend to voluntarily cancel the pesticide registration(s). Required documentation is attached.

2.5. I intend to reformulate the product(s) to exclude this chemical from the formulation. Required documentation is attached.

2.6. I am claiming a *Formulators' Exemption*. Required documentation is attached.

These Response Options Apply Only to Chemicals that are Other Ingredients (aka inerts):

2.7. I have/am in the process of discontinuing the manufacture/import of this chemical. Required documentation is attached.

2.8. I do not and will not sell my chemical for use as an inert ingredient to the pesticide market.
 Required documentation is attached.

Options for Test Order Recipient's Initial Response

- Option 1 Generate data
- Option 2 Submit or Cite Existing data
- Option 3 Form a task force or offer to join a task force
- Option 4 Claim not subject to the order/DCI
- 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
- Option 8 Discontinue the manufacture/import of this chemical
- Option 9 Will not sell chemical for use as an inert to the pesticide market.



Things to Check as OSRI Submission is Prepared

- Is the Test Order Recipient Initial Response Form (Parts 2 and 3) completed appropriately?
- If the Test Order Recipient is citing OSRI, is a rationale and appropriate documentation included?
- If the Test Order Recipient is submitting existing data, is the existing data part of the submission?
- Does the submission include MRID numbers for existing data?
- If the existing data are from published journal articles, is the full citation provided (e.g., author, year, volume, name of journal, pages)?
- If an option other than agreeing to conduct the studies or citing OSRI is being selected, is the required documentation attached?

OSRI Review Objectives

- In order to be accepted as satisfaction of the requirements imposed in this Order, the Agency expects that any such hazard related data would be of high quality and achieves the objective of Tier 1 assays to provide **reasonable assurance that a chemical does or does not have the potential to interact with the estrogen, androgen thyroid systems.**
- EPA's decisions about whether the other scientifically relevant information (OSRI) cited or submitted satisfies part or all of the Tier 1 Order will be based on the weight-of-evidence from all relevant information available to the Agency.

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.

EDRT

The goal of the EDRT is to review the rationale and OSRI submitted in lieu of conducting T1S and requests to consider alternate test protocols.

Their objective is to reach consistent, transparent and defensible conclusions on responses to the test orders including OSRI. This will be particularly challenging in light of the diversity of approaches to OSRI, as well as the volume and frequency that responses to test orders will be received.

EDRT evaluations will be made on a chemical basis, rather than an individual response basis. EDRT will confirm the claims made for OSRI, and will make the Agency recommendation on T1 test order requirements based on the OSRI rationale.

Review Process for Part 158 OSRI

The OPP science divisions are responsible for:

- Verifying that endpoints cited in OSRI rationale for Part 158 data have been evaluated
- the adequacy of the existing DERs for cited endpoints/studies
- revision of DERs if needed

They will evaluate the cited data/DER relative to the OSRI rationale and present their findings to the Endocrine Disruptor Review Team (EDRT).

Review Process for Journal Articles Cited as OSRI

- Agency scientists will review the cited Journal Articles for adequacy as OSRI. All of the cited OSRI will be considered by the EDRT in their weight-of-evidence determinations regarding satisfaction of the test order.

Alternate Test Protocols

- The Agency may receive requests to conduct T1S using different species or methodologies that will require science review.
- These requests should be submitted to the Agency through PRD.
- Review of alternate test protocols will be conducted by the EDRT.
- The Agency determination on alternate test protocols will be included in the EDRT memorandum.

Challenges

- This is the first time OPP has issued DCI's for a test battery for 50+ chemicals at one time with the offer to consider requests for other scientifically relevant information.
- We will consider responses from TOR and the public.
- The level of detail, nature and volume of OSRI responses is unknown; therefore LOE is uncertain.
- The goal is for OPPTS to complete all aspects of the response to test orders within 90 days. This includes potential contractor reviews.
- Because this is a new process, the Agency is still developing the workflow design and reporting formats.
- Production for PRIA, registration review and litigation must continue on time.