Endocrine Disruptor Screening Program Update

November 15, 2023
PPDC Meeting

Office of Chemical Safety and Pollution Prevention

Announced New Strategies

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EPA Rebuilds Endocrine Disruptor Screening Program to Better Assess Human Endocrine Effects of Pesticides

October 26, 2023

Contact Information
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WASHINGTON – Today, the U.S. Environmental Protection Agency (EPA) is announcing a strategic plan to ensure that its assessments of pesticides more closely, quickly, and effectively evaluate the potential for endocrine effects in humans. These strategies will also improve EPA's ability to protect against those effects as part of its pesticide decisions under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and to implement the Endocrine Disruptor Screening Program (EDSP) under section 408(p) of the Federal Food, Drug, and Cosmetic Act (FFDCA).

"This plan is a major milestone in our efforts to ensure that pesticide decisions continue to protect human health," said **Deputy**

Why New Strategies?

- Office of Inspector General Report (July 2021)
- NGO lawsuit (Dec. 2022)
  Alianza Nacional de Campesinas, et al v. EPA
- Longstanding questions about EDSP implementation
- EDSP for registration review final actions

What Does FFDCA Require?

- Federal Food, Drug, and Cosmetics Act (Section 408(p)) requirements:
  - Create and implement screening program (**EDSP**)
  - Provide for **testing** of “all pesticides” and issue **test orders**
  - **Protect** public health against endocrine effect substances [**§408(p)(6)**]
  - May **exempt** chemical from EDSP

Two-Tiered Testing Framework

- **Tier 1 screening**:
  - To screen for potential to interact with estrogen, androgen, or thyroid systems.
  - 11 assays: 6 *in vivo* and 5 *in vitro* (Green rows have NAMs alternative)
- **Tier 2 testing**:
  - To identify, characterize, and quantify adverse effects for risk assessment.

EDSP Tier 1 Battery	Type	Tier 1 Test Guideline
Estrogen Receptor (ER) Binding	In vitro	OCSPP 890.1250
Estrogen Receptor Transactivation (ERTA)	In vitro	OCSPP 890.1300
Uterotrophic (UT)	In vivo	OCSPP 890.1600
Androgen Receptor (AR) Binding	In vitro	OCSPP 890.1150
Aromatase	In vitro	OCSPP 890.1200
Steroidogenesis (STR)	In vitro	OCSPP 890.1550
Hershberger	In vivo	OCSPP 890.1400
Female Rat Pubertal	In vivo	OCSPP 890.1450
Male Rat Pubertal	In vivo	OCSPP 890.1500
Fish Short Term Reproduction (FSTRA)	In vivo	OCSPP 890.1350
Amphibian Metamorphosis (AMA)	In vivo	OCSPP 890.1100

EDSP Tier 2 Tests	Type	Tier 2 Test Guideline
Rat 2-generation Reproduction	In vivo	OCSPP 870.3800
Rat Extended 1-Gen Reproduction (alternative to rat 2-gen)	In vivo	OECD TG 443
Medaka Extended 1-Gen Reproduction	In vivo	OCSPP 890.2200
Larval Amphibian Growth & Development	In vivo	OCSPP 890.2300
Avian Multi-Generation Reproduction	In vivo	OCSPP 890.2100

Scope of Strategies

- New AI registrations and registration review
- Conventional pesticide active ingredients
- Human health

Four Documents

Near-Term Strategies (FRN)

- Describes three strategies
- Background on EDSP
- Starts 60-day public comment for data

Science Paper

- Explains when and how EPA will use FIFRA data to address EDSP

Conventional AIs List

- Lists 400+ registered AIs, and how we prioritized them for any data collection based on initial analysis of existing data

List 1

- Describes EDSP status of all 50 List 1 chemicals

Overall Approach

- Use FIFRA to address EDSP data and decisions.
  - Determine what endocrine data we already have in order to identify data needs for EDSP.
  - Integrate EDSP decisions and data needs into FIFRA decisions.
  - Get any additional endocrine data with new AI registrations or registration review.
  - Make §408(p)(6) decision when we finish E-A-T analysis for humans.

Three Strategies

- **<u>One</u>: Prioritize *human* endocrine effects**
  - Maintain current FIFRA approach for wildlife effects.

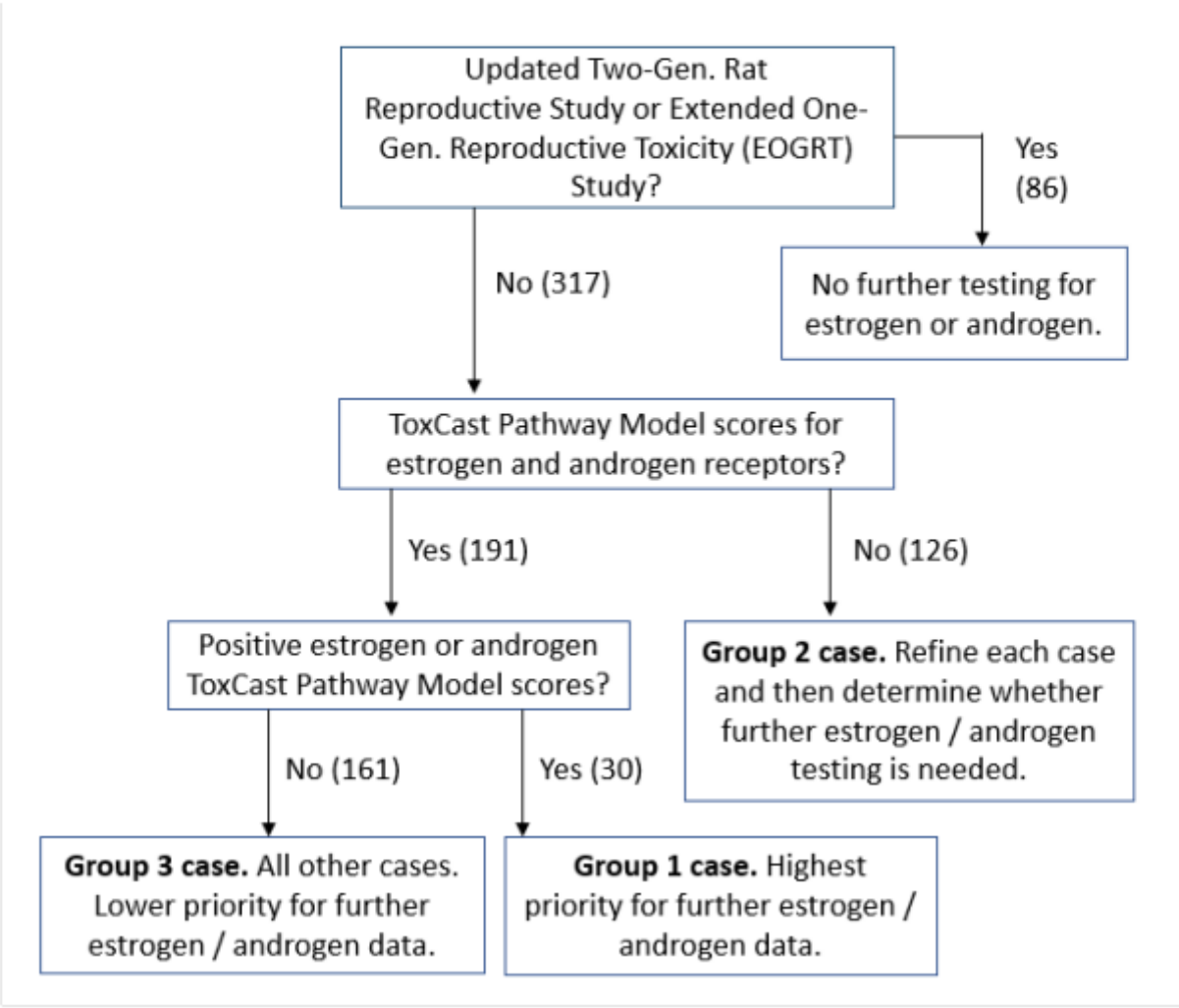
- **<u>Two</u>: Using existing endocrine data to determine whether more endocrine data are needed for FIFRA <u>and</u> EDSP**
  - For estrogen and androgen:
    - Updated rodent reproductive study.
    - But other data might also be adequate.

  - For thyroid:
    - Maintain current approach.
    - FIFRA SAP expected in 2025.

Three Strategies

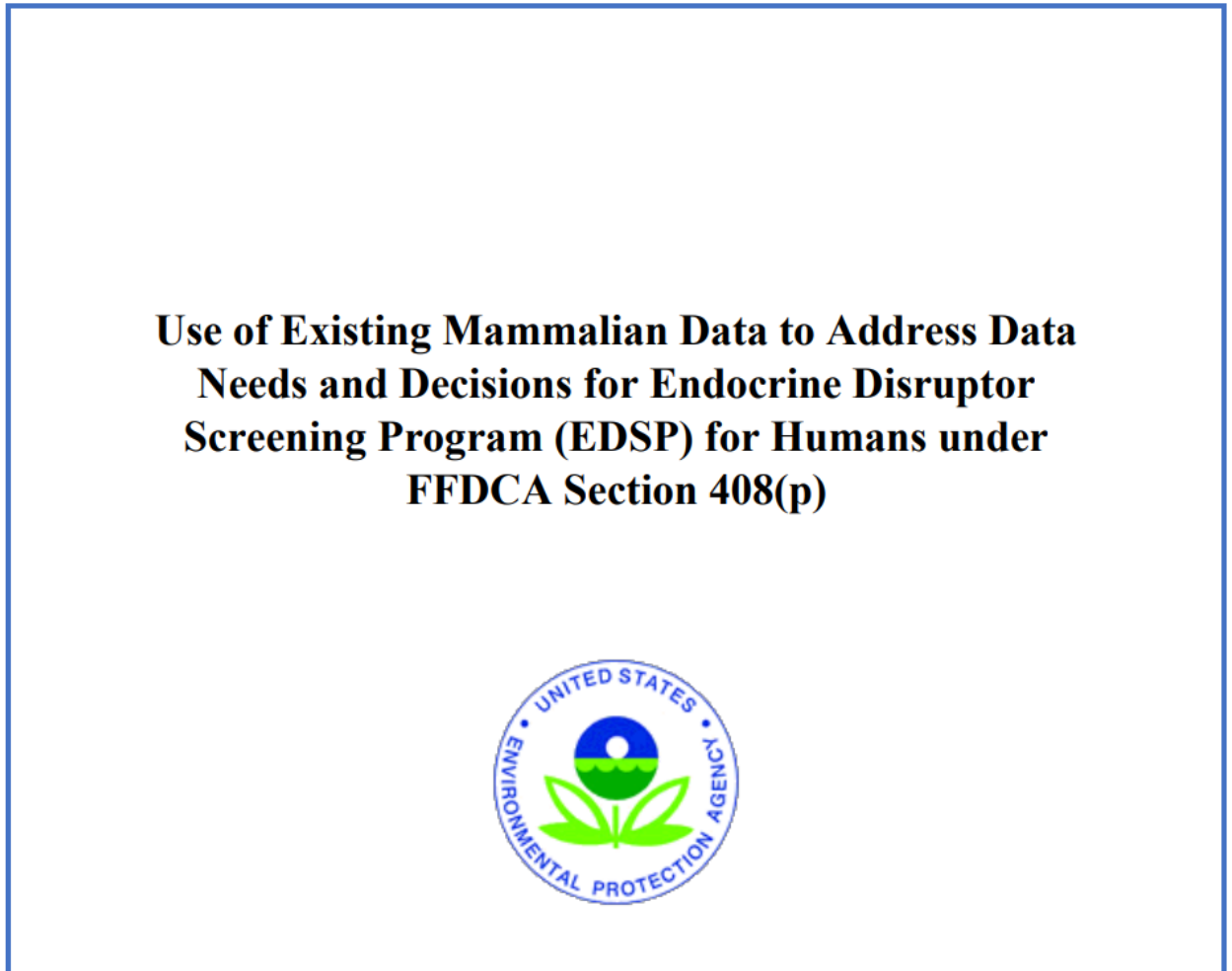
- **<u>Three</u>: Integrate data requirements through registration review, starting with priority chemicals**

Figure 1. Framework for prioritizing the 403 conventional pesticide cases currently in registration review for which an FFDCA section 406(p)(6) determination is needed.



Science Paper

- Discusses existing studies with endocrine-related endpoints:
  - Two-generation reproductive toxicity study (post-1998)
  - Extended one-generation reproductive toxicity (EOGRT)
  - Comparative thyroid assay (CTA)
- Crosswalk endpoints in existing studies with those in Tier 1 assays



Conventional AI List

- List of chemicals for each Group
- Also includes list of chemicals with adequate estrogen and androgen data for humans (repro. studies)
- Some chemicals are dual use (e.g., also an antimicrobial)

List of Conventional Registration Review Chemicals for Which an FFDCA Section 408(p)(6) Determination is Needed

Conventional AI List

- Updated reproductive toxicity studies available (adequate estrogen and androgen data) for 20% of conventional chemicals.

- For other 80% of chemicals, divided into three groups:

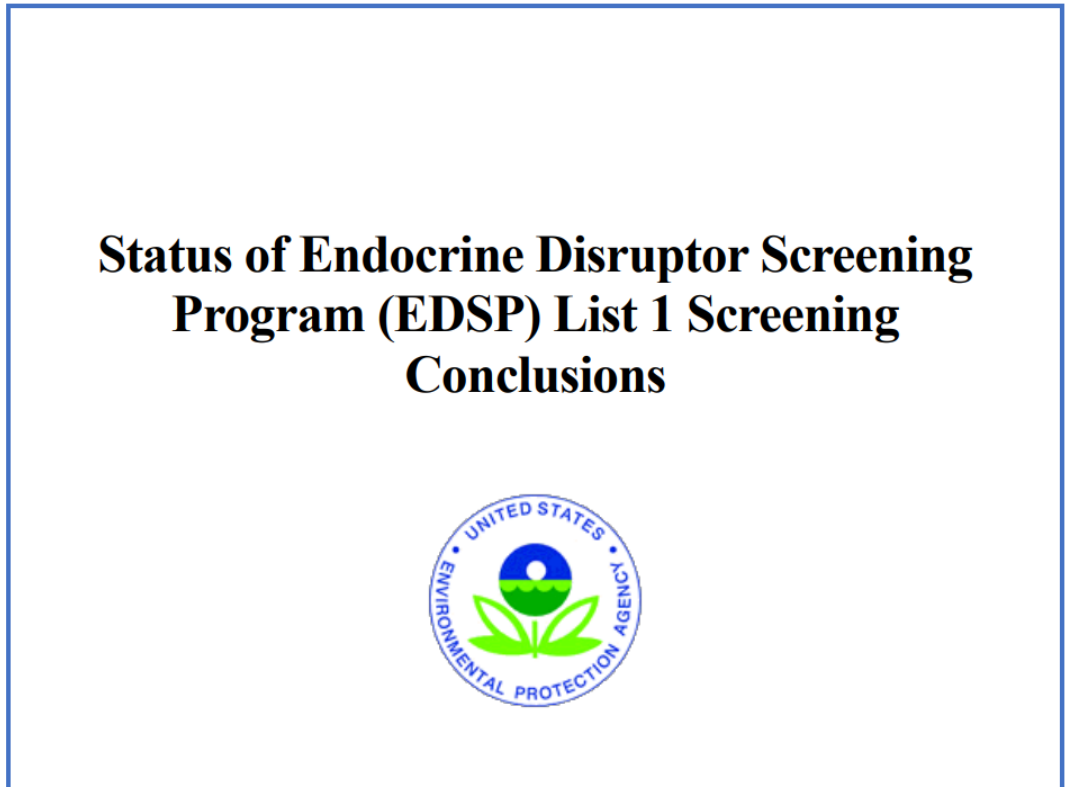
  Group 1: 30 chemicals show activity in ER/AR pathway models
  - DCI for additional Tier 1 testing in spring 2024

  Group 2: 126 chemicals not tested in ER/AR pathway models

  Group 3: 161 other chemicals with no activity in ER/AR pathway models

List 1 Document

- 52 chemicals (50 actives and 2 inerts)
- Concludes EPA review of potential human endocrine effects for all 52 chemicals
- For 35 chemicals, EPA determined that available data are sufficient to assess potential wildlife endocrine effects
- For other 17 chemicals, EPA recommends additional testing. Will address in future EDSP updates.



Questions