

# U.S. Environmental Protection Agency Endocrine Disruptor Screening Program Comprehensive Management Plan

Jointly developed by the Office of Chemical Safety & Pollution Prevention and the Office of Water

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## February 14, 2014

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This comprehensive management plan was developed by the EPA to describe activities envisaged between FY 2014 through FY 2019 and supersedes the original comprehensive management plan issued in June 2012; the management plan provides strategic guidance to the EPA staff and managers participating in the internal activities associated with EDSP. This comprehensive management plan does not create or confer legal rights or impose any legally binding requirements on the EPA or any other party. This comprehensive management plan is distributed solely for the purpose of sharing this information with the public, consistent with the EPA transparency objectives. It is not intended to serve any other purpose, and should not be construed to represent formal dissemination of any agency determination or policy. As such, the information correction process under the agency's Information Quality Guidelines does not apply to this document.

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## 1. Introduction

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One of the U.S. Environmental Protection Agency's highest priorities is to assure chemicals are safe for both people and the environment. The EPA developed the Endocrine Disruptor Screening Program (EDSP) in response to the statutory mandate in the Federal Food, Drug, and Cosmetic Act (FFDCA) to "develop a screening program...to determine whether certain substances may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or such other endocrine effects as the Administrator may designate."<sup>1</sup> As part of the EDSP, the statute also provides the EPA with authority to "provide for the testing of any other substance that may have an effect that is cumulative to an effect of a pesticide chemical if the Administrator determines that a substantial population may be exposed to such a substance."<sup>2</sup> In addition to FFDCA, the Safe Drinking Water Act (SDWA) provides the EPA with authority to provide for testing "of any other substances that may be found in sources of drinking water if the Administrator determines that a substantial population may be exposed to such substance."<sup>3</sup> Beyond testing and determining endocrine effects, FFDCA also authorizes the EPA to take action: "In the case of any substance that is found...to have an endocrine effect...the Administrator shall, as appropriate, take action under such statutory authority as is available to the Administrator...to ensure the protection of public health."<sup>4</sup>

To begin meeting this statutory mandate, the EPA in 1996 chartered a Federal Advisory Committee to address endocrine disruption: the Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC). After considering the EDSTAC recommendation in its final report<sup>5</sup> the EPA largely adopted the EDSTAC recommendations, and in an August 1998 Federal Register notice established the EDSP.<sup>6</sup> In its final report, EDSTAC made several key recommendations to:

- Address both potential human and ecological effects from chemical exposures
- Examine effects of these chemicals on estrogen, androgen and thyroid hormone-related processes
- Include pesticide and non-pesticide chemicals, contaminants, and (after evaluating single chemicals) mixtures
- Develop a two-tiered screening and testing strategy, now known as the Endocrine Disruptor Screening Program

The two-tiered screening and testing process is intended to ensure that only those chemicals that were screened to have potential endocrine activity would be advanced for further testing. Before initiating the screening process, EDSTAC recommended EPA establish a priority setting approach to determine which chemicals should undergo Tier 1 screening. The purpose of Tier 1 screening is to identify chemicals that have the potential to interact with the estrogen, androgen or thyroid hormone systems. This is done by using a battery of assays. The purpose of Tier 2 testing is to identify whether there is an interaction with the endocrine system and establish a quantitative, dose-response relationship for any adverse effects that might result from that interaction.

On April 15, 2009, the EPA announced the policies and procedures for initial EDSP screening<sup>7</sup> and the first list of chemicals to be screened (List 1 chemicals), with the Tier 1 battery of assays, for their

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<sup>1</sup> 21 U.S.C. § 346a(p)(1).

<sup>2</sup> 21 U.S.C. § 346a(p)(3)(B).

<sup>3</sup> 42 U.S.C. § 300j-17.

<sup>4</sup> 21 U.S.C. § 346a(p)(6).

<sup>5</sup> U.S. EPA, *Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC), Final Report*, August 1998.

<sup>6</sup> 63 Federal Register (FR) 42852-42855 (August 11, 1998), *Endocrine Disruptor Screening Program*.

<sup>7</sup> 74 FR 17560-17579 (April 15, 2009), *EDSP; Policies and Procedures for Initial Screening*.

*potential* to interact with the endocrine system. This is known as Tier 1 screening.<sup>8</sup> The agency began issuing these test orders for the first list of chemicals on October 29, 2009. As stated in the April 15, 2009 Federal Register Notice, "For the initial screening, EPA generally intends to issue 'Tier 1 Orders' pursuant to section 408(p)(5) of FFDCA." As demonstrated in the revised second list of chemicals (List 2 chemicals) issued in June of 2013,<sup>9</sup> screening and testing will include chemicals that may occur in sources of drinking water to which a substantial population may be exposed as stipulated in SDWA section 1457.

While the agency has validated Tier 1 assays to determine potential endocrine activity, we recognize the need to enhance and improve the current efforts, by adopting newer high-throughput assays, computational technology and state-of-the-science testing methods. In this evolution, the program will shift and transition through several incremental phases. The current phase focuses on establishing a solid foundation of scientifically validated screening and testing methods, systematic and efficient issuance of test orders for screening and testing, and development of an interoperable standardized information technology data system that allow for technology management of test order issuance, electronic submission of study data and electronic data reviews. Within the next five years, the EDSP plans to fully embrace new technology to enable a more efficient and effective chemical screening, testing, data entry, storage and review processes, with a specific focus on the regulatory application of new computational risk-based tools. This shift to utilization of computational tools will enable the agency to more efficiently and effectively prioritize and screen chemicals for review under the EDSP.

## **EDSP Mission Statement**

The Endocrine Disruptor Screening Program was developed to protect public health and the environment by screening and testing chemicals. If perturbation of the endocrine system leads to alterations in the function(s) of the endocrine system and consequently causes adverse health effects in humans and wildlife, the agency will fully assess the risks and will develop risk mitigation measures to protect against those effects. Advancements in risk assessment methodologies, risk assessment policies and toxicity pathway understanding have rapidly evolved over the past decade; these progressive changes affect the evolution of the Endocrine Disruptor Screening Program and are more fully described in the EDSP21 Work Plan.<sup>10</sup>

## **Executive Summary: Comprehensive Management Plan**

This EDSP comprehensive management plan is intended to provide strategic guidance for FY 2014 and through FY 2019. This management plan is a living document. It will be evaluated on an annual basis for necessary revisions reflecting adjustments to program priorities and resources and to shift the time horizon. The plan covers the current fiscal year (FY) plus five years into the future of the program. Annual revisions of this plan will be released to coincide with the annual review process and for alignment with the agency's fiscal year planning and budgeting cycle. It is important to note that, although this overarching, management plan will be evaluated on an annual basis; certain elements of

<sup>8</sup> 74 FR 17579-17585 (April 15, 2009), *Final List of Initial Pesticide Active Ingredients and Pesticide Inert Ingredients to be Screened under the FFDCA*.

<sup>9</sup> 75 FR 70248-70254 (November 17, 2010), *EDSP, Second List of Chemicals for Tier 1 Screening*.

<sup>10</sup> U.S. EPA, *Endocrine Disruptor Screening Program for the 21st Century: (EDSP21 Work Plan), Summary Overview*, September 30, 2011. [http://www.epa.gov/endo/pubs/edsp21\\_work\\_plan\\_summary%20\\_overview\\_final.pdf](http://www.epa.gov/endo/pubs/edsp21_work_plan_summary%20_overview_final.pdf)

the plan (e.g., the list of activities and distribution of resources) may be evaluated and adjusted on a more frequent basis throughout each year.

This plan was developed by the EPA to provide strategic guidance to the EPA staff and managers participating in the internal activities associated with EDSP. This plan is not intended to establish any policy or procedures or impose any requirements. While the requirements in the statutes, agency regulations, and the EDSP orders are binding, it is important to note that nothing in this plan is binding on either the EPA or others. As such, the EPA may depart from this plan where circumstances warrant and without prior notice. The use of non-mandatory language such as "may," "can" or "should" in this plan does not connote a requirement but does indicate the EPA's current intentions and provides strategic guidance to internal EPA staff and managers.

Although this plan does not identify or describe all of the internal procedures or administrative requirements that might apply to the activities contemplated by this plan, the agency recognizes the need to identify those details as part of its efforts. To the extent applicable, internal procedures or administrative requirements may influence the activities outlined in this plan.

## **Targeted Objectives for 2014 through 2019**

In FY 2013, the EDSP underwent four significant external FIFRA Scientific Advisory Panel (FIFRA SAP) peer reviews on the critical science supporting the program: 1) the application of advanced computational toxicological methods for chemical prioritization;<sup>11</sup> 2) the performance of the Tier 1 screening assays and battery for the initial list of chemicals;<sup>12</sup> 3) scientific validation of the Tier 2 ecological species test methods, inclusive of bird, frog, fish and invertebrate;<sup>13</sup> and 4) interpreting Tier 1 and other scientifically relevant data in accordance with the EDSP Weight of Evidence Guidance,<sup>14</sup> issued in September of 2011.<sup>15</sup> Following these four external peer reviews, the agency will be carefully considering all of the FIFRA SAP recommendations for this revision of the EDSP comprehensive management plan and other modifications to the program as we advance forward.

### **List 1 Chemicals: Data Reviews and Risk Assessments**

Between 2014 and 2019, the agency will be actively engaged in programmatic implementation, which will proceed with the scientifically rigorous technical review of all Tier 1 assay results from the initial list of chemicals that received EDSP Tier 1 orders, and review of that collective data along with other scientifically relevant data to complete the weight of evidence decisions. If the weight of scientific evidence indicates a need for Tier 2 testing, the agency will issue test orders accordingly. The agency will allow four years for Tier 2 data generation and 1 year for data review. Different from Tier 1 screening data, results from the Tier 2 data reviews will be integrated directly into the risk assessments supporting registration review and new registration actions (as appropriate). Also, to the extent that the Tier 2 data indicate a risk of concern, the agency can/will act accordingly to address that risk scenario, even outside the registration review schedule.

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<sup>11</sup> <http://www.epa.gov/scipoly/sap/meetings/2013/012913meeting.html>

<sup>12</sup> <http://www.epa.gov/scipoly/sap/meetings/2013/052113meeting.html>

<sup>13</sup> <http://www.epa.gov/scipoly/sap/meetings/2013/062513meeting.html>

<sup>14</sup> U.S. EPA OCSPP, *EDSP, Weight-of-Evidence: Evaluating Results of EDSP Tier 1 Screening to Identify the Need for Tier 2 Testing*, September 14, 2011. <http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPPT-2010-0877-0021>

<sup>15</sup> <http://www.epa.gov/scipoly/sap/meetings/2013/073013meeting.html>

If the assessment warrants additional testing via Tier 2 methods, the agency intends to ensure that test guidelines and standard evaluation procedures are publically available. To that end, the agency plans to finalize the test guidelines for the remaining ecological species (*e.g.*, bird, fish, frog and invertebrates) and ensure that any additional guidance documents and standard evaluation procedures are publically available on the EDSP website (<http://www.epa.gov/endo>).

## **List 2 Chemicals: Tier 1 Test Orders for Pesticide Chemicals and Drinking Water Contaminants**

List 2 chemicals were proposed on November 2010 and finalized in June 2013 when the agency issued the policies and procedures document for SDWA chemicals. As stated in 2013, the agency anticipates issuing test orders for Tier 1 data incrementally over the course of three (3) years, pending the approval of the information collection request. Consistent with the agency's commitment to begin applying 21<sup>st</sup> century computational methods during the time frame in which List 2 test orders will be issued, it is possible that, over the course of the three-year period, 21<sup>st</sup> century computational data may be applied to List 2 chemicals that lead to further prioritization of List 2, elimination of some assay requirements from some test orders, and potentially considered along with other scientifically relevant information as part of the rationale to support whether to exempt some List 2 chemicals from Tier 1 screening. Applicable for List 2 chemicals, the agency is developing an integrated information system to increase efficiency in test order issuance, data submission, transfer, storage, tracking and reviews.

## **List 3 Chemicals: Computational Risk Based Prioritized Chemicals**

While the agency will continue its current operations for Lists 1 and 2, EDSP will be actively pursuing the application of computational toxicology and exposure methods to create a more efficient and robust screening program. This is in reflection of recent advances in computational toxicology and exposure methods that are heralding an accelerated pace for chemical screening, allowing simultaneous testing of thousands of compounds in high-throughput methods. The EDSP is collaborating with EPA's Office of Research and Development (see Section 5), and our federal Tox21 partners at National Institute of Health and the Food and Drug Administration, to bring these new, cutting-edge, computational exposure and risk based prioritization methods to FIFRA SAP review starting in 2014-2015 (see Table 1), with potential regulatory application in 2016 with a draft third list of chemicals (List 3 chemicals) for possible Tier 1 screening. List 3 will primarily focus on inert ingredients and drinking water contaminants that meet requirements stipulated under the Federal Food, Drug and Cosmetic Act, section 408(p) and the Safe Drinking Water Act, section 1457; pesticide active ingredients will be prioritized for Tier 1 screening based on the existing registration review schedule. Continuing the agency's steadfast commitment to ensuring an open and transparent process, we will be soliciting public comment and engaging with our public stakeholders in revising the draft List 3 chemicals based on public comment prior to the finalization and subsequent issuance of Tier 1 test orders.

Table 1 briefly summarizes many of the targeted goals with corresponding targeted completion dates.<sup>16</sup>

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<sup>16</sup> Targeted dates for completion are approximations and may change due to limitations of resources and unanticipated shifts in programmatic priorities.

**Table 1: EDSP Management Plan – Milestones by Fiscal Year**

Fiscal Year	EDSP Activity	Category of Activity	Period of Activity
2014	Completion of List 1, Tier 1 scientific review, data evaluation records (DERs), and weight of evidence decisions for 52 pesticide chemicals	List 1	2014-2015
2014	Completion of Tier 2 Test Methods Validation, development of test guidelines, guidance documents and standard evaluation procedures	Test Methods	2014
2014	Issuance of List 1 Chemicals, Tier 2 test orders and review of other Scientifically relevant information	List 1	2014-2015
2014	Develop Interoperable data storage, integration and management solutions to increase efficiency and effectiveness through electronic submission, tracking, and systematic data reviews	Information Technology	2014-2015
2014	Issuance of List 2 Chemicals, Tier 1 test orders and review of Other Scientifically Relevant Information; test orders will be issued incrementally over three (3) years	List 2	2014-2016
2014	FIFRA Scientific Advisory Panel Review of high-throughput, computational exposure predictive model (ExpoCast)	Peer Review	2014-2015
2015	FIFRA Scientific Advisory Panel Review of high-throughput, computational risk-based prioritization method for the universe of chemicals	Peer Review	2015-2016
2016	Issuance of proposed List 3 chemicals, based on the risk-based prioritization method, for public comment and finalization of revised List 3 chemicals for Tier 1 screening	List 3	2016-2017
2017	Data Review List 2 Chemicals, Tier 1 assay scientific data reviews, data evaluation records (DERs) and weight of evidence decisions	List 2	2017-2019
2018	Completion of List 1 Chemicals, Tier 2 assay scientific data reviews, data evaluation records and risk assessments	List 1	2019-2020
2018	Issuance of List 3 Chemicals, Tier 1 test orders and review of other scientifically relevant information; test orders issued incrementally over three (3) years, using existing ICR for registration review for pesticide actives	List 3	2018-2020
2021	Completion of List 3, Tier 1 scientific review, data evaluation records, and weight of evidence decisions	List 3	2021-2023

## 2. Scope of the Document

The EDSP management plan will describe how the agency intends to continue implementation of the EDSP by focusing primarily on five core areas:

- 1) Management organizational structure that ensures efficient decision making at multiple levels and inclusive of representatives from multiple offices across the agency (Section 3),
- 2) Systematic and efficient test order management and implementation of data reviews (Section 4),
- 3) Scientific advancement in chemical priority setting, screening, targeted testing (Section 5),
- 4) Data management by developing an enhanced and consolidated informational technology infrastructure (Section 6), and
- 5) Optimization of extant resources, development of sound performance measures and achievement of performance targets (Section 7).

In consideration of the multiple milestones described in Table 1 and the many steps and complex challenges that remain ahead, it is increasingly important to ensure seamless coordination and communication between partnering regulatory offices within the agency. To that end, the EDSP has a management organizational structure that is inclusive of multiple programs and offices, with each office equally represented at every level of the management organization. This management structure ensures

that focused decisions are made at appropriate management levels and that decisions of increasing and broader importance are elevated through the management hierarchical structure. (See Section 3, Project Organization, below.) In addition to the management organizational structure, task-focused workgroups (*e.g.*, *EDSP21 Workgroup*) will report to specific relevant committees.

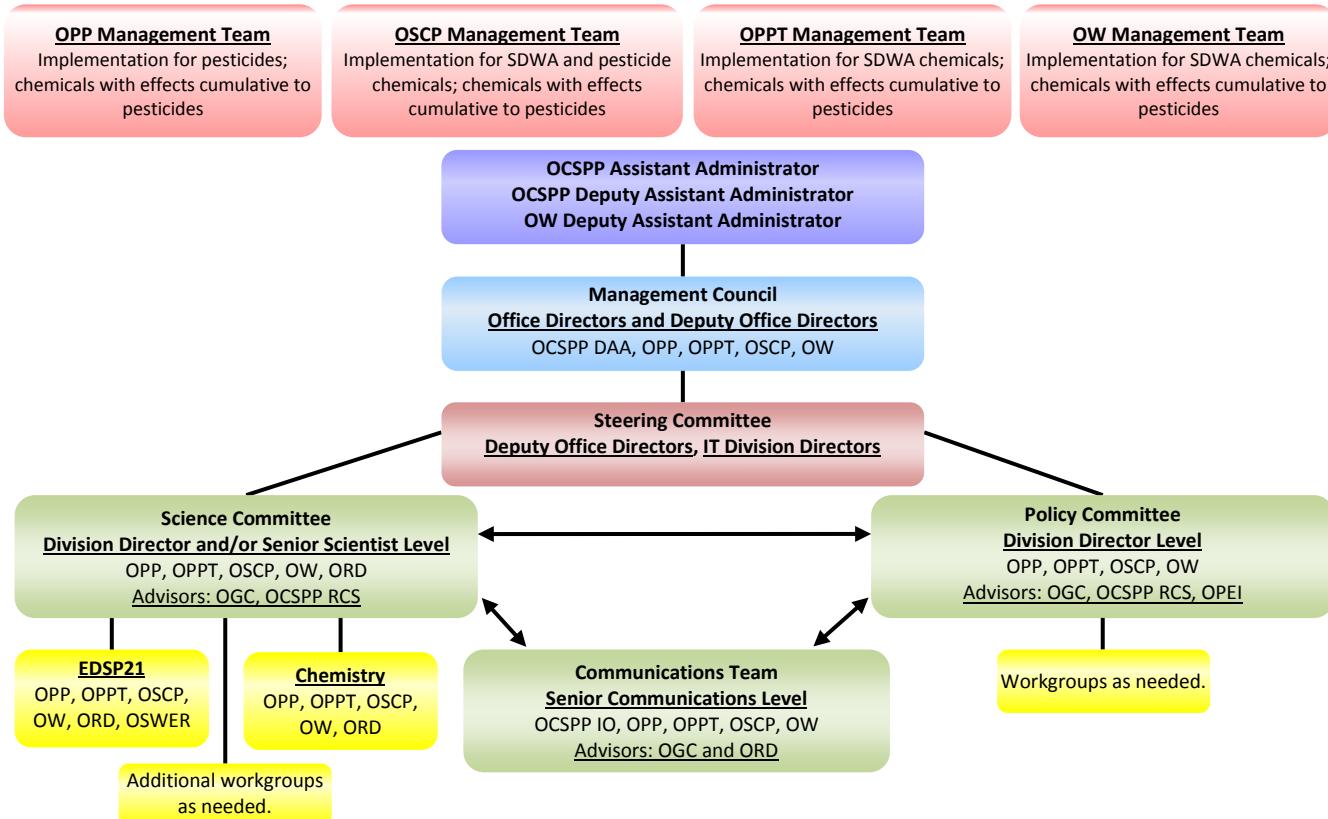
### **3. Program Organization**

This section describes the management organizational structure, identifies organizational boundaries and interfaces, and defines individual responsibilities for the various EDSP elements.

#### **Management Organizational Structure**

As illustrated in the figure below, the majority of work in EDSP will be conducted by cross-office workgroups and five major committees.

**Figure 1: Organizational Structure for EDSP Development and Implementation**



**Table 2: EDSP Committees**

Committee	Targeted Mission	Committee Membership
Management Council	Overall EDSP Management Decisions	OCSPP DAA and Office Directors from OW, OPP, OPPT and OSCP
Steering Committee	Provides management oversight of the science, policy budgetary and IT issues	Deputy Office Directors from OW, OPPT, OPP and OSCP; IT Division Directors from OPPT, OPP. OGC and ORD may participate when necessary.
Science Committee	Develop scientific methodologies/guidances for evaluation of the Tier 1 and Tier 2 data and providing oversight and advice on complex and novel scientific issues.	Scientific Risk Assessment Division Directors and Senior Science Advisors from OW, OPPT, OPP, ORD and OSCP. Other ORD experts may participate when necessary.

Committee	Targeted Mission	Committee Membership
Policy Committee	Develop and codify policies and procedures to reflect the current state of the art EDSP issues. Coordinate the development of policies and procedures, responses to petitions, congressional inquiries and ICRs.	Risk Management Division Directors from OW, OPPT, OPP and OSCP. RCS, OGC and OPEI participation when needed.
Communications Team	Coordinate all internal and external communications to ensure a consistent EPA message. This committee will provide development and oversight of the EDSP Management Database.	Senior communications officers from OPPT, OPP, OSCP, OW. OGC and ORD will provide advice when necessary.

The EDSP management structure ensures seamless communication and coordination among the partnering offices, while ensuring that decisions are made at the appropriate levels of management. When decisions cannot be reconciled at any management level, issues will be elevated to the *Management Council* for consideration.

To demonstrate how the management structure operates, the following examples are provided. If a complex scientific issue arises when evaluating other scientifically relevant information (OSRI) or the Tier 1 and Tier 2 assay data, the issue would be brought before the *Science Committee* for deliberation and determination. Committee recommendations would be elevated to the *Steering Committee* for final determination and if warranted, the *Steering Committee* would brief the *Management Council* before a final decision is made. Another example is the construction of a response to public comments that may be submitted to the *Communications Team*; while this committee may have the lead on addressing the issues, they will consult with the *Policy and Science Committees* in addressing some of the broader issues in those domains. It is emphasized that while the management structure exists to enhance coordination among the decision makers, it is intended neither to be rigid nor to restrict lines of communications that may occur outside of its structure.

Flexibility and agility are built into the management decision making structure, increasing responsiveness to change and innovation. For example, task-specific, temporary focus groups have been formed to address task-specific efforts; these workgroups will brief the relevant committees for formalization or approval to proceed, but once the objective has been met, these workgroups would disband. In the past year, a decision was made to merge the *IT and Infrastructure Steering Committee* with the *Budget and Management Steering Committee* to form the *Steering Committee*. EDSP is committed to seeking opportunities to streamline its process. As the program moves forward, the agency will continue to implement an "adaptive management" approach by ensuring process efficiencies by either streamlining the process and/or merging committees to optimize resources.

## **EDSP Community Communications Strategy**

As the management organizational structure allows for efficient decision making, the communication of these decisions is critical in promoting a highly functional and informed program. This section describes the plans for EDSP's overall communication and coordination procedures.

A *Communications Team* composed of representatives from each of the partnering programs will actively coordinate all internal and external outreach efforts, including the tracking of all incoming, outgoing and internal items related to communication of the EDSP. This ensures the expeditious tracking, production, vetting and dissemination of final responses for EDSP communication materials related to such items as:

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| <ul style="list-style-type: none"> <li>• Congressional Inquiries</li> <li>• Congressional Reports</li> <li>• Court-ordered Reports</li> <li>• Internal EPA Reports</li> </ul> | <ul style="list-style-type: none"> <li>• Questions from EDSP Order Recipients</li> <li>• Freedom of Information Act (FOIA) Requests</li> <li>• Questions from the Public</li> </ul> |
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Some of the recurring reporting requirements appear in Table 3.

**Table 3: Examples of Recurring Reporting Requirements**

Report Origin	General Description	Schedule
<b>Congressional Reporting Requirements</b>		
HAC 110-187 pp. 108-109. <sup>17</sup>	Cumulative information regarding the number of pesticides registered/reregistered through the OPP programs since August 3, 1999; the number of pesticides for which testing for endocrine disrupting effects have been conducted and the number of determinations that have been made; and the status of the assay development and validation efforts.	Annual
HAC 112-151 p. 72. <sup>18</sup>	Information regarding the use of 21 <sup>st</sup> century tools and other scientifically relevant information (OSRI) within the EDSP (requires coordination with ORD).	Semi-Annual
<b>Other Reporting Requirements</b>		
NRDC et al. v. Whitman, No. C-99-03701 WHA (Northern District of California) – Settlement Agreement	Information regarding EDSP assay development, validation and initial issuance of Tier 1 Screening and Tier2 Test Orders.	Semi-Annual (June and December)
OMB	Information regarding EDSP assay development and validation.	Quarterly

## Coordination Procedures

The EDSP requires coordination across several offices within the agency. To supplement the organizational structure described earlier, this section provides information on how the workgroups and management groups in the structure will coordinate, and how information will be transmitted to individuals and offices involved in the EDSP.

### ***Methods for Coordination***

To improve coordination between all EPA offices and levels of groups working on the EDSP, the following methods have been used:

- Biweekly Newsletter will be issued with summaries of highlighted EDSP activities.
- Committee chairs will meet at least once a month to discuss crosscutting issues. This will promote efficiency and coordination on issues that overlap science, policy, communication and infrastructure.
- Decisions made by committees, the *Steering Committee* and the *Management Council* will be appropriately documented and distributed through the committees to their members, who will in turn distribute it to the workgroup members, providing prompt and complete communication of important decisions or milestones to all offices.

<sup>17</sup> U.S. Congress, House Appropriations Committee Report 110-187, pp. 108-109.

<http://www.gpo.gov/fdsys/pkg/CRPT-110hrpt187/pdf/CRPT-110hrpt187.pdf>

<sup>18</sup> U.S. Congress, House Appropriations Committee Report 112-151, p. 72.

<http://www.gpo.gov/fdsys/pkg/CRPT-112hrpt151/pdf/CRPT-112hrpt151.pdf>

## **Roles and Responsibilities**

The EDSP is developed and implemented by the following four offices: 1) the Office of Science Coordination and Policy (OSCP); 2) the Office of Pesticide Programs (OPP); and 3) the Office of Pollution Prevention and Toxics (OPPT), and the 4) Office of Water (OW); with support and collaboration with the Office of Research and Development (ORD) and the Office of General Counsel (OGC). These offices are all involved; they either regulate the chemicals identified in the statutes or manage the potential routes of exposure that may occur from certain chemicals. For the most part, these entities all play a role in developing the vision statement, implementation plan, and ensuring strong execution of the EDSP comprehensive management plan.

**Table 4: Roles and Responsibilities**

<b>Lead Office</b>	<b>Activity</b>	<b>Supporting Offices</b>
OSCP	Tier 2 assay –development/validation, peer review, regulatory implementation	OPP, OPPT and ORD
	EDSP21 Work Plan Development and Implementation	OPP, OPPT, OW, OSWER and ORD
	Coordination, communication and EDSP website	All
	Information Collection Request (ICR) Development	OPP, OPPT, OPEI, OGC, OCSPP IO (RCS), OW
	Any Revisions to Tier 1 Assays/Battery or Tier 2 test methods	OPP, OPPT, OW and ORD
OPP	Order issuance and management of pesticides active ingredients; pesticide inert ingredients	OSCP
	Data review (OSRI, Tier 1, Tier 2) of pesticide active ingredients; pesticide inert ingredients	OSCP, OPPT, OW and ORD
	Technical questions for pesticide chemicals	ORD, OSCP
	Weight of evidence and regulatory decisions for pesticide chemicals	ORD, OSCP, OPPT, OW
OPPT/ OW Team	Makes exposure finding under SDWA identifying chemicals to receive SDWA/FFDCA orders (OW)	ORD, OPP, OSCP, OGC
	Policy and procedures for SDWA/FFDCA	OGC, OCSPP IO (RCS)
	Order Issuance and management of drinking water chemicals	OSCP
	Data Review and addressing technical questions (OSRI, Tier 1 and Tier 2) for SDWA chemicals	OSCP, ORD
	Technical questions for drinking water chemicals	ORD, OSCP
	Review weight of evidence and regulatory decisions for drinking water chemicals	ORD, OSCP, OPP, ORD

The organizational roles and responsibilities for information technology, budget and resources may be found in later sections of this document.

## **Policies and Procedures**

On April 15, 2009, following several rounds of public review and comment, the EPA published the policies and procedures for issuing and enforcing EDSP Tier 1 orders pursuant to the authority provided by section 408(p)(5) of the FFDCA. The policies and procedures, which apply to pesticide chemicals, provide specific details on the requirements associated with section 408(p) of FFDCA, format of the orders, and the associated agency policies and procedures.

Subsequently, in November 2010, the EPA sought public comment on draft policies and procedures it generally intends to use to issue and enforce EDSP Tier 1 orders pursuant to the authority provided by

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FFDCA section 408(p)(5) and as authorized under section 1457 of SDWA. On June 14, 2013, EPA published the final version of these policies and procedures to address drinking water contaminants.<sup>19</sup>

Collectively, both policies and procedures documents describe how the EPA intends to:

- Minimize duplicative testing.
- Promote fair and equitable sharing of test costs.
- Address relevant issues surrounding data compensation and confidentiality.
- Determine to whom Tier 1 orders would generally be issued.
- Identify how Tier 1 order recipients should respond to test orders, including procedures for challenging the orders.
- Ensure compliance with FFDCA section 408(p) Tier 1 and SDWA section 1457 test orders

As activities relate to updating the existing policies and procedures, over the next five years, the agency expects to:

- Revise the current policies and procedures for initial screening to reflect the lessons learned in issuance of test orders; and evaluation and review of the List 1 and subsequent List 2 chemicals.
- Review Tier 1 data for the initial list of chemicals and subsequent List 2 chemicals and perform weight of evidence determinations for all 52 chemicals associated with the initial list of chemicals.
- Incorporate technological advancements in science and risk assessment methodologies as they may apply to the policies and procedures (e.g., EDSP21 Work Plan<sup>20</sup>).
- Improve the procedures to reflect advances in new technology by providing web based electronic submission of information in response to the orders to the agency, including the DER composers for submission of electronic data reviews.

#### **4. Technical Review Processes**

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The current EDSP technical process involves:

- a) Selection of the universe of chemicals for prioritization and use of computational tools for future chemical prioritization, targeted testing, and in support of potential EDSP exemption decisions
- b) Issuance of test orders for the Tier 1 screening assays,
- c) Review of Tier 1 assay data,
- d) Develop a weight of evidence determination on whether the chemical should be advanced to Tier 2 assay testing for interaction with the endocrine system and the dose-response relationship,
- e) Issuance of test orders for Tier 2 assays, data review and integration into the risk assessment and completion of risk determinations

The elements of these processes are described in more detail below.

a) Universe of Chemicals for Prioritization

The agency believes that FFDCA and SDWA provide a clear scope for the universe of approximately 10,000 chemicals under the EDSP. In addition, the agency believes this

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<sup>19</sup> 78 FR 35922-35928 (June 14, 2013), *Endocrine Disruptor Screening Program; Final Second List of Chemicals and Substances for Tier 1 Screening*. <http://www.gpo.gov/fdsys/pkg/FR-2009-04-15/pdf/E9-8709.pdf>

<sup>20</sup> U.S. EPA, *Endocrine Disruptor Screening Program for the 21st Century: (EDSP21 Work Plan)*, Summary Overview, September 30, 2011. [http://www.epa.gov/endo/pubs/edsp21\\_work\\_plan\\_summary%20\\_overview\\_final.pdf](http://www.epa.gov/endo/pubs/edsp21_work_plan_summary%20_overview_final.pdf)

characterization of the universe addresses such factors as public nominations and exposure considerations. Additional information on future prioritization concepts are provided in a supplemental document, "*EDSP Universe of Chemicals and General Validation Principles*" that may be found on <http://www.epa.gov/endo/pubs/prioritysetting/index.htm>.

b) Issuance of Tier 1 Assay Test Orders

As previously stated, the agency announced the first list of chemicals (67 pesticides and inert ingredients) to be screened with the Tier 1 battery on April 15, 2009 and the test orders were issued starting on October 29, 2009. Registrants were given two years to complete the Tier 1 assays, with an ability to request time extensions on an assay by assay basis. Similar procedures are anticipated for the issuance of List 2 chemical Tier 1 test orders.

c) Review of Tier 1 Assay Data and Battery

Per the recommendation of a joint Scientific Advisory Board and FIFRA SAP in 1999 (EPA-SAB-EC-00-013, July 1999), the agency held a mid-course review of the functionality of each assay and the battery as a whole. These performance evaluations of the Tier 1 battery were conducted on an adequate sample of chemicals and these Tier 1 performance review results were submitted for external scientific peer review by the FIFRA SAP in May 2013. The SAP final report was submitted to the agency in August 2013.<sup>21</sup>

d) Develop Weight of Evidence Determination

After the Tier 1 assay reviews have been completed for a chemical, a weight of evidence determination will be developed in accordance with the weight of evidence guidance document. In September 2011, the agency issued a weight of evidence guidance document for evaluation of results for the Tier 1 assay, other scientifically relevant information, and additional data submitted under 40 CFR part 158 and available for the weight of evidence evaluation.<sup>22</sup> EPA's methodology was externally peer reviewed by the FIFRA SAP in a July 30 to August 2, 2013 FIFRA SAP meeting. The SAP final report was submitted to the agency in November 2013.<sup>23</sup>

e) Issuance of Tier 2 Assay Test Orders

When a weight of evidence determination for a chemical concludes that there is a potential for endocrine interaction and that it warrants additional data, the agency may either require some of the Tier 2 tests or more targeted testing. Unlike Tier 1 assays, Tier 2 testing is not a battery of assays, but rather the selection of key targeted study(s) to provide the quantitative dose-response level information needed to inform risk assessment and risk management decisions, if needed.

Chemicals that are selected to undergo Tier 2 testing will be issued test orders and data will be evaluated using routine hazard evaluation criteria that are commonly used by EPA's regulatory programs to assess potential risk to human and ecological health. EPA's risk assessment guidance and underlying scientific rationale for that guidance are publicly available and have been extensively peer reviewed (see Section 9, Appendix A).

The current Tier 2 studies include longer term studies in rats, Medaka, Xenopus Laevis, Japanese Quail and Mysid. The mammalian two generation reproduction study is already validated and the four remaining ecological Tier 2 studies have undergone inter-laboratory validation testing across

<sup>21</sup> <http://www.epa.gov/scipoly/sap/meetings/2013/052113meeting.html>

<sup>22</sup> U.S. EPA OCSPP, *EDSP, Weight-of-Evidence: Evaluating Results of EDSP Tier 1 Screening to Identify the Need for Tier 2 Testing*, September 14, 2011. <http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPPT-2010-0877-0021>

<sup>23</sup> <http://www.epa.gov/scipoly/sap/meetings/2013/073013meeting.html>

independent contract laboratories. During this intense inter-laboratory validation phase, the agency was focused on identifying opportunities to streamline these studies from a multi-generational approach to a single generation where appropriate, similar to the determination made for the mammalian two-generation reproduction study to an extended one-generation reproduction study. Such decisions will be based on an outcome-neutral finding, or one that does not sacrifice the ability to identify potential effects of concern within the second generation. All four assays underwent external scientific peer review by the FIFRA SAP (June 25-28, 2013) for measure of performance, reproducibility and reliability. The FIFRA SAP final report was submitted to the agency on September 30, 2013. The compilation of the inter-laboratory data and preliminary agency conclusions in the integrated summary reports were made publically available.<sup>24</sup>

## **5. Endocrine Disruption Screening Program Toxicology in 21<sup>st</sup> Century Work Plan**

### **Advances in Science and Technology**

While the agency has invested resources in developing and validating Tier 1 and Tier 2 test methods, the need for a more comprehensive review of new, state-of-the-science and emerging technologies for toxicity testing has been recognized. In this recognition, the EPA requested the National Research Council to compile a document to propose a strategy for implementation of toxicity testing. The results of this 2007 review, *Toxicity Testing in the 21<sup>st</sup> Century: A Vision and Strategy*<sup>25</sup> (Tox21) provides a strategic plan for implementation and adoption of these newer technologies to reduce the use of animals and accelerate the pace of typical animal-based traditional toxicity testing. In response to the NAS report in 2007, the EDSP issued its plan for how the agency will incorporate computational toxicological tools into the Endocrine Screening Program and this is described more specifically within the *Endocrine Disruptors Screening Program for the 21<sup>st</sup> Century: (EDSP21 Work Plan)*,<sup>26</sup> issued on September 30, 2011.

The work plan includes several efforts to integrate computational or *in silico* models and molecular-based *in vitro* high-throughput screening assays for prioritizing chemicals for Tier 1 screening, promote targeted *in vivo* Tier 1 testing and eventual Tier 1 battery replacement. The timeframe for application is dependent on when new computational methodologies become available and validated for specific regulatory application; for chemical prioritization, the universe of chemicals may be analyzed and prescreened using a suite of high-throughput system assays and computer-based expert systems (e.g. Quantitative Structure Activity Relationship models, High-Throughput assays, Exposure models, etc.). During this initial or prescreening phase, chemicals identified using a combination of these computational models and specific consideration of exposure will be prioritized for the issuance of Tier 1 screening battery test orders. In the intermediate-term, chemicals would only be queued for and evaluated by certain Tier 1 screening assays based on the biological activity identified by high-throughput *in vitro* assays and expert computer-based models as appropriate (*i.e.*, targeted endocrine screening). In addition, where appropriate, the results of certain *in vivo* Tier 1 screening assays would be replaced by one or a combination of validated *in vitro/in silico* models. The long-term goal is to use information derived from *in vitro*, *in silico* and existing *in vivo* data to fully replace the current EDSP Tier 1 screening battery, so that animal-based testing is eliminated or greatly reduced.

<sup>24</sup> <http://www.regulations.gov/#!docketBrowser;rpp=78;so=ASC;sb=docId;po=0;dct=SR%252BN;D=EPA-HQ-OPP-2013-0182>

<sup>25</sup> National Academy of Sciences, *Toxicity Testing in the Twenty-first Century: A Vision and a Strategy* (Report in Brief). [http://dels.nas.edu/resources/static-assets/materials-based-on-reports/reports-in-brief/Toxicity\\_Testing\\_final.pdf](http://dels.nas.edu/resources/static-assets/materials-based-on-reports/reports-in-brief/Toxicity_Testing_final.pdf)

<sup>26</sup> U.S. EPA, *Endocrine Disruptor Screening Program for the 21st Century: (EDSP21 Work Plan), Summary Overview*, September 30, 2011. [http://www.epa.gov/endo/pubs/edsp21\\_work\\_plan\\_summary%20\\_overview\\_final.pdf](http://www.epa.gov/endo/pubs/edsp21_work_plan_summary%20_overview_final.pdf)

The computational methods work plan is also a key component of advancing the goals in the President's proposed fiscal year 2012 budget, "In FY 2012 EPA will begin a multi-year transition from the [EDSP] to validate and more efficiently use computational toxicology methods and high-throughput assays that will allow the agency to more quickly and cost-effectively assess potential chemical toxicity."<sup>27</sup>

The EDSP21 Work Plan also addressed the goal set within the President's proposed fiscal year 2012 budget: To advance the goals in the President's proposed fiscal year 2012 budget, "In FY 2012 EPA will begin a multi-year transition from the Endocrine Disruptor Screening Program (EDSP) to validate and more efficiently use computational toxicology methods and high-throughput screens that will allow the Agency to more quickly and cost-effectively assess potential chemical toxicity."<sup>28</sup>

## Approach for Evolving EDSP

Evolving the EDSP to incorporate computational toxicology methodologies will be a multi-year process with incremental steps for adoption and integration of new tools for certain applications (*e.g.*, chemical prioritization, targeted testing, *in vivo* replacement), as described in the EDSP21 Work Plan. Four major activities are necessary to achieve this evolution:

1. A transparent methodology for building confidence in the reliability of new assays and models must be developed. Thus, any new method needs to undergo expert peer review and public comment (see Table 1, line items for FIFRA Scientific Advisory Panel reviews for high-throughput exposure predictive model and new risk-based prioritization method in 2014-2015).
2. The high-throughput assays must be evaluated to build confidence that they can indicate the biological activities of interest for EDSP screening and to develop an understanding of how they compare to the current, validated Tier 1 assays and other scientific information.
3. The *in silico* models will be evaluated to build confidence that they can adequately predict biological activity in the relevant regulatory chemical inventory and exposure to better inform our ability to prioritize chemicals to go through the EDSP.
4. Optimizing the existing agency activities to build additional efficiencies with existing registration review schedules for pesticide active ingredients and research efforts established in the Office of Research and Development.

## *Office of Pesticide Program: Registration Review Schedule*

In addition to the use of computational tools for chemical prioritization, the agency will also ensure that, to the extent possible, all resources are optimized by temporally aligning EDSP with currently scheduled reviews and extant processes, such as the registration review schedule for pesticide active ingredients. Registration review was mandated by FIFRA. With some exceptions, all pesticides distributed and sold in the United States must be registered by the EPA, and, based on scientific data, they must show that they will not cause unreasonable adverse effects on the environment when used as directed on product labeling. The registration review program under FIFRA section 3(g) ensures that as the ability to assess risk evolves and as policies and practices change, all registered pesticide active ingredients continue to meet the statutory standard of no unreasonable adverse effects on the environment. Changes in science, public policy and pesticide use practices occur over time. Through the registration review program, the

<sup>27</sup> U.S. EPA, FY 2012, *Justification of Appropriation Estimates for the Committee on Appropriations*, EPA-190-R-11-003, p. 53. <http://www.epa.gov/planandbudget/archive.html>

<sup>28</sup> *Ibid.*

agency reevaluates currently registered pesticide active ingredients at least once every 15 years to make sure that as these changes occur, products in the marketplace can still be used safely. The registration review program challenges the EPA to continuously improve its processes, science and information management while maintaining a collaborative and open process for decision-making. One goal of this plan is the integration of the endocrine disruptor screening activities for pesticide active ingredients into this re-evaluation effort; for example, OPP could seek opportunities to cluster similar chemicals into chemical categories and select representative chemicals within those classes for endocrine screening to reduce the need to test all chemicals. This type of strategic testing could occur with the next list of chemicals for Tier 1 screening.

### ***EPA's Office of Research and Development Endocrine Disruptors Research Program***

EPA's ORD has a number of research and development projects underway to support the EDSP21 transition to computational toxicology and high-throughput approaches. The individual projects are managed under ORD's national research program for Chemical Safety for Sustainability (CSS) and, collectively, constitute a portion of the Endocrine Disruptors Research Program. The EDRP is funded through a different appropriation than the EDSP and is therefore outside the scope of this management plan. However, the interplay between the EDRP and the EDSP must be accounted for in the establishment of performance measures and resource requirements for the EDSP.

Chemical Safety for Sustainability (CSS) is one of several newly developed priority research areas for EPA. Through collaboration between the agency's program and research offices, CSS research will advance environmental sustainability while continuing to ensure chemical safety. Protecting the health of humans and wildlife in the 21<sup>st</sup> Century will require an integrative approach among research and regulatory scientists of various disciplines to develop contemporary tools for prediction, toxicity screening and testing, and guidance for evaluation, characterization and management of potential risks to chemical exposure.

The EDSP21 Work Plan provides a framework for cross-office collaboration that promotes the integration by regulatory scientists of CSS research into the EDSP. In the near-term, EDSP-related CSS projects are designed to develop and evaluate the applicability of high-throughput assays and computational models and databases to aid in prioritizing the order in which chemicals are selected for screening in the current Tier 1 battery. As science and technology progress, and experience and confidence are gained using these new assays and models, alternative methodologies will begin to replace part or all of the current Tier 1 screening battery. A longer-term goal of CSS research is to develop the methods that characterize effects, absorption, distribution, metabolism, excretion, and exposure estimation that will eventually replace whole animal testing in Tier 1. Thus, a future version of the EDSP Tier 1 battery is expected to be a more efficient and sustainable screening process. More detailed information on CSS research is available at the website:

<http://www.epa.gov/research/priorities/chemicalsafety.htm>.

### **EDSP21 Scientific Workgroup**

To ensure that the EDSP program collaborates and coordinates on these research areas, the *EDSP21 Workgroup* was formed under the auspices of the EDSP *Science Committee* (see Section 3, Figure 1), includes key participants from ORD and will be responsible for ensuring that EDRP results and the associated transition to computational toxicology and high-throughput approaches are appropriately incorporated into the formulation of EDSP performance measures, performance targets and resource requirements.

To address 2014-2019 EDSP milestones described in Table 1, the *EDSP21 Workgroup* will ensure close coordination and leadership in the development of state of the science documents for the planned FIFRA SAP reviews. These peer review recommendations will guide the agency towards application of computation methods and their incremental use of *in silico* models and high-throughput *in vitro* assays for risk-based prioritization and screening purposes in the EDSP. More broadly, to ensure national and global harmonization, the workgroup will engage in frequent and productive cross-agency and international interactions through the Tox21 effort and Global and International coordination with the Organisation for Economic Co-operation and Development (OECD), Endocrine Disruptor Testing and Assessment (EDTA) Committee as well.

## 6. Consolidated Information Technology (IT) Infrastructure

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In addition to computational methods for toxicity determinations, the EDSP consolidated information infrastructure focuses on developing more efficient information technology (IT) tools for issuing EDSP test orders and subsequently receiving test order responses and data. Current efforts are focused on the use of electronic submission tools (*e.g.*, the agency's central data exchange or CDX), management databases and scientific data management. These IT objectives include:

### IT Objectives

- Building information technology components that can be leveraged across the EPA to streamline processes and create efficiencies for both the EPA and external users
- Promote "One EPA" by providing industry with simple, streamlined and unified approach to reporting information
- Leverage information technologies to improve the quality and timeliness of accomplishing the EPA's mission
- Increase electronic submissions, resulting in greater transparency and speed/efficiencies in generating automated program reports

The EDSP program has two major IT efforts planned:

- 1) A single, administrative system to issue and manage/track test orders, as well as receive and review studies and data, and to track regulatory progress/status.
- 2) A single, scientific system/database to store, integrate and analyze study results.

### Administrative System Development Work

The agency's goal is to develop a single administrative system. This system will issue test orders and track recipient responses to those test orders. Those responses include 90-day responses, other scientifically relevant information (OSRI), extension and waiver requests, as well as actual study submissions, Data Evaluation Records (DERs), and summary data. Studies will be electronically stored in this system, and are not just scanned Adobe Portable Document Format (PDF) files of paper documents. The administrative system will also track the progress/status of primary, secondary and final review of submitted studies with the ability to communicate status to the EPA (and potentially, to registrants). Finalized study results (summary data from DERs) will be exported to the scientific system or EDSP DER database. In accordance with the EPA's August 2011, *Final Plan for Periodic*

*Retrospective Review of Existing Regulations,*<sup>29</sup> OCSPP will leverage the technologies of this system to increase electronic reporting.

The benefits of the administrative system include: 1) Actual electronic submission of documents (no scanning to PDF), 2) Streamlined flow of data submission—one entry port for all submissions, registrants will do much of the submission data field entries resulting in less redundant work between the EPA and registrants to process the submissions and increasing the data integrity of submissions, 3) Potentially, the EPA receives actual study and summary data so that it can easily be stored in a database where the EPA scientists and regulators can search, sort and analyze it with a few key strokes.

## Scientific System Development Work

The agency's goal is to develop a single scientific data system. An essential element of this scientific system is the EDSP DER database which houses the EDSP summary review data. This database is available to various internal agency work groups for analysis and validation purposes once the reviews are finalized (*i.e.*, the weight of evidence has been finalized along with associated data reviews [DERs]). ORD will consider the DERs in the EDSP DER database for use in validating and comparing them to computational toxicology models, as well as high-throughput assays. In addition, the agency will determine whether a non-sensitive subset of the database can be made available to the public via the Web after the weight of evidence and data reviews are finalized.

The expected benefits of this scientific data system include: 1) standardized content of DER composer documents will speed the process of writing and storing data reviews. It will also standardize DERs and keep format and content consistent across agency program offices; 2) study summary data from standardized DERs can be automatically exported to the EDSP DER database; 3) actual study summary data and endpoints could quickly be mined and analyzed; 4) the database will support consistent weight of evidence determinations; and 5) the agency can use the EDSP DER database for analyzing the performance of Tier 1 and eventual Tier 2 assays.

## 7. Resource Requirements and Performance Management

The management of EDSP's resource requirements and performance is conducted within the existing structure of the agency's budget, planning and results cycle.



Figure 3, EPA Budget, Planning & Results Cycle

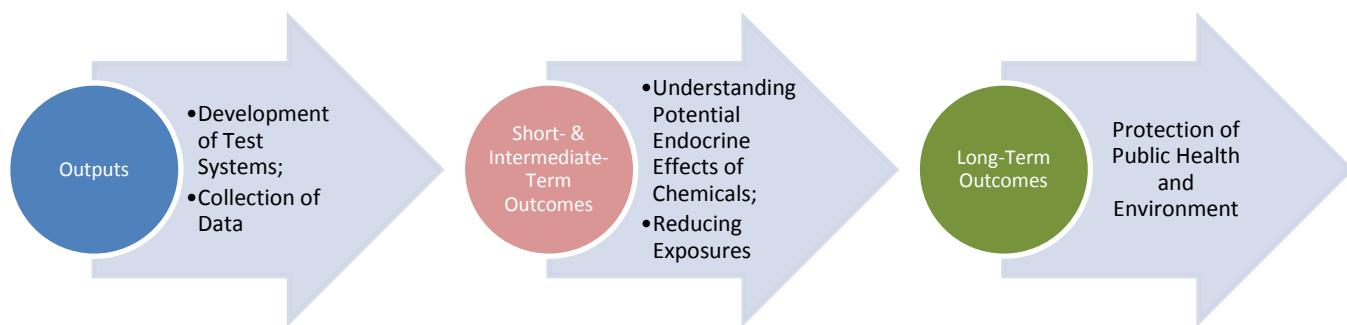
<sup>29</sup> U.S. EPA, *Improving Our Regulations: Final Plan for Periodic Retrospective Reviews of Existing Regulations*, August 2011. <http://www.epa.gov/regdarrt/retrospective/documents/eparetreviewplan-aug2011.pdf>

## Strategic Planning

The strategic objectives of the EDSP are defined by statute in the FFDCA<sup>30</sup> and the SDWA.<sup>31</sup> Specifically, the objectives are to develop and implement a screening program to determine whether certain substances may have endocrine effects and, in the case of any substance that is found to have endocrine effects, to take action as is necessary to ensure the protection of public health.

Conceptually, these statutory objectives can be organized into three categories of possible performance measures, as depicted in Figure 3 (below). As will be described more fully under the *Annual Planning and Budgeting* section, outputs are focused on program activities and work products; short and intermediate term outcomes are focused on changes in knowledge or behavior needed to achieve program objectives; and long-term outcomes are focused on the ultimate goals of the program.

**Figure 2: Conceptual Model for Performance Measures**



For the Draft Fiscal Year 2014 - 2018 EPA Strategic Plan, the agency developed a strategic measure that is consistent with these statutory objectives for the EDSP and is measurable during the period covered by the plan. By 2018, the agency plans to complete Endocrine Disruptor Screening Program (EDSP) decisions for 100 percent of chemicals for which complete EDSP data is expected to be available by the end of 2017. Baseline is 15 decisions have been completed through 2012 for any of the chemicals for which complete EDSP information is anticipated to be available by the end of 2017.

In this context, EDSP decisions for a chemical are defined broadly and include short- to intermediate-term outcomes ranging from determining a chemical's potential to interact with the estrogen, androgen or thyroid hormone systems to otherwise determining whether further endocrine related testing for the chemical is necessary.

The EDSP organizational structure includes a *Management Council* with senior representation from all offices with primary responsibility for implementing the program (OCSPP and OW). The *Management Council*, in consultation with the Assistant Administrator and Deputy Assistant Administrators for OCSPP and OW, will provide guidance to the EDSP *Steering Committee* for the development of future strategic measures. Future strategic measures will continue to focus on program outcomes and will attempt to capture long-term outcomes to the extent practicable in the covered period.

<sup>30</sup> 21 U.S.C. § 346p.

<sup>31</sup> 42 U.S.C. § 300j-17.

## Annual Planning and Budgeting

The EPA's annual planning and budgeting process requires the consideration of three fiscal years at the same time. For the current fiscal year, efforts focus on budget execution while for subsequent years, efforts will focus on formulation and planning. The Table 5 depicts the generic budget process used in fiscal year 2012 which continues to be relevant to date.

For the EDSP, annual planning focuses on establishing performance measures and associated targets and estimating the resource requirements for major program activities. The major EDSP activities are currently focused on advancing assay validation, continuing program implementation, and developing a consolidated information infrastructure. In the future, the emphasis will shift to computational toxicology and high-throughput approaches supported by the EPA's Office of Research and Development (ORD) Endocrine Disruptors Research Program (EDRP).

### **Performance Measures**

In fiscal year 2010, the agency developed three performance measures for the EDSP. These measures were intended to cascade from the strategic measure and to capture a shift in the program's emphasis associated with beginning to issue test orders for the first pesticide chemicals to undergo screening. Though developed as part of the fiscal year 2012 planning process, the measures were retroactively applied to fiscal year 2011.

In fiscal year 2012, while planning for fiscal year 2014, the *Policy Committee* addressed performance related recommendations from the EPA's Office of the Inspector General (OIG). OIG has recommended that the EPA:

*Develop short-term, intermediate, and long-term outcome performance measures, and additional output performance measures, with appropriate targets and timeframes, to measure the progress and results of the program [EDSP].*

As guidance, OIG provided the definitions listed in Table 6 (below). The *Policy Committee* evaluated existing performance measures (generally focused on outputs) and determined what revisions and additional measures were needed. In addition, the committee explored whether additional outcome

**Table 5: Planning and Budgeting Process**

Phase	FY 2014 Planning		FY 2013 Budget Formulation	FY 2012 Budget Execution								
	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep
2011									OMB Hearings			Appropriations bill or CR Enacted
									OMB Pass back			Enacted Operating Plan Developed
									EPA Appeals and Resolution			
									Budget Request to Congress Developed			
									Budget Submitted to Congress			
									Congressional Hearings			
												Monitoring and Accounting
2012												
Spending												

performance measures could be developed that capture the policy objectives of the EDSP: to determine which chemicals have endocrine effects and take any necessary actions to protect public health.

**Table 6: OIG Guidance Regarding Performance Measures**

In developing additional performance measures for the EDSP, the *Policy Committee* considered an important transition for the EDSP. As stated in the fiscal year 2012 Congressional Justification: "In FY 2012 EPA will begin a multi-year transition from the Endocrine Disruptor Screening Program (EDSP) to validate and more efficiently use computational toxicology methods and high-throughput screens that will allow the agency to more quickly and cost-effectively assess potential chemical toxicity."<sup>33</sup> The EDSP21 Work Plan outlines the steps needed to effect this transition that will require a close partnership between the EDSP implementing offices and the agency's ORD (see Section 5).

Key performance measurement terms and definitions <sup>32</sup>	
Term	Definition
Outputs	Quantitative or qualitative measures of activities, work products, or actions
Short-term outcomes	Changes in learning knowledge, attitude, skills, or understanding that result from program activities and are needed to achieve the end outcome
Intermediate outcomes	Changes in knowledge, behavior, or conditions that result from program activities and are needed to achieve the end outcome
Long-term outcomes	The ultimate outcomes of program activities

During the planning of FY 2014 Presidential Budget, the *Policy Committee* made further considerations to the EDSP performance measures for FY 2014 to better focus and update the EDSP measures. In reflection of the anticipated application of advanced computational methods and completion of validated methods, the committee opted to delete two measures, E02 and E03, in favor of newly developed measures, E04, E05 and E06. These performance measures changes are effective starting in FY 2014.

Performance measure rationales to delete existing measures include: E02 (Number of chemicals for which EDSP Tier 1 test orders have been issued) is an output measure that is implicitly captured in other measures that are more directly related to program outcomes; measure E03 (Number of screening and testing assays for which validation decisions have been reached) will become obsolete in FY 2014 as Tier 2 test method validation concludes and activities shift to implementation of 21<sup>st</sup> century tools (captured under measure E06). New performance measure E04 tracks the number of chemicals with Tier 1 screening assay results reviewed. While this is linked to E01, it differs by accounting for those scientific data evaluation records that have undergone primary and secondary technical reviews and does not include the specific regulatory decisions accounted for in E01. Performance measure E05 tracks the number of chemicals for which weight of evidence determinations have been completed. This measure differs from E04 in that it accounts for the number of scientific weight of evidence and hazard characterizations completed. These hazard characterizations will be based on the integrated scientific reviews of the 1) Tier 1 data in combination with, 2) other scientifically relevant information, and 3) existing toxicity information (e.g., 40 CFR part 158). New performance measure E06 tracks the number of High-Throughput (HTP) assays and Quantitative Structure Activity Relationship (QSAR) tools validated for use in a chemical prioritization scheme, screening or data replacement for EDSP. This measure reflects the advancement in technology replacing validation of traditional screening and

<sup>32</sup> U.S. EPA, OIG Evaluation Report, *EPA's EDSP Should Establish Management Controls to Ensure More Timely Results*, Report No. 11-P-0215, May 3, 2011, p. 17. <http://www.epa.gov/oig/reports/2011/20110503-11-P-0215.pdf>

<sup>33</sup> U.S. EPA, FY 2012, *Justification of Appropriation Estimates for the Committee on Appropriations*, EPA-190-R-11-003, p. 53. <http://www.epa.gov/planandbudget/archive.html>

testing methods with new computational tools, as recommended by the NAS 2007 report. The measures and their current performance results and targets are listed in the Table 7 below.

Overall, the performance measures changes made for FY 2014 will continue to reflect the progressive transition in FY 2015 that moves the program from a focus on test order issuance to implementation of state-of-the science, risk assessment and data review. These new performance measures also proactively signal the evolution of the program from one based on low throughput, traditional whole animal test methods towards the use of computational toxicology and high-throughput methods, with less reliance on animal testing.

Selected measures are supported by a Data Quality Record that includes a definition of the data being collected and their sources; associated information systems and data quality procedures; and information related to results reporting and oversight.

### **FY 2012 and FY 2013 Performance Measures and Targets**

In FY 2012 and FY 2013, the Endocrine Program continued to review public comments submitted for the second list of EDSP chemicals and did not accomplish the goal of issuing additional test orders on the subsequent list of EDSP chemicals for screening. This second list includes drinking water contaminants in addition to pesticide active ingredients was revised and issued in June 2013 and pending approval of the Information Collection Request (ICR), the agency anticipates issuing test orders across three years of the duration of the ICR. The single decision accomplished in 2012 was the decision to exempt a biopesticide, *agrobacterium radiobacter* that the agency determined to have met the requirements under FFDCA 408(p), section 4. This decision was announced on the EDSP website ([www.epa.gov/endo](http://www.epa.gov/endo)) in June of 2012.

In FY 2013, to address performance measure E03(Number of screening and testing assays for which validation decisions have been reached), the Endocrine Program completed the validation efforts for five ecological Tier 2 test methods, including an additional Tier 1 test method that seeks to replace the use of whole animals with human recombinant cell lines. All six test methods have been submitted for external peer review as of September 30, 2013. The FIFRA Scientific Advisory Panel report for the review of the interlaboratory validation data for the bird, fish, frog, mysid and copepod species have been submitted to the agency as of September 30, 2013 and the Human Recombinant Estrogen Receptor (HRER) Tier 1 test method integrated summary report had been submitted for external peer review on September 30, 2013 (Table 7).

**Table 7: Current EDSP Performance Measures**

	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014
<b>Measure (E01) Number of chemicals for which EDSP decisions have been completed</b>					
Target		3	5	20	59
Actual		3	1	0	
<b>Measure (E02) Number of chemicals for which EDSP Tier 1 test orders have been issued</b>					
Target		40	40	40	Deleted
Actual		0	0	0	
<b>Measure (E03) Number of screening and testing assays for which validation decisions have been reached</b>					
Target		2	4	6	Deleted
Actual		2	1	6	

	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014
Measure (E04) Number of chemicals with Tier 1 screening assay results reviewed					
Target					52
Actual					
Measure (E05) Number of chemicals for which weight of evidence determinations have been completed					
Target					52
Actual					
Measure (E06) Number of HTP assays validated for use in prioritization, screening, or data replacement					
Target					8
Actual					

As noted in Section 3 (Program Organization), EDSP activities are currently supported by several EPA offices including all three offices within OCSPP (OSCP, OPP, OPPT), OW, ORD and OGC. Therefore, the development of performance measures and associated targets requires broad input. The EDSP organizational structure includes a *Policy Committee* with representation from the division level management of each office. The *Policy Committee*, or a workgroup under its direction, will continue to develop EDSP performance measures and associated targets during annual planning. To develop measures, the *Policy Committee* will work in consultation with the *Steering Committee*, and will also obtain feedback and approval from the *Management Council*.

### ***Resources Requirements***

The agency receives resources for the EDSP under appropriations for Environmental Programs and Management (EPM). The appropriated funds are allocated, primarily, to OCSPP, the Responsible Program Implementation Office (RPIO). Table 8 contains EDSP budget figures from the fiscal year 2014 Congressional Justification.

**Table 8: EDSP Budget – FY 2014 Congressional Justification**

	FY 2012 Actual	FY 2013 Annualized CR	FY 2014 President's Budget
Environmental Program and Management	\$6,807	\$8,358	\$6,891
Total Budget Authority / Obligations	\$6,807	\$8,358	\$6,891
Total Work Years	20.7	10.8	10.0

(Dollars in Thousands)

As noted previously, EDSP implementation activities are currently supported by several EPA offices, including all three offices within OCSPP, as well as OW. To ensure that resource needs are identified in a corporate manner, the EDSP organizational structure includes a *Steering Committee* with representation from each office. The *Steering Committee* will develop estimates of EDSP resource requirements so that senior management has sufficient information to consider program needs during planning and budget formulation.

In consultation with the *Policy Committee*, the *Steering Committee* will use project management tools to maintain a comprehensive list of EDSP activities and associated timelines and resource needs. The portfolio will cover a time horizon extending from the prior and current fiscal years (budget execution) to at least five years into the future of the program (formulation and planning). Consultations with the *Policy and Steering Committees* will ensure that resource decisions are reflected in setting and adjusting performance targets and in developing budget supporting fact sheets and narratives.

Though the resource requirements portfolio will capture a time horizon that extends to at least five years into the future of the EDSP, it is important to note that there will be considerable uncertainty with respect to activities and associated resource needs beyond the publicly released President's budget. The development of the longer-term portfolio is intended to provide general guidance, not to preempt the agency's annual planning and budgeting process. Detailed information from the portfolio will only be publicly released when appropriate to do so within the annual planning cycle.

Generally, over the next five years, the EDSP will continue to see a shift from traditional assay validation efforts to computational toxicology and high-throughput approaches supported by the EPA's Office of Research and Development (ORD) Endocrine Disruptors Research Program (EDRP). (See discussion in Section 5.) Concurrent with this decrease in resources for assay validation, the agency anticipates an increase in the proportion of EDSP resources devoted to issuing test orders, evaluating computational toxicology data and building interoperable informational databases.

## Budget and Spending

The EDSP *Steering Committee* will meet periodically (at least quarterly) to examine the distribution of available EDSP resources and the progress of program spending. In particular, the committee, in consultation with the *Policy Committee*, *Management Council* and Deputy Assistant Administrators, will examine whether adjustments to the distribution of available EDSP resources, both within and among offices, are necessary to address program priorities. The *Steering Committee* also will provide periodic budget updates to the *Management Council* and Deputy Assistant Administrators. These updates will be coordinated with the *Policy Committee*'s periodic updates on the overall status of program activities.

## Reporting Results

### *Annual Reporting*

The EPA's annual performance results are reported in two documents: the agency Financial Report (AFR) and the Annual Performance Report (APR). The AFR contains primarily financial information from agency databases and includes audited financial statements. The AFR also includes a Management Discussion and Analysis (MD&A) narrative highlighting major accomplishments and performance management issues and addresses other reporting requirements under the Federal Management and Financial Integrity Act (FMFIA). The APR presents detailed performance results as measured against targets developed during annual planning (e.g., see Table 7). The APR also summarizes program reviews conducted during the year.

For the EDSP, a major input for the AFR relates to the Program's characterization as a management challenge. Each year, the OIG provides a list of areas they consider to be key management challenges confronting the agency. In FY 2011, the OIG listed the EPA's Framework for Assessing and Managing Chemical Risks as a management challenge and, within this context, specifically highlighted the EDSP as follows:

*The EPA's framework for assessing and managing chemical risks from endocrine disruptors is also failing to show results. In August 1996, Congress passed both the Food Quality Protection Act and amendments to the Safe Drinking Water Act, calling for the screening and testing of chemicals and pesticides for possible endocrine-disrupting effects (i.e., adverse effects on the development of the brain and nervous system, the growth and function of the reproductive system, as well as the metabolism and blood-sugar levels). The EPA established the Endocrine*

*Disruption Screening Program in 1998. The Endocrine Disruption Screening Program was mandated to use validated methods for the screening and testing of chemicals to identify potential endocrine disruptors. In 2000, the EPA estimated that approximately 87,000 chemicals would need to be screened for potential endocrine-disrupting effects. As of February 25, 2010, the EPA issued test orders to industry for 67 pesticide active ingredients and high-production volume chemicals with some pesticide inert uses. Thus, 14 years after the passage of the Food Quality Protection Act and amendments to the Safe Drinking Water Act, the EPA has yet to regulate the endocrine-disrupting effects of any chemicals.*

As part of the AFR, the EPA provides a narrative discussion of each challenge that summarizes the issues and highlights key activities demonstrating how the agency is addressing the challenge and otherwise making progress within the program. The EDSP *Policy Committee*, or a workgroup under the committee's direction, will develop this narrative in consultation with the *Steering Committee*, and will obtain feedback and approval from the *Management Council*.

The major inputs for the APR are the performance results for each of the EDSP measures (see Table 7). This includes the numerical results for each measure and explanations and additional information as needed. The EDSP *Policy Committee* will develop these APR inputs in the same manner as described above for the AFR.

The APR also contains summaries of program reviews completed during the fiscal year. In fiscal year 2011, the APR included a summary of the OIG's evaluation of the EDSP. The EDSP *Policy Committee*, in consultation with the *Steering Committee* and the *Management Council* will determine whether any significant program reviews of the EDSP were completed during the year and will prepare summaries for the APR, as needed.

#### ***Annual Review***

Based on their evaluation of the EDSP, the OIG recommended that OCSPP conduct an annual review of the program.

*Annually review the EDSP program results, progress toward milestones, and achievement of performance measures, including explanations for any missed milestones or targets.*

In response, OCSPP has committed to conducting an annual review of the EDSP. The review process will be conducted internally, within OCSPP, and will be designed to ensure that proper management controls are in place so that progress and accountability within the EDSP can be determined.

The EDSP *Steering Committee* will lead the annual review of the EDSP and, in October of each year, will report findings to the *Management Council*, Deputy Assistant Administrators and Assistant Administrators. The specific timing of the presentation to senior management is anticipated to coincide with the development of final (or at least penultimate) program inputs for the AFR and APR.

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## **8. Cross-Agency EDSP Training Plans**

Training is an essential component to the continued improvement of the EDSP. The innovation, flexibility and dedication that are necessary to build a truly dynamic EDSP will come from well-trained and supported employees. A thoughtful and targeted training plan will be instituted to support three comprehensive goals:

1. Technical Endocrine Seminar Series: Supporting Cultural Changes within the EDSP  
*e.g., as the EDSP moves more towards the use of computational toxicology, staff will need not only to be trained in the use of new *in silico* tools, but also supported in terms of building their confidence with these tools.*
2. Technology Transfer: Retention of Institutional Knowledge  
*e.g., as staffing changes (retirement, promotion, etc.) occur, EDSP will use training as mechanism to ensure smooth transitions when facing these challenges.*
3. IT Training that Addresses the "Mechanics" of the EDSP  
*e.g., EDSP uses certain computer systems that are EDSP specific such as OPP's EDSP PRISM module. Staff will be trained on the Pesticide Registration Information System (PRISM) as well as tools such as ORD's Tox21, etc.*

The training plan will not only focus on information technology transfer with the EDSP but will deal with the process that allows expertise to be transferred across EPA offices and groups in order to facilitate evaluation of test results, make determinations of the potential for disrupting the endocrine system, and facilitate cross-organizational learning.

## **9. Appendices**

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### **Appendix A - Specific References for Risk Assessment Guidance**

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## Appendix B - List of Acronyms

AA	Assistant Administrator (EPA)
AFR	Agency Financial Report
APA	Administrative Procedures Act
APR	Annual Performance Report
CCL	Contaminant Candidate List
CDX	Central Data Exchange
CFR	Code of Federal Regulations
CR	Continuing Resolution
CSS	Chemical Safety for Sustainability
DCI	Data Call-In
DER	Data Evaluation Record
EDRP	Endocrine Disruptors Research Program
EDSP	Endocrine Disruptor Screening Program
EDSP21	Endocrine Disruptor Screening Program for the 21 <sup>st</sup> Century
EDSTAC	Endocrine Disruptor Screening and Testing Advisory Committee (pre-EDSP)
EDTA	Endocrine Disrupter [sic] Testing and Assessment [Committee] (OECD)
EPA	U.S. Environmental Protection Agency
EPM	Environmental Programs and Management
ER	Estrogen Receptor
FFDCA	Federal Food, Drug, and Cosmetic Act
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
FMFIA	Federal Management and Financial Integrity Act
FOIA	Freedom of Information Act
FQPA	Food Quality Protection Act (amended FFDCA and FIFRA)
FR	Federal Register
FY	Fiscal Year
HAC	House Appropriations Committee
IO	Immediate Office
IT	Information Technology
MD&A	Management Discussion and Analysis
NRDC	Natural Resources Defense Council
OCSPP	Office of Chemical Safety and Pollution Prevention (EPA)
OECD	Organisation for Economic Co-operation and Development
OGC	Office of General Counsel (EPA)
OIG	Office of the Inspector General (EPA)
OMB	Office of Management and Budget
OPP	Office of Pesticide Programs (in OCSPP)
OPPT	Office of Pollution Prevention and Toxics (in OCSPP)
ORD	Office of Research and Development (EPA)
OSCP	Office of Science Coordination and Policy (in OCSPP)
OSRI	Other Scientifically Relevant Information
OST	Office of Science & Technology (In OW)
OW	Office of Water (EPA)
PDF	Adobe® Portable Document Format
PRISM	Pesticide Registration Information System
QSAR	Quantitative Structure Activity Relationship
RCS	Regulatory Coordination Staff (in OCSPP)
RPIO	Responsible Program Implementation Office
SAB	Science Advisory Board (for EPA)
SAP	Scientific Advisory Panel (for OPP)
SDWA	Safe Drinking Water Act
Tox21	EPA Computational Toxicology Research Program - Toxicity Testing in the 21 <sup>st</sup> Century
TSCA	Toxic Substances Control Act
U.S.	United States
U.S.C.	United States Code
.xml	Extensible Markup Language

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## Appendix C - References

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