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

June 2012

This EDSP comprehensive management plan was developed for release in June 2012 to coincide with the EPA's internal planning process for FY 2014. This initial plan is intended to provide strategic guidance for the remainder of FY 2012 through FY 2017. The agency anticipates that this management plan will be a living document and will be evaluated for revision on an annual basis.

This comprehensive management 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 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 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

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."[1] 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."[2] 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."[3] 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."[4]

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[5] the EPA largely adopted the EDSTAC recommendations, and in an August 1998 Federal Register notice established the EDSP.[6] 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 to determine whether the chemical does interact with the endocrine system. 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 and establish a quantitative, dose-response relationship for any adverse effects that might result from the interactions with the endocrine system. EDSTAC also recommended that the EPA establish a priority-setting approach for choosing chemicals to undergo Tier 1 screening.

On April 15, 2009, the EPA announced the policies and procedures for initial EDSP screening[7] and the first list of chemicals to be screened, with the Tier 1 battery, for their potential to interact with the

[1] 21 U.S.C. § 346a(p)(1).
[2] 21 U.S.C. § 346a(p)(3)(B).
[3] 42 U.S.C. § 300j–17.
[4] 21 U.S.C. § 346a(p)(6).
[5] U.S. EPA, *Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC), Final Report*, August 1998.
[6] 63 Federal Register (FR) 42852-42855 (August 11, 1998), *Endocrine Disruptor Screening Program*.
[7] 74 FR 17560-17579 (April 15, 2009), *EDSP; Policies and Procedures for Initial Screening*.

endocrine system. This is known as Tier 1 screening.[8] 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 proposed second list of chemicals,[9] 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.

To enhance and improve the current efforts, the program must evolve 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 phases. The current phase focuses on creating 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, electronic submission of study data and electronic data reviews. Within the next five years, the EDSP plans to embrace new technology to enable a more efficient and effective chemical screening, testing, data entry, storage and review processes, with a focus on embracing new Tox21 tools. This will allow the agency to better optimize the ability to prioritize 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.[10]

Executive Summary: Comprehensive Management Plan

This EDSP comprehensive management plan is intended to provide strategic guidance for the remainder of FY 2012 and through FY 2017. The agency anticipates that this management plan will be a living document. It will be evaluated on an annual basis for necessary revisions to reflect adjustments to program priorities and resources and to shift the time horizon. The plan will always cover the current fiscal year (FY) plus five years into the future of the program. Any future revisions of this plan will be released to coincide with the annual review process and for temporal alignment with the agency's fiscal year planning and budgeting cycle. It is important to note that, although this overarching, management plan document will be evaluated on an annual basis; certain elements of 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.

[8] 74 FR 17579-17585 (April 15, 2009), *Final List of Initial Pesticide Active Ingredients and Pesticide Inert Ingredients to be Screened under the FFDCA*.
[9] 75 FR 70248-70254 (November 17, 2010), *EDSP, Second List of Chemicals for Tier 1 Screening*.
[10] 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

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 the 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 within 2012 and 2017

Between 2012 and 2017, the agency will be actively engaged in implementation, which will proceed with the scientifically rigorous technical review of all Tier 1 assay results from the chemicals that received EDSP Tier 1 orders, and review of that collective data. This analysis will be focused on the performance of each assay and the performance of the combined Tier 1 battery. The review of a subset of chemicals for the functionality of each assay and the battery as a whole will be submitted for Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) Scientific Advisory Panel (SAP) review in FY 2013. In parallel with these Tier 1 activities, the agency will continue its scientific validation of Tier 2 assays for inter-laboratory reproducibility, reliability and transferability with the development of integrated summary reports for each assay, respectively. These Tier 2 validation efforts will be submitted for FIFRA SAP review in FY 2013 to coincide with the Tier 1 weight of evidence determinations that may warrant the need for further Tier 2 testing which will necessitate Tier 2 test order issuance, which is anticipated to initiate in FY 2013.

In addition to the review of Tier 1 data and completion of regulatory determinations for whether additional testing is warranted, the agency anticipates finalizing the second list of chemicals for Tier 1 screening in FY 2013. The corresponding policies and procedures will also be completed at that time. Additional test orders for the second list of chemicals will be issued, incrementally over a three-year period.

After issuance of the List 2 test orders, the agency anticipates that all associated activities will be completed (e.g., two years for data generation, and one year for data review and weight of evidence determinations).

Table 1 briefly summarizes many of the targeted goals with corresponding targeted completion dates.

Table 1: EDSP Management Plan – Milestones by Fiscal Year

Fiscal Year	EDSP Activity	Period of Activity
2013	Develop Data Evaluation Record Composers (.xml) for all Tier 1 assays and Data Management Capture Tools	2013-2014
2013	Tier 2 Inter-laboratory Validation External FIFRA SAP Peer Review and development of standard evaluation procedures	2013-2014
2013	FIFRA SAP External Peer Review of Re-evaluation of Tier 1 battery and weight of evidence determinations (several FIFRA SAPs)	2013-2014

Fiscal Year	EDSP Activity	Period of Activity
2013	Issuance of List 2 Chemicals, Tier 1 test orders and review of Other Scientifically relevant Information	2013-2016
2014	Completion of List 1 Chemicals, Tier 1 assay scientific data reviews, data evaluation records (DERs) and weight of evidence decisions	2014
2014	Issuance of List 1 Chemicals, Tier 2 test orders and review of other Scientifically relevant information	2014-2015
2015	Data Review List 2 Chemicals, Tier 1 assay scientific data reviews, data evaluation records (DERs) and weight of evidence decisions	2015-2018
2016	Completion of List 1 Chemicals, Tier 2 assay scientific data reviews, data evaluation records.	2016-2018

2. Scope of the Document

The EDSP management plan will describe how the agency intends to continue implementation of the EDSP in three major parts:

1) Scientific Advancement of Tier 1 data reviews and Tier 2 assay development and validation including advancing the state of the science in chemical priority setting and screening,
2) Test Order Management and Implementation: including prioritizing chemicals, developing policies and procedures, and issuing and managing test orders, and
3) Data Management by developing an enhanced and consolidated information infrastructure.

In the immediate future, the agency will focus on the scientific review of Tier 1 battery results, and development of weight of evidence determinations for the first list of chemicals. This includes an overall review of the performance of each assay and the entire battery. It is the agency's intention to submit the weight of evidence reviews and assay by assay review and battery performance reviews to the FIFRA SAP for external peer review.

Beyond the Tier 1 screening assays, the Tier 2 assays are critical to identifying and establishing a dose-response relationship for any adverse effects from the interactions identified through the Tier 1 screening assays. These Tier 2 assays are expected to include multiple generation reproduction studies in laboratory rats, fish, amphibians and birds. While the multi-generation reproduction study and extended one-generation study in rats are validated, the intra- and inter-laboratory validations of the remaining four species (e.g., fish, frog, bird and invertebrate) will be completed for several chemicals. Additionally, external scientific peer review of the inter-laboratory testing results will also be completed.

Scientific advancement of EDSP also relies upon incorporating advanced, 21st century tools. The EDSP21 Work Plan includes efforts to integrate computational or *in silico* models and molecular-based *in vitro* high-throughput screening assays for prioritizing chemicals for Tier 1 screening. It sets forth a plan for the incremental transition to incorporate computational or *in silico* models and molecular-based *in vitro* high-throughput screening assays into Tier 1 screening to replace current *in vitro* assays including their validation.[11] This EDSP21 Work Plan sets the initial stages for incorporating the advancements of scientific methodologies into the EDSP that eventually will result in improved efficiency, fewer animals being tested, less resource demand and higher throughput in Tier 1 screening

[11] 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

assays results.[12] This workplan is also a key component of advancing the goals in the President's proposed fiscal year 2012 budget, "In FY2012 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."[13]

In addition to scientific advancements, this management plan summarizes how existing and procedures will be applied to prioritize chemicals for Tier 1 assay screening. Implementation will include, issuance of FFDCA 408(p) and/or SDWA screening and testing orders, establishing the policies and procedures by which test orders are sent to importers and manufacturers and joint data development, cost sharing, data compensation and data protection, managing the test orders, managing the data submitted in response to the test orders, evaluating the Tier 1 assay results and reaching weight of evidence conclusions to determine whether Tier 2 data are warranted.

The EDSP consolidated information infrastructure focuses on developing 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.

This management plan also describes the resources required for successful achievement of the goal targeted for 2012-2017. These resources include scientific expertise, information technology and financial resources. Moreover, considering the many steps and complex challenges ahead, it is increasingly important to ensure seamless coordination and communication between partnering offices within the agency. To that end, the EDSP has developed 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 can 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.

[12] The initial work to initiate the use of computational tools for priority setting is within the scope, however full Tier 1 assay replacement will not be completed within the five-year time frame (by FY 2017) of the management plan.
[13] 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

Figure 1: Organizational Structure for EDSP Development and Implementation

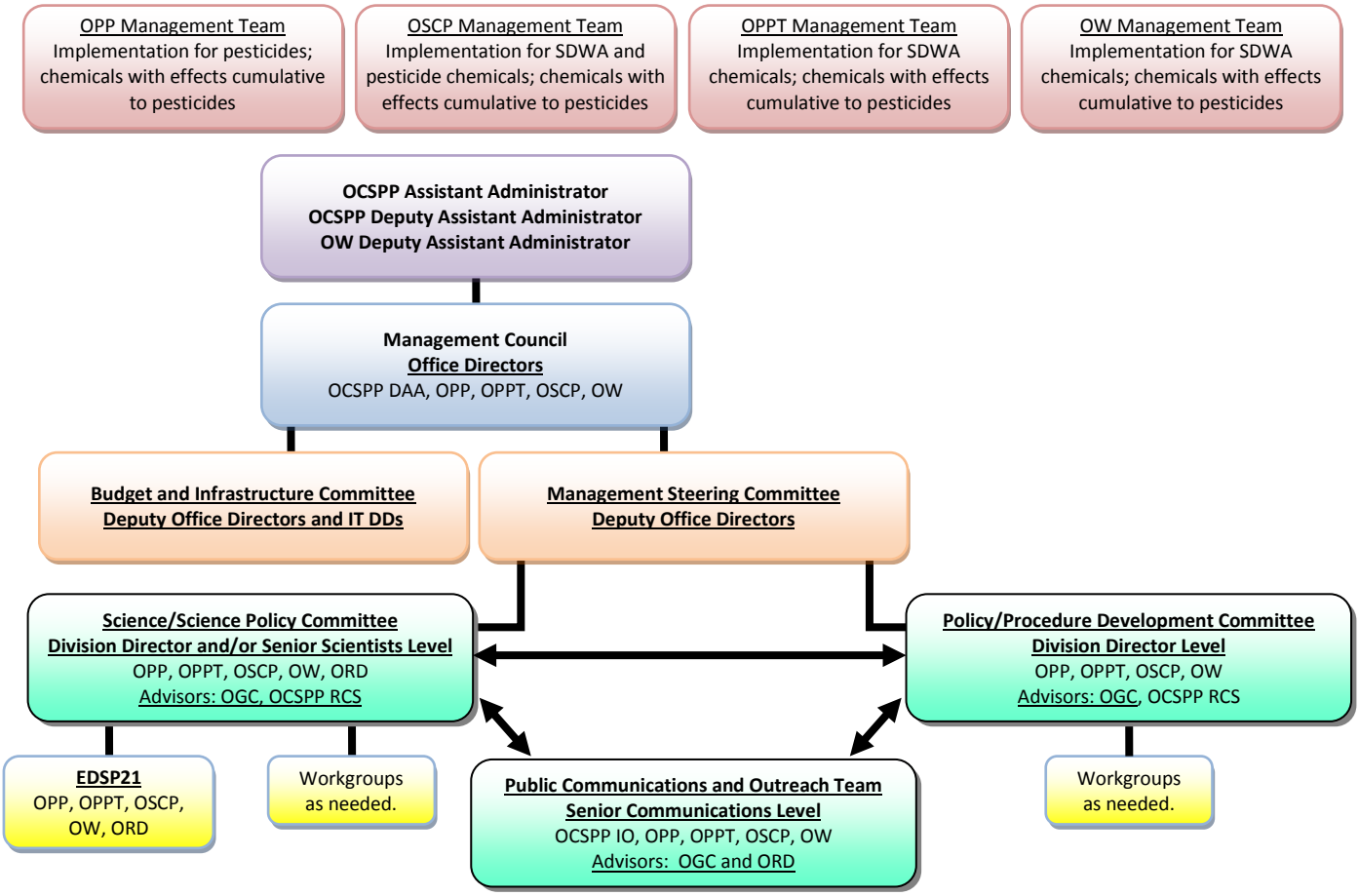


Table 2: EDSP Committees

Committee	Targeted Mission	Committee Membership
Management Council	Overall EDSP Management Decisions	OCSPP DAA and Office Directors from OW, OPP, OPPT and OSCP
Management Steering Committee	Provides management oversight of the science, policy and budgetary issues	Deputy Office Directors from OW, OPPT, OPP and OSCP. OGC and ORD may participate if necessary.
Budget and Infrastructure Committee	Provides fiscal management oversight and ensures budgetary allocations and IT resources are targeted towards full optimization to achieve EDSP programmatic goals.	Deputy Office Directors on Budget and IT Division Directors from OW, OPPT, OPP and OSCP.
Science/Science Policy Committee	Develop scientific methodologies 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 if necessary.
Policy/Procedure Development 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, and ICRs.	Risk Management Division Directors from OW, OPPT, OPP and OSCP. RCS and OGC participation if needed.
Public Communications and Outreach 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 and OW. OGC and ORD will provide advice as 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 show how the management structure operates, the following examples are provided. If a complex scientific issue arises when evaluating OSRI or the Tier 1 and Tier 2 assay data, the issue would be brought before the Science/Science Policy Committee for deliberation and determination. Committee recommendations would be elevated to the Management Steering Committee for final determination and if warranted, the Management 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 Public Communications and Outreach 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 provide better coordination among the decision makers, it is neither intended to be rigid nor to restrict communications that may occur outside of its structure.

Task-specific, temporary workgroups will continue to form to address task-focused efforts; these workgroups will brief the relevant committees for formalization or approval to proceed. In addition, as the process moves forward, the agency will implement an adaptive management approach by ensuring process efficiencies by either streamlining the process and/or merging committees to optimize resources.

Communication and Coordination Process

This section describes the plans for EDSP's overall communication and coordination procedures.

Strategy

A communication strategy plan has been developed for two distinct types of communication:

1. Event-Driven Communication
   - To communicate activities that are event-driven or irregular
2. Ongoing Communication
   - Internal Coordination Plan: How we communicate within the EPA to our colleagues in other offices and regions
   - External Communication Plan: How we communicate externally to other executive branch agencies, other branches of the federal government, the regulated community, other EDSP stakeholders and the public. This would contain a plan for developing proactive outreach efforts including those to other stakeholders.

The Public Communications and Outreach Team will track 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:

- Congressional Inquiries
- Congressional Reports
- Court-ordered Reports
- Internal EPA Reports
- Questions from EDSP Order Recipients
- Freedom of Information Act (FOIA) Requests
- Questions from the Public

Some of the recurring reporting requirements appear in table 3:

Table 3: Examples of Recurring Reporting Requirements

Report Origin	General Description	Schedule
Congressional Reporting Requirements		
HAC 110-187 pp. 108-109.[14]	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.[15]	Information regarding the use of 21st century tools and other scientifically relevant information (OSRI) within the EDSP (requires coordination with ORD).	Semi-Annual
Other Reporting Requirements		
NRDC et al. v. Whitman, No. C-99-03701 WHA (Northern District of California) – Settlement Agreement	Information regarding EDSP assay development and validation.	Semi-Annual (June and December)
OMB	Information regarding EDSP assay development and validation.	Quarterly

Coordination Procedures

The EDSP requires coordination across several offices. 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 will be used:

- An EDSP intranet site to provide consistent and up-to-date information to EPA personnel working on the EDSP.[16]
- Committee chairs will meet at least once a month to discuss issues that cross between several areas. This will promote efficiency and coordination on issues that overlap science, policy, communication and infrastructure.
- Decisions made by committees, the Management 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.

[14] U.S. Congress, House Appropriations Committee Report 110-187, pp. 108-109. http://www.gpo.gov/fdsys/pkg/CRPT-110hrpt187/pdf/CRPT-110hrpt187.pdf
[15] U.S. Congress, House Appropriations Committee Report 112-151, p. 72. http://www.gpo.gov/fdsys/pkg/CRPT-112hrpt151/pdf/CRPT-112hrpt151.pdf
[16] U.S. EPA, Environmental Science Connector, EDSP Project. http://ofmpub.epa.gov/portal/page/portal/ESConnector/CNTR_ESC/ESCHOME

Roles and Responsibilities

The EDSP is developed and implemented by the following three offices within the Office of Chemical Safety and Pollution Prevention: the Office of Science Coordination and Policy (OSCP); the Office of Pesticide Programs (OPP); and the Office of Pollution Prevention and Toxics (OPPT), and the Office of Water (OW) with support from the Office of Research and Development (ORD) and the Office of General Council (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 the development, implementation and execution of the EDSP.

Table 4: Roles and Responsibilities

Lead	Activity	Support
OSCP	Tier 2 assay –development/validation, peer review, regulatory implementation	OPP, OPPT and ORD
	EDSP21 Work Plan Implementation	OPP, OPPT, OW and ORD
	Coordination, communication and website	All
	Information Collection Request (ICR) Development	OPP, OGC, OCSPP IO (RCS)
	Re-evaluation of the Tier 1 Battery Performance	OPP and ORD
OPPT	Policy and procedures for SDWA/FFDCA	OW, OGC, OCSPP IO (RCS)
	Order Issuance and management of SDWA chemicals	OPP
OPPT/ OW Team	Data Review and addressing technical questions (OSRI, Tier 1 and Tier 2) for SDWA chemicals	OPP, OSCP, ORD
OPP	Order issuance and management of pesticides active ingredients; pesticide inerts not found in water	OSCP
	Data review (OSRI, Tier 1, Tier 2) of pesticide active ingredients; pesticide inerts not found in water	OSCP, ORD
	Technical questions for List 1 chemicals	ORD, OSCP
	Weight of evidence and regulatory decisions List 1 chemicals	ORD, OSCP
OW	Makes finding under SDWA identifying chemicals to receive FFDCA/SDWA orders	ORD, OPPT, OPP, OGC

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. They also describe how the EPA intends to:

- Minimize duplicative testing.
- Promote fair and equitable sharing of test costs.
- Address 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 FFDCA section 408(p) test orders, including procedures for challenging the orders.
- Ensure compliance with FFDCA section 408(p) Tier 1 orders.

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 FFDCA section 408(p)(5) and as authorized under section 1457 of SDWA.

Over the next five years, the agency expects to:

- Revise the 2009 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 List 2 chemicals.
- Review Tier 1 data for the initial list of chemicals and perform weight of evidence determinations and review of the Tier 1 assay batter for overall performance.
- Finalize List 2 Chemical Lists, and the policies and procedures as they apply to the drinking water chemicals authorized by SDWA prior to issuance of the test orders for List 2 chemicals.
- Incorporate technological advancements in science and risk assessment methodologies as they may apply to the policies and procedures (e.g., EDSP 21 Work Plan[17]).
- 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

The overall EDSP technical process involves:

a) Universe of chemicals for prioritization and use of computational tools for future chemical prioritization
b) Issuance of test orders for the Tier 1 screening assays,
c) Review of Tier 1 assay data review,
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,
e) Issuance of test orders for Tier 2 assays and completion of hazard 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 chemicals under the EDSP. In addition, the agency believes this characterization of the universe addresses such factors as public nominations and exposure considerations. Additional information will be provided in a supplemental document, "Endocrine Chemical Prioritization" that may be found on http://www.epa.gov/endo/pubs/prioritysetting/index.htm.

As new 21st century computational toxicology methodologies become available, the universe of chemicals may be analyzed and prescreened using a suite of high-throughput system assays and computer-based expert systems (e.g. QSAR models). During this initial or prescreening phase, chemicals identified using a combination of these computational models and a consideration of exposure will be prioritized for the issuance of test orders under the current Tier 1 screening battery. 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*

[17] 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

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 *in vivo* data to fully replace the current EDSP Tier 1 screening battery, so that animal-based testing is eliminated or greatly reduced.

New methods developed or considered for replacement of the current Tier 1 set of screening assays will go through a validation process to confirm the new methods are fit for that purpose. This is an important component of this overall effort and is consistent with the language in FFDCA, which is discussed in more detail below. It is likely a new validation framework would need to be developed to rapidly evaluate the new high-throughput methods and computer models. This new framework would be evaluated by the FIFRA SAP and the FIFRA SAP process will also provide an opportunity for public comment.

In addition to the use of computational tools for chemical prioritization, the agency will also ensure that all resources are optimized by temporally aligning EDSP with currently scheduled reviews, 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 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.

Additional information on the chemical prioritization for EDSP will be provided in a supplemental document, "Endocrine Chemical Prioritization."[18]

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 and to date, Tier 1 assay data information are being submitted to the agency for technical review. The agency anticipates data will be incrementally submitted to the agency for evaluation.

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 plans to conduct a mid-course review of the functionality of each

[18] U.S. EPA, Endocrine Disruptor Screening Program (EDSP) [Home Page]. http://www.epa.gov/endo/

assay and the battery as a whole. These performance evaluations of the Tier 1 battery will be conducted on an adequate sample of chemicals and it is further anticipated that these Tier 1 performance review results will be submitted for external scientific peer review by the FIFRA SAP in fiscal year 2013, pending the availability of complete Tier 1 assay data sets for a sufficient and representative number of chemicals.

d) Develop Weight of Evidence Determination

After the Tier 1 assay reviews have been completed, 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 available information, and additional data submitted under 40 CFR part 158 and available for the weight of evidence evaluation.[19]

e) Issuance of Tier 2 Assay Test Orders

When a weight of evidence determination for a chemical has been made that there is a potential for endocrine interaction based on current available data, and if additional data are warranted, 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 management decisions.

Chemicals that are ultimately selected to undergo Tier 2 testing will be evaluated, after completion of the selected Tier 2 or more targeted tests, 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 8, Appendix A).

The current Tier 2 studies include complex multiple generation studies in Sprague Dawley rats, Medaka, Xenopus Laevis, Japanese Quail and Mysid. Four of the five multiple generation studies are undergoing inter-laboratory validation testing across three independent contract laboratories. During this intense inter-laboratory validation phase, the agency will be focused on determining whether there are opportunities to streamline these studies from a two-generation to a one-generation study, similar to the determination made for the mammalian two-generation reproduction study to an extended one-generation reproduction study. This decision would 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. Once completed, all four assays will undergo external scientific peer review through the FIFRA SAP for measure of performance, reproducibility and reliability. Additional documents such as the integrated summary reports, test guidelines and scientific evaluation procedures will also be made available.

Endocrine Disruption Screening Program Toxicology in 21st Century Work Plan

The pesticide active ingredient library has been prioritized for the EDSP as described above, with the goal of following the pesticide registration review schedule. The non-active, or inert, ingredient library will be analyzed using a suite of high-throughput assays. Expert computer-based models such as QSAR

[19] 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

can be used as a prescreen tool. For example, the agency has developed and peer-reviewed a chemical prioritization approach for pesticide inert ingredients and antimicrobial pesticide active ingredients using an expert system/QSAR model for estrogen receptor (ER) binding and gene activation. Work is ongoing to expand this ER binding predictive model to other chemicals as well as to develop expert systems/QSAR models for the androgen receptor binding and thyroid pathways.

During the initial or prescreening phase, chemicals that have been identified using a combination of computational models as well as exposure considerations will be prioritized for the issuance of test orders under the current Tier 1 screening battery. 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, the results of certain *in vivo* Tier 1 screening assays could 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 *in vivo* data to fully replace the current EDSP Tier 1 screening battery so that animal-based testing is eliminated or greatly reduced.

New methods developed or considered for replacement of the current Tier 1 set of screening assays will go through a validation process to confirm the new methods are fit for that purpose. This is an important component of this overall effort and consistent with the language in Food Quality Protection Act (FQPA). It is likely a new validation framework will need to be developed to rapidly evaluate the new high-throughput methods and computer models. This new framework will be evaluated by the FIFRA SAP before implementation.

Advances in Science and Technology (EDSP21)

> 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."[20]

Recognizing the need for a more comprehensive review of new, state-of-the-science and emerging technologies for toxicity testing, 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 21st Century: A Vision and Strategy*[21] (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. To this end, the EPA's National Center for Computational Toxicology has developed *in silico* models for predicting quantitative physiochemical relationships and high-throughput *in vitro* assays as methods for quickly and efficiently assessing the adverse outcome potential of chemical targets.

The EDSP has a vested interest in using these methods for screening and hazard identification of chemicals for potential endocrine interactions. A plan for how the agency will incorporate computational

[20] 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
[21] 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

toxicological tools into the Endocrine Screening Program is described more specifically within the *Endocrine Disruptors Screening Program for the 21st Century: (EDSP21 Work Plan)*,[22] issued on September 30, 2011.

The EDSP21 Work Plan proposes a multi-level and integrated approach to determine whether a chemical has the potential to interact with the endocrine system in incremental stages. The first stage relies on computational methods to prioritize chemicals for screening. The second phase involves replacing current validated *in vitro* screening assays with validated *in vitro* high-throughput assays, using results to inform and target current *in vivo* endocrine assays, and, where possible, to reduce the use of whole animal toxicity tests. The third phase is to replace the current Tier 1 screening assays by incorporating advances in computational modeling and molecular biology, our understanding of endocrine-specific pathways, and use of robotics for conducting rapid assays on hundreds of chemicals.

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. Three 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. This will include definition of the "validation" process for the methodology in the context of how it will be used or applied (e.g., chemical prioritization versus *in vivo* replacement). The legislative directive of FFDCA indicated that the agency should use "validated test systems." Thus a validation approach of the new methodologies will be necessary to assess the reliability or validity of priority setting and, ultimately, to determine which tools can replace current, validated Tier 1 screening assays.
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 cataloged and 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.

The overall EDSP21 effort will be coordinated by OSCP with the agency's computational toxicology and programmatic technical expertise focused on three main areas: assay and model validation, high-throughput assay evaluation and *in silico* or expert computer-based model evaluation.

EDSP21 Validation and Implementation Workgroup

An EDSP21 Workgroup will be formed with senior level scientists with appropriate expertise across the relevant program offices and the agency's ORD to manage the development of the confidence-building processes. This will enable the incremental use of *in silico* models and high-throughput *in vitro* assays for prioritization and screening purposes, in the EDSP. The workgroup will also ensure that there is cross-agency and international interaction through the Tox21 effort and Global and International

[22] 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

coordination with the Organisation for Economic Co-operation and Development (OECD), Endocrine Disruptor Testing and Assessment (EDTA) Committee as well.

5. Consolidated Information Technology (IT) Infrastructure

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 reporting, 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 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*,[23] 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 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

[23] U.S. EPA, *Improving Our Regulations: Final Plan for Periodic Retrospective Reviews of Existing Regulations*, August 2011. http://www.epa.gov/regdarrt/retrospective/documents/eparetroreviewplan-aug2011.pdf

various agency 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. The agency will use the EDSP DER database for analyzing the performance of Tier 1 and Tier 2 assays. 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 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) 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.

6. 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 2: EPA Budget, Planning and Results Cycle

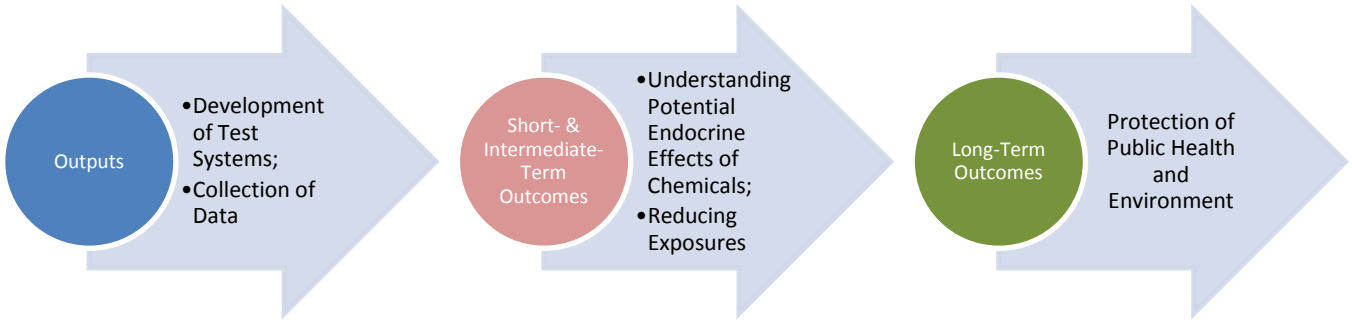
Strategic Planning

The strategic objectives of the EDSP are defined by statute in the FFDCA[24] and the SDWA[25] 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.

[24] 21 U.S.C. § 346p.
[25] 42 U.S.C. § 300j-17.

Figure 3: Conceptual Model for Performance Measures



For the Fiscal Year 2011 - 2015 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:

Goal 4: Ensuring the Safety of Chemicals and Preventing Pollution

Objective 4.1: Ensure Chemical Safety

Strategic Measure:

By 2015, complete endocrine disruptor screening program (EDSP) decisions for 100 percent of chemicals for which complete EDSP information is expected to be available by the end of 2014.

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 Management Steering Committee and the Budget and Infrastructure 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.

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.

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.

Table 5: Planning and Budgeting Process

	Phase	FY 2014 Planning	FY 2013 Budget Formulation	FY 2012 Budget Execution	
2011	Oct		OMB Hearings	Spending	Appropriations bill or CR Enacted
2011	Nov		OMB Passback	Spending	Enacted Operating Plan Developed
2011	Dec		EPA Appeals and Resolution	Spending	
2012	Jan		Budget Request to Congress Developed	Spending	Monitoring and Accounting
2012	Feb		Budget Submitted to Congress	Spending	Monitoring and Accounting
2012	Mar		Congressional Hearings	Spending	Monitoring and Accounting
2012	Apr	EPA Internal Planning Process	Congressional Hearings	Spending	Monitoring and Accounting
2012	May	EPA Internal Planning Process	Congressional Hearings	Spending	Monitoring and Accounting
2012	Jun	EPA Internal Budget Process	Congressional Mark-ups	Spending	Sweeps and Close-out
2012	Jul	EPA Budget Forum	Congressional Mark-ups	Spending	Sweeps and Close-out
2012	Aug	Administrator's Passback	Congressional Mark-ups	Spending	Sweeps and Close-out
2012	Sep	EPA Budget Submission to OMB	Congress Passes Budget / CR	Spending	Sweeps and Close-out

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. The measures and their current performance results and targets are listed in the table 6 below.

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.

Table 6: Current EDSP Performance Measures

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

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/Procedure Development Committee with representation from the division level management of each office. The Policy/Procedure Development Committee, or a workgroup under its direction, will develop EDSP performance measures and associated targets during annual planning. To develop measures, the Policy/Procedure Development Committee will work in

consultation with the Budget and Infrastructure Committee and the Management Steering Committee, and will also obtain feedback and approval from the Management Council.

In fiscal year 2012, while planning for fiscal year 2014, the Policy/Procedure Development Committee will address 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 7 (below). The Policy/Procedure Development Committee will need to evaluate existing performance measures (generally focused on outputs) and determine what revisions and additional measures may be needed. In addition, the committee will need to explore whether additional outcome performance measures can 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 7: OIG Guidance Regarding Performance Measures

Key performance measurement terms and definitions [26]	
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

In developing additional performance measures for the EDSP, the Policy/Procedure Development Committee will need to consider 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."[27] 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.

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 2013 Congressional Justification.

[26] 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
[27] 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

Table 8: EDSP Budget – FY 2013 Congressional Justification

	FY 2011 Actual	FY 2012 Enacted	FY 2013 President's Budget
Environmental Program and Management	$9,624.6	$8,255.0	$7,238.0
Total Budget Authority / Obligations	$9,624.6	$8,255.0	$7,238.0
Total Work Years	14.9	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 Budget and Infrastructure Committee with representation from each office. The Budget and Infrastructure Committee will develop estimates of EDSP resources requirements so that senior management has sufficient information to consider program needs during planning and budget formulation.

In consultation with the Management Steering Committee and the Policy/Procedure Development Committee, the Budget and Infrastructure 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/Procedure Development and Management Committees also 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 cover 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 decrease in the proportion of resources expended on assay validation efforts with the shift in focus 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 below.) Concurrent with this decrease in resources devoted to assay validation, the agency anticipates an increase in the proportion of EDSP resources devoted to issuing test orders and evaluating data.

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 and 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 21st Century will require an integrative approach among basic 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.

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/Science Policy 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.

Budget and Spending

The EDSP Budget and Infrastructure 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/Procedure 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 Budget and Infrastructure Committee also will provide periodic budget updates to the Management Council and Deputy Assistant Administrators. These updates will be coordinated with the Policy/Procedure Development 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 6). 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/Procedures Development Committee, or a workgroup under the committee's direction, will develop this narrative in consultation with the Budget and Infrastructure 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 6). This includes the numerical results for each measure and explanations and additional information as needed. The EDSP Policy/Procedures Development 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/Procedures Development Committee, in consultation with the Budget and Infrastructure 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 Budget and Infrastructure and Management Steering Committees will jointly 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.

7. 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. 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. 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. 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.

8. Appendices

Appendix A - Specific References for Risk Assessment Guidance

U.S. EPA, *Guidelines for Reproductive Toxicity Risk Assessment*, October 31, 1996. EPA/630/R-96/009. National Center for Environmental Assessment, Office of Research & Development, Washington, DC, 61 FR 56273. http://www.epa.gov/raf/publications/pdfs/REPRO51.PDF

U.S. EPA, *Assessment of Thyroid Follicular Cell Tumors*, March 1998. EPA/630/R-97/002. National Center for Environmental Assessment, Office of Research & Development, Washington, DC. http://www.epa.gov/raf/publications/pdfs/THYROID.PDF

U.S. EPA, *Science Policy Council Handbook: Risk Characterization*, December 2000. EPA 100-B-00-002. Science Policy Council, Office of Research and Development, Washington, DC. http://www.epa.gov/ORD/spc/rchandbk.pdf

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 21st 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 21st Century
TSCA	Toxic Substances Control Act
U.S.	United States
U.S.C.	United States Code
.xml	Extensible Markup Language

Appendix C - References

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