Contact: Lance J Rakovan 301–415–2589.

Revision to FR Notice Published 09/08/2023; Extending the Comment Period from 10/23/2023 to 11/07/2023.

EIS No. 20230116, Draft Supplement, BLM, USFWS, AK, Coastal Plain Oil and Gas Leasing Program, Comment Period Ends: 11/07/2023, Contact: Serena Sweet 907–271–4543.

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Dated: October 23, 2023.

Nancy Abrams,

Associate Director, Office of Federal Activities.

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ENVIRONMENTAL PROTECTION AGENCY

[EPA–HQ–OPP–2023–0474; FRL–11384–01–OCSPP]

Endocrine Disruptor Screening Program (EDSP); Near-Term Strategies for Implementation; Notice of Availability and Request for Comment

AGENCY: Environmental Protection Agency (EPA).

ACTION: Notice.

SUMMARY: The Environmental Protection Agency (EPA) is announcing the availability of and soliciting comment on the near-term strategies described in this document to help the Agency meet its obligations and commitments under the Federal Food, Drug, and Cosmetic Act (FFDCA), which requires, among other things, that EPA screen for and protect against endocrine disrupting effects in humans. An important part of these obligations and commitments is the Endocrine Disruptor Screening Program (EDSP), which EPA established in 1998 as a two-tier endocrine screening and testing process for pesticides and other chemicals. After over two decades of implementing the EDSP and other aspects of the mandate in FFDCA, EPA has developed near-term strategies to begin addressing the challenges it has encountered and to rebuild the EDSP. This document covers only the initial strategies that EPA is taking over the next several years to generate momentum toward its longer-term goal of timely addressing all its endocrine screening data needs and decisions. Through this notice and to help implement its strategies, EPA is also seeking additional endocrine data on two groups of active ingredients currently undergoing registration review, or explanations of why the additional data are unnecessary for EPA to make its FIFRA and FFDCA decisions.

DATES: Comments must be received on or before December 26, 2023.

ADDRESSES: Submit your comments, identified by docket identification (ID) number EPA–HQ–OPP–2023–0474, using the Federal eRulemaking Portal at *https://www.regulations.gov.* Follow the online instructions for submitting comments. Do not submit electronically any information you consider to be Confidential Business Information (CBI) or other information whose disclosure is restricted by statute. Additional instructions on commenting or visiting the docket, along with more information about dockets generally, is available at *https://www.epa.gov/.*

FOR FURTHER INFORMATION CONTACT: Catherine Aubee, Endocrine Disruptor Screening Program (7505T), Office of Pesticide Programs, Environmental Protection Agency, 1200 Pennsylvania Ave. NW, Washington, DC 20460–0001; main telephone number: (202) 566–1030; email address: *pesticidequestions@epa.gov.*

SUPPLEMENTARY INFORMATION:

I. Executive Summary

A. Does this action apply to me?

You may be potentially affected by this action if you produce, manufacture, use, or import pesticide/agricultural chemicals and other chemical substances; or if you are or may otherwise be involved in the testing of chemical substances for potential endocrine effects. Potentially affected entities, identified by the North American Industrial Classification System (NAICS) codes, may include, but are not limited to:

- Chemical manufacturers, importers and processors (NAICS code 325), *e.g.,* persons who manufacture, import or process chemical substances.
- Pesticide, fertilizer, and other agricultural chemical manufacturing (NAICS code 3253), *e.g.,* persons who manufacture, import or process pesticide, fertilizer and agricultural chemicals.
- Scientific research (NAICS code 5417).

B. What is the Agency's authority for taking this action?

FFDCA section 408(p)(1) requires, among other things, that EPA ''develop a screening program, using appropriate validated test systems and other scientifically relevant information 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 effects as [EPA] may designate.'' (21 U.S.C. 346a(p)). FFDCA sections 408(p)(2) and (p)(7) require EPA to implement the EDSP by August 1999 and report to Congress on the program's progress by August 2000, respectively.

FFDCA section 408(p)(3) requires that EPA ''shall provide for the testing of all pesticide chemicals.'' FFDCA section 201 defines ''pesticide chemical'' as ''any substance that is a pesticide within the meaning of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), including all active and pesticide inert ingredients of such pesticide.'' (21 U.S.C. 231(q)(1)). However, FFDCA section 408(p)(4) authorizes EPA to, by order, exempt a substance from the EDSP if the EPA ''determines that the substance is anticipated not to produce any effect in humans similar to an effect produced by a naturally occurring estrogen.'' FFDCA section 408(p)(5) identifies the requirements and processes for issuing test orders, requiring testing under the EDSP, and submitting information obtained from the testing to EPA. (21 U.S.C. 346a(p)(5)). Finally, FFDCA section 408(p)(6) requires EPA to ''as appropriate, take action under such statutory authority as is available to the Administrator, including consideration under other sections of this chapter, as is necessary to ensure the protection of public health'' for ''any substance that is found, as a result of testing and evaluation under this section, to have an endocrine effect on humans.''

The Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) precludes the distribution and sale of any pesticide that is not registered under FIFRA. (7 U.S.C. 136a(a)). Applications for registration of a pesticide may be submitted to EPA but must meet the requirements in FIFRA sections 3(c) and 33, which include providing complete data in support of that registration request. (7 U.S.C. 136a and 136w-8). The data required to support these applications are identified in EPA regulations at 40 CFR part 158. EPA may issue Data Call-In (DCI) notices under FIFRA section 3(c)(2)(B) to require additional data during the registration process to address a risk or after registration to maintain a registered pesticide. (7 U.S.C. 136a(c)(2)(B)). To grant a pesticide registration, FIFRA requires EPA to consider whether the pesticide has ''unreasonable adverse effects'' to human health and the environment. (7 U.S.C. 136a(c)(5)). FIFRA section 2(bb) defines ''unreasonable adverse effects on the

environment'' to mean, among other things, ''any unreasonable risk to man or the environment, taking into account the economic, social, and environmental costs and benefits of the use of any pesticide.'' (7 U.S.C. 136(bb)). EPA is required to review each pesticide registration every 15 years to determine whether the pesticide continues to satisfy this FIFRA standard for registration. (7 U.S.C. 136a(g)). EPA regulations at 40 CFR part 155, subpart C apply to the conduct of this registration review process.

C. What action is the Agency taking?

This document describes three near-term strategies the Agency is taking to further implement its obligations and commitments under FFDCA section 408(p) relating to the EDSP, which EPA established in 1998 as a two-tier endocrine screening and testing process for pesticides and other chemicals. EPA is pursuing these strategies to generate momentum toward its longer-term goal of timely addressing all its endocrine data needs and decisions.

Under strategy one, EPA will prioritize addressing potential human estrogen, androgen, and thyroid effects for conventional pesticide active ingredients. Although the Agency will continue to address wildlife endocrine effects and endocrine effects from other pesticide chemicals (*e.g.,* inert ingredients and active ingredients intended solely for biological or antimicrobial uses), updates and activities relating to that work are on a longer-term timeline for the reasons discussed in the strategy. Under strategy two, EPA will use existing data, routinely obtained through FIFRA registration and registration review, to determine whether additional human health-related endocrine data are needed and to make endocrine decisions under FIFRA and FFDCA section 408(p). This strategy also describes the endocrine data that EPA considers sufficient to register a new conventional active ingredient and how EPA will address endocrine data deficiencies for those registration submissions and for registration review cases. Under strategy three, EPA will phase into its registration review processes any new data requirements to address potential human estrogen, androgen, and thyroid effects for conventional pesticide active ingredients, starting with 30 registration review cases (''Group 1'' cases) that EPA has identified using a new framework for prioritizing estrogen and androgen data needs. In this notice, EPA is requesting comments and the voluntary submittal of existing information on these 30 cases and, during the comment period, plans to begin preparing DCIs with the goal of issuing those them in spring of 2024 for specified EDSP Tier 1 data for these cases.

To support the strategies described in this document, EPA has posted the following three reference documents in the docket:

1. *Use of Existing Mammalian Data to Address Data Needs and Decisions for Endocrine Disruptor Screening Program (EDSP) for Humans under FFDCA Section 408(p)* (Ref. 1). This endocrine science paper explains when and how EPA will rely on data it has already received under FIFRA to address the data needs and decisions under FFDCA section 408(p), providing the scientific support for strategies two and three.

2. *List of Conventional Registration Review Chemicals for Which an FFDCA Section 408(p)(6) Determination is Needed* (Ref. 2). This paper lists each currently registered conventional pesticide active ingredient, and how the types of data EPA has for each active ingredient inform where it fits within EPA's priorities for obtaining any additional endocrine data for those pesticides in registration review. Commenters should use this list to identify the active ingredients for which EPA is seeking information through this document.

3. *Status of Endocrine Disruptor Screening Program (EDSP) List 1 Screening Conclusions* (Ref. 3). This paper explaining EPA's decisions under FFDCA section 408(p) relating to the human endocrine system (estrogen, androgen, and thyroid endpoints) for all 52 EDSP List 1 chemicals. In 2009, EPA published the List 1 chemicals and issued test orders for them (the original List 1 had 67 chemicals). The Agency later revised the list to 52 chemicals because 15 were canceled or discontinued. The actions to address the remaining List 1 chemicals are unrelated to the development of Group 1 chemicals in this document.

Many aspects of this document overlap with policies described in a notice issued in the **Federal Register** of August 11, 1998 (63 FR 42852) (FRL–6021–3) (hereinafter referred to as the ''1998 Notice''), that established the basic components of the EDSP. EPA views this document as consistent with the policies in the 1998 Notice and thus is not rescinding or modifying those policies. Rather, this document augments the notice with complementary strategies and priorities that reflect advances in science, EPA's experience administering the EDSP, and the Agency's recent efforts to more quickly meet its FFDCA section 408(p) obligations and commitments.

D. Why is the Agency taking this action?

After over two decades of implementing FFDCA section 408(p), EPA has developed the near-term strategies in this document to begin to transparently address the challenges it has encountered and rebuild the EDSP. This document explains how the Agency currently obtains and will obtain data needed to assess a conventional pesticide active ingredient's interaction with the human estrogen, androgen, and thyroid pathways, and when and how EPA intends to make the requisite FFDCA section 408(p)(6) finding that the pesticide use adequately protects human health. This document also addresses the confusion about when and how EPA obtains data in the registration and registration review processes to assess the potential for effects to the endocrine system from use of a conventional pesticide active ingredient. These near-term strategies also help EPA respond to specific recommendations in a 2021 EPA Office of Inspector General (OIG) Report to develop a strategic plan for the EDSP and to a legal complaint filed in the Federal District Court for the Northern District of California raising similar issues.

E. Does this document contain binding requirements?

This document describes EPA's near-term strategies over the next several years to accelerate how the Agency meets its FFDCA section 408(p) obligations and commitments. The requirements in the statutes and any future FIFRA DCIs or FFDCA test orders are binding on EPA and the order recipients, respectively, but this document does not impose any binding requirements on EPA or outside parties. The strategies outlined in this document further the general goals of the program, and EPA may depart from the strategies where circumstances warrant and without prior notice. In general, however, EPA will continue to offer notice and comment on chemical-specific proposed decisions that implement these strategies.

F. What should I consider as I prepare my comments for EPA?

1. Scope of Request for Comments

As discussed further in strategy three of this document, EPA encourages the public to submit any relevant estrogen, androgen, and thyroid data for the Group 1 and Group 2 cases of pesticide

active ingredients currently in registration review. The public may also submit any explanations for why additional endocrine data are unnecessary to inform the Agency's findings under FIFRA and FFDCA section 408(p) for potential endocrine effects in humans.

Please submit any relevant endocrine data, Other Scientifically Relevant Information (OSRI), or explanations of why the additional data are unnecessary for EPA to make its FIFRA and FFDCA section 408(p) decisions to the ''Registration Review'' section of EPA's Pesticide Submission Portal (PSP). The PSP can be accessed through EPA's Central Data Exchange (CDX) using the link *https://cdx.epa.gov/.*

2. Submitting CBI

Do not submit CBI to EPA through *https://www.regulations.gov* or email. If you wish to include CBI in your comment, please follow the applicable instructions at *https://www.epa.gov/dockets/commenting-epa-dockets#rules* and clearly mark the part or all of the information that you claim to be CBI. In addition to one complete version of the comment that includes information claimed as CBI, a copy of the comment that does not contain the information claimed as CBI must be submitted for inclusion in the public docket. Information so marked will not be disclosed except in accordance with procedures set forth in 40 CFR part 2.

3. Tips for Preparing Your Comments

When preparing and submitting your comments, see the commenting tips at *https://www.epa.gov//commenting-epa-dockets.*

II. Background

A. What is the endocrine system?

Endocrine systems, also referred to as hormone systems, are found in all mammals, birds, fish, and many other living organisms. These systems are made up of glands located throughout the body, the hormones synthesized by these glands and released into the bloodstream or the fluid surrounding cells, and the receptors in various organs and tissues that recognize and respond to the hormones.

B. What is the relevant history of the EDSP?

In 1996, Congress amended the FFDCA with the Food Quality Protection Act, 21 U.S.C. 346a(p), requiring EPA 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 [EPA] may designate.'' In response, EPA established the EDSP, the basic components of which were described in the 1998 Notice (63 FR 42852). Further, when carrying out the EDSP, EPA ''shall provide for the testing of all pesticide chemicals,'' which includes active and inert ingredients, and ''may 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.'' The FFDCA required EPA to implement the EDSP by August 1999 and report to Congress on the program's progress by August 2000. EPA met both requirements on time, as the Agency began implementing the EDSP after issuing the 1998 **Federal Register** Notice (the statute does not specify when implementation ends nor steps for implementing the EDSP, and thus EPA views implementation as an ongoing activity) and the Agency issued its report to Congress in August 2000.

FFDCA section 408(p) requires EPA to screen only for estrogen effects in humans that are similar to an effect produced by a naturally occurring estrogen. Through the 1998 **Federal Register** Notice, however, EPA permissibly expanded the scope of the EDSP in two important ways. One is to include screening for androgen and thyroid effects, based on the recommendations of the Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC), which EPA formed to advise on designing a screening and testing program for chemicals. EPA had explained that it will focus on estrogen, androgen, and thyroid because they are among the most studied of the approximately 50 known vertebrate hormones, with a relatively large body of relevant data and screening tests. EPA also explained that including these three hormone systems will help the Agency understand effects on reproduction, development, and growth. Further, EPA adopted the EDSTAC recommendation to screen for effects in the same endocrine systems in wildlife because adverse effects on wildlife can forewarn of potential risks to humans and because strong evidence existed for endocrine disruption from pesticides in natural wildlife and fish populations. Throughout this document, when EPA refers to section 408(p) ''obligations and commitments,'' the Agency is describing both the mandatory aspects of this section (obligations) and the discretionary aspects (commitments), as summarized in Table 1.

TABLE 1—SUMMARY OF FFDCA SECTION 408(p) MANDATORY OBLIGATIONS AND DISCRETIONARY COMMITMENTS FOR PESTICIDE ACTIVE INGREDIENTS

FFDCA provision	Mandatory obligation	Status of obligation	EPA discretionary commitment and status
408(p)(1)	Must create estrogen screening program	Completed when EPA created the EDSP in 1998.	In 1998, expanded screening program to include androgen, thyroid, and wildlife.
408(p)(2)	Must implement screening program by Aug. 1999.	Completed the deadline obligation, but ongoing implementation.	Ongoing (currently implementing expanded screening).
408(p)(3)	Must provide for testing of all pesticide chemicals and may provide for testing of other substance with cumulative effect to a pesticide chemical.	Ongoing (currently obtaining data through FIFRA regulations and processes).	Ongoing (currently obtaining data through FIFRA regulations and processes).
408(p)(4)	None, but EPA may exempt chemical from 408(p).	Ongoing (established the Endocrine Disruptor Science Policy Council (EDSPOC) to make recommendations on exemptions).	Ongoing (established the EDSPOC to make recommendations on exemptions).
408(p)(5)	Must issue test orders	Ongoing (currently implementing for pesticide active ingredients through FIFRA regulations and processes).	Ongoing (currently implementing for pesticide active ingredients through FIFRA regulations and processes).

TABLE 1—SUMMARY OF FFDCA SECTION 408(p) MANDATORY OBLIGATIONS AND DISCRETIONARY COMMITMENTS FOR PESTICIDE ACTIVE INGREDIENTS—Continued

FFDCA provision	Mandatory obligation	Status of obligation	EPA discretionary commitment and status
408(p)(6)	Must take action to protect public health against a substance with endocrine effect.	Ongoing (working to address protections for pesticide active ingredients in FIFRA decisions).	Through this notice, EPA will begin issuing determinations for pesticide active ingredients when 408(p)(6) is met for human estrogen, androgen, and thyroid.
408(p)(7)	Must report to Congress by August 2000	Completed	N/A.

C. What is the screening and testing process under the EDSP?

Through the 1998 Notice, EPA also adopted the EDSTAC recommendation to create a two-tier EDSP screening and testing process. The purpose of the first tier of testing (Tier 1) is to screen chemicals for the *potential* to interact with the estrogen, androgen, or thyroid systems and inform the need for any additional data (*e.g.,* Tier 2) to evaluate possible adverse effects in humans or wildlife. The purpose of Tier 2 testing is to identify, characterize, and quantify those adverse effects for risk assessment. The Tier 1 screening battery consists of 11 assays, six of which are *in vivo* (performed with living organisms) and five of which are *in vitro* (performed outside of living organisms, with biological material such as cells or tissues).

As described in its January 2023 white paper on new approach methodologies (NAMs; Ref. 4), EPA has now validated two computational models that integrate bioactivity data from multiple *in vitro* assays, referred to as the ToxCast Pathway Models for estrogen and androgen receptors, which can serve as alternatives to four of the 11 assays. Specifically, the validated estrogen receptor ToxCast Pathway Model can serve as an alternative for three of the Tier 1 assays that detect estrogen activity and the validated androgen receptor ToxCast Pathway Model can serve as an alternative for one of the Tier 1 assays that detect androgen activity. Research is ongoing to develop validated models as alternatives for other Tier 1 and Tier 2 assays.

Under the EDSP two-tier process, analysis of Tier 1 screening data, in conjunction with OSRI on the endocrine system, results in one of two outcomes: a recommendation for additional data (*e.g.,* through Tier 2 testing of the chemical) to establish a dose-response relationship for any adverse effects that may result from interactions with the endocrine system, or an explanation for why no further testing is needed to assess the chemical for potential impacts to the estrogen, androgen, and thyroid hormone pathways. If more testing is recommended, the Tier 1 analysis also informs which tests may be performed.

D. How is FIFRA involved in EPA's implementation of the EDSP?

FFDCA section 408(p) is not limited to EDSP screening and testing, as paragraph (p)(6) also requires EPA to ''as appropriate, take action under such statutory authority as is available to the Administrator, including consideration under other sections of this chapter, as is necessary to ensure the protection of public health'' for ''any substance that is found, as a result of testing and evaluation under this section, to have an endocrine effect on humans.'' Because FFDCA section 408(p) does not itself provide legal authority to ''ensure the protection of public health,'' EPA must rely on authorities in other sections of FFDCA and other laws, such as FIFRA, to satisfy FFDCA section 408(p)(6). In this respect, EPA's implementation of FFDCA section 408(p) and FIFRA are closely linked.

The two are closely linked in another important manner. To meet the FIFRA requirement of ensuring that a pesticide will not cause ''unreasonable adverse effects on the environment,'' EPA reviews numerous studies to assess potential adverse outcomes from exposure to chemicals. These studies include acute, sub-chronic, and chronic toxicity, including assessments of a wide range of potential toxic effects for carcinogenicity, neurotoxicity, developmental, reproductive, and general or systemic toxicity, and other effects. These studies include endpoints that may be susceptible to endocrine influence, including effects on endocrine target organ weights and histopathology, estrus cyclicity, sexual maturation, fertility, pregnancy rates, reproductive loss, and sex ratios in offspring.

In the past, however, EPA's Office of Pesticide Programs (OPP) has generally focused on endocrine-related activities under FIFRA separate from the EDSP testing strategy. Thus, OPP's FIFRA decisions have not been explicit about how its review of required and submitted data for FIFRA informs EPA's obligations and commitments under FFDCA section 408(p). For instance, OPP amended its FIFRA data requirements at 40 CFR part 158 to incorporate an updated reproductive study, which is the same study identified in EDSP Tier 2 and which allows the Agency to fully evaluate the potential for a conventional pesticide active ingredient to interact with the estrogen and androgen pathways. However, EPA did not explain how that effort informs the obligations and commitments under FFDCA section 408(p).

In addition, while prior FIFRA decisions often referred to the FFDCA section 408(p) screening program, those decisions have not expressly discussed whether or how the data EPA reviews for its FIFRA decisions address FFDCA section 408(p) obligations or commitments. For example, FIFRA actions protect for the most sensitive endpoints in humans, which in many cases are not endocrine endpoints. In these situations, EPA did not take the final step of explaining whether or how the FIFRA decision fully addresses the data needs and decisions under FFDCA section 408(p) and protects the public from potential endocrine effects.

One reason EPA has not completed these FFDCA section 408(p) actions is that it had focused on developing the science and technology to rapidly screen for chemicals that may have the potential to disrupt the estrogen, androgen, and thyroid systems of humans and wildlife. In recent years, for example, the Agency has focused on NAMs, particularly with high-throughput testing approaches, because of their central role in supporting the screening of the thousands of chemicals covered by the EDSP. This includes EPA testing of over 1,800 chemicals using the estrogen receptor and androgen receptor ToxCast Pathway Models, which, as explained in a separate white paper previously released, fulfill the data

needs for four separate EDSP Tier 1 assays for those chemicals. Through the strategies in this document, EPA is planning to expand the scope of its EDSP work to emphasize obtaining any additional human endocrine data as part of the Agency's FIFRA decisions and to issue FFDCA section 408(p)(6) decisions where possible.

E. What concerns have been raised about EPA's implementation of the EDSP?

The issues discussed earlier have led to confusion and criticism about the extent to which EPA has implemented FFDCA section 408(p) for pesticides. These criticisms have included concerns that EPA has been failing to obtain data and assess whether a pesticide active ingredient may cause adverse endocrine effects at the regulated levels and failing to make decisions under FFDCA section 408(p)(6) that consider those data and effects. In addition, EPA understands that some stakeholders have heard different messages over the years about whether EPA would require Tier 1 data when it has adequate Tier 2 data to make FIFRA determinations and FFDCA section 408(p) findings. Through this notice, EPA seeks to transparently address some of these criticisms and concerns.

In July 2021, EPA's OIG issued a report concluding that the Agency has made limited progress in implementing the EDSP (Ref. 5). The report identified several reasons for this limited progress, including delays in testing pesticides for endocrine disruption, and lack of strategic guidance, performance measures, and other actions needed to implement the EDSP. The report offered ten recommendations for OCSPP, which the office generally agreed with and proposed to address. This document represents the Agency's strategic plan for rebuilding the EDSP that OCSPP will augment in the future. OCSPP has also begun implementing several other OIG recommendations, including publishing an EDSP white paper on NAMs, conducting an annual internal program review, and periodically updating the program website.

In December 2022, EPA received a complaint in *Alianza Nacional de Campesinas et al.* v. *EPA,* alleging that EPA has violated the FFDCA and Administrative Procedures Act by not implementing the EDSP and not testing all pesticide chemicals for possible endocrine effects. (Ref. 6).

III. Strategies To Further Implement FFDCA Section 408(p)

EPA recognizes that its past practice has created questions about whether and how the Agency has been implementing FFDCA section 408(p), and now seeks to address these questions and accelerate progress in further implementing the EDSP, beginning with the three strategies described in this section. Before discussing the strategies, EPA is identifying the two overall approaches for expediting its ability to meet its FFDCA section 408(p) obligations and commitments.

A. Obtain Needed Endocrine Data During FIFRA Registration or Registration Review

EPA will use the FIFRA registration and registration review processes to obtain data as needed to assess potential human estrogen, androgen, and thyroid effects for its FIFRA and FFDCA section 408(p) decisions. In general, EPA is already receiving some endocrine data through these processes as part of its standard FIFRA processes and regulatory data requirements. For example, for over a decade, EPA has routinely received data on mammalian estrogen and androgen effects for new conventional pesticide registrations through either a two-generation reproductive study (typically performed in the rat (Ref. 7)) or an extended one-generation reproductive toxicity (EOGRT) study (also normally performed in the rat) (Organization for Economic Cooperation and Development (OECD) TG443) (Ref. 8). In these situations, EPA will generally not need to obtain additional data for these endpoints, including Tier 1 data, as explained in strategy three. Further, EPA understands that some registrants may have generated endocrine data to meet registration requirements in other countries but never submitted those data to EPA. EPA will consider those data, if submitted, to assess the need for additional endocrine data and to make the relevant FIFRA and FFDCA section 408(p) decisions, while avoiding unnecessary duplicative testing.

Where EPA has identified outstanding endocrine data needs for a pesticide active ingredient, it will generally obtain the data through the FIFRA registration or registration review process, rather than through the FFDCA section 408(p)(5) process for issuing FFDCA test orders, as EPA already has a well-established process of seeking data through FIFRA. Further, EPA will generally obtain the data based on prioritized lists of pesticide active ingredients that it has begun developing and describes in strategy three.

B. Integrate FFDCA Data and Decisions into FIFRA Decisions

For conventional pesticide active ingredients, EPA will integrate its FFDCA section 408(p) endocrine data and decisions into its FIFRA decisions, so that the Agency can efficiently use its FIFRA process and timelines to also address its FFDCA obligations and commitments for those chemicals. This approach will significantly increase EPA's consistency and transparency about how and when the Agency is meeting its FFDCA section 408(p) obligations and commitments as part of FIFRA decisions.

Moving forward, when EPA has addressed those obligations and commitments for a pesticide active ingredient, it will clearly indicate that it has sufficient endocrine data and completed taking action under FFDCA section 408(p)(6) to ''ensure the protection of public health.'' This can occur in one of three scenarios. In scenario one, the most sensitive human endpoint identified in the pesticide's database is not an endocrine endpoint and is protective of endocrine effects at higher doses, if any are present. In scenario two, EPA exempts a pesticide active ingredient from the requirements of FFDCA section 408(p) because the Agency determines that the chemical meets the section 408(p)(4) statutory standard that it ''is anticipated not to produce any effect in humans similar to an effect produced by a naturally occurring estrogen.'' In its 2023 decision for citric acid, for instance, EPA concluded the acid is not anticipated to produce in humans or other organisms any effect similar to an effect produced by naturally occurring estrogen, androgen, or thyroid hormones, because it has no endocrine activity and no toxic effects at levels that people consume (Ref. 9).

In both scenarios, EPA will issue a determination as part of a FIFRA decision for a pesticide that the Agency has completed taking action under FFDCA section 408(p)(6) to ''ensure the protection of public health'' by regulating exposure based on the most sensitive endpoint. Although FFDCA section 408(p)(6) does not obligate EPA to issue this determination and explanation, EPA is committing to do so because the Agency recognizes the benefits of more clarity and transparency about how it implements FFDCA section 408(p). This is another example where EPA distinguishes between mandatory obligations and

discretionary commitments, as summarized in Table 1.

In scenario three, an endocrine effect is the most sensitive endpoint, so EPA would directly regulate to protect against that effect and issue a determination that it has completed taking action under FFDCA section 408(p)(6) through its FIFRA decision that uses the endocrine endpoint to regulate exposure to that pesticide. For example, the thyroid is a target organ for the insecticide fipronil, and thyroid effects were used as the basis for deriving most of the risk assessment endpoints and points of departure in the most recent human health risk assessment for this chemical (Ref. 10).

Throughout this document, when EPA refers to a FFDCA section 408(p)(6) ''decision,'' it is referring to one of these three scenarios. Strategies two and three explain when and how EPA will integrate these FFDCA section 408(p) data and decisions into its FIFRA registration and registration review decisions for conventional pesticide active ingredients.

In implementing these strategies, EPA recognizes that it cannot address all past and present challenges simultaneously. For example, EPA is concerned about overwhelming the capacity of testing laboratories if it were to immediately impose testing for the hundreds of pesticide active ingredients in registration review. In addition, EPA does not have the resources to immediately assess each active ingredient case to identify all endocrine data gaps and to begin obtaining all outstanding data immediately. Thus, EPA developed this document to help prioritize how the Agency will implement these strategies. To summarize, the three strategies discussed are as follows:

- EPA will prioritize addressing potential human estrogen, androgen, and thyroid effects for conventional pesticide active ingredients (see strategy one), starting with the use of existing data routinely obtained through FIFRA registration and registration review activities, to determine whether additional endocrine data are needed (see strategy two).
- If existing data are adequate to inform the FFDCA section 408(p)(6) and FIFRA decisions for any of the three endocrine pathways, EPA will make those decisions without obtaining additional endocrine data for that pathway (*e.g.,* Tier 1), because any additional data would be duplicative and would not alter those decisions (see strategy three).
- EPA will continue to require that all applications for conventional new active ingredient registrations include adequate data to assess potential interaction with the human estrogen, androgen, and thyroid pathways. Those data will inform the FIFRA registration decision, which will include whether or how it addresses FFDCA section 408(p) endocrine data and decisions (see strategy two).

Similarly, to ensure all existing registrations for conventional pesticide active ingredients are supported by adequate human health-related endocrine data, EPA will phase into the registration review process, using the framework discussed in this document (see strategy three), any additional data needs for evaluating potential interaction with human estrogen, androgen, and thyroid pathways. For 30 high priority conventional pesticide active ingredients, however, EPA is seeking any comments, existing endocrine data, and explanations on the need for additional endocrine data for any chemical on this list. During the public comment period, EPA will initiate the process for issuing DCIs in spring 2024 to require specified data for each of these active ingredients to address gaps in the data. EPA expects to include in the DCIs for these chemicals the requirement for the following EDSP Tier 1 studies or equivalent data: steroidogenesis, aromatase, Hershberger, female rat pubertal, and male rat pubertal studies. EPA also expects to include in the DCIs the potential for requiring submission of Tier 2 studies, based on the results of the Tier 1 studies submitted and any OSRI that may inform the weight-of-evidence analyses on those data. In the alternative, EPA expects to accept Tier 2 data in response to the DCIs to assess for potential effects to the estrogen and androgen pathways. Thus, if EPA receives an acceptable two-generation reproductive or EOGRT study, the study would fully satisfy the EDSP Tier 1 DCI for estrogen and androgen endpoints. As discussed in strategy three, EPA has prioritized the 30 chemicals because it lacks sufficient Tier 2 data for the chemicals but does have screening-level data indicating potential activity in the mammalian estrogen and/or androgen system. Further, as with new conventional active ingredient applications, EPA will explain in registration review documents for conventional active ingredients whether or how EPA's assessment or decision addresses FFDCA section 408(p) data and decisions.

1. Scope

EPA's resources for the EDSP are limited, so the Agency must prioritize which aspects of the EDSP to address first. For these near-term strategies, EPA has prioritized the registration of new conventional active ingredients and the registration review of conventional active ingredients, because they comprise the majority of registered active ingredients. The strategies are not intended to apply at this time to pesticide active ingredients that are solely intended for biological and antimicrobial uses or inert ingredients. Those ingredients span a wider range of uses and modes of action and can often present very different chemistries than conventional pesticides. EPA is still evaluating how best to prioritize human endocrine assessments for those active and inert ingredients and to develop strategies for the chemicals.

2. Strategy One: Prioritize Human Endocrine Effects

The FFDCA section 408(p)(1) mandate is limited to developing a screening program to identify potential estrogen effects in humans, but EPA in 1998 expanded the scope of the program to include potential androgen and thyroid effects in humans and potential wildlife estrogen, androgen, and thyroid effects. Because of limited resources, however, EPA will initially focus on ensuring that the potential for human endocrine effects is transparently and sufficiently addressed for conventional pesticide active ingredients.

Meanwhile, EPA will maintain its current approach in its FIFRA decisions of addressing wildlife endocrine effects if it already has adequate endocrine data for a species or group of species, supported by multiple lines of scientific evidence, as part of a new conventional registration or registration review action. EPA will also prioritize resources for research and risk assessment methods development to better understand endocrine effects in wildlife.

There are several reasons for this decision to first address EPA's statutory requirement to more fully assess human endocrine effects before assessing discretionary wildlife effects. First, EPA's scientific understanding of the impacts of chemical interactions on the human endocrine system is generally more developed than for most wildlife. Thus, the data and science currently available to EPA enable the Agency to make progress in evaluating effects on humans using the approaches presented in this document. This is especially true considering the large number of non-mammalian species that are covered by the EDSP (*e.g.,* birds, fish, amphibians). Second, EPA is already taking unprecedented steps to reduce pesticide

exposure to wildlife through its work under FIFRA and the Endangered Species Act (ESA) (16 U.S.C. 1531 *et seq.*). Through its ESA–FIFRA Workplan released in April 2022 and subsequent updates, EPA has prioritized mitigating pesticide effects on endangered species earlier in the FIFRA registration and registration review processes (Ref. 11). In addition, EPA has developed and will be implementing FIFRA Interim Ecological Mitigation measures for agricultural crop uses of conventional pesticide active ingredients in registration review. EPA expects that these mitigation measures will reduce pesticide exposures for ESA-listed species. EPA is also pursuing several pilot projects to expedite mitigation for listed species (*e.g.,* herbicide strategy, Hawaiian species initiative) and continuing to implement the mitigation measures from ESA biological opinions for individual pesticide active ingredients, such as certain organophosphates (Ref. 11). These mitigation measures are also expected to reduce pesticide exposure to wildlife, which will also reduce the potential for endocrine disruption.

EPA will continue to advance the science and develop strategies to consider the potential for endocrine effects on wildlife under the EDSP. For example, as outlined in the EDSP NAMs white paper, EPA is continuing to refine and apply species extrapolation processes and tools, which will help EPA understand how test results on laboratory animals extrapolate to effects on wildlife (Ref. 4). EPA is also involved in international efforts to assess the addition of thyroid endpoints to fish assays and tests that are commonly submitted to support pesticide registrations. Lastly, EPA is building datasets to support the development and validation of models that would allow *in vitro* to *in vivo* extrapolation for Tier 1 ecological studies. EPA will further discuss its approach to wildlife under the EDSP in future strategy documents. For the remainder of this document, all discussions are limited to the human endocrine system.

3. Strategy Two: Use Existing Data To Determine Whether Additional Endocrine Data Are Needed and To Inform FIFRA and FFDCA Endocrine Findings

As a key part of rebuilding the EDSP, EPA is committing to transparency when assessing the adequacy of data on whether a conventional pesticide active ingredient has the potential to interact with the estrogen, androgen, and thyroid pathways. EPA is also committing to ensure that when it authorizes a new pesticide through registration and reauthorizes its use through registration review, those decisions adequately protect human health, as required by FFDCA section 408(p)(6). EPA can make these determinations more promptly when they are based on existing data, supplemented by targeted requests for additional data and explanations to address any potential data gaps. In most cases, the existing data will already have been submitted through registration or registration review to inform the FIFRA unreasonable adverse effects finding.

In this strategy, EPA explains the overall status of what data are already typically available to the Agency on conventional pesticide active ingredients as part of its registration and registration review program. If EPA determines that available Tier 2 or other data are sufficient to fully inform the FIFRA registration/registration review and FFDCA section 408(p)(6) decisions for estrogen, androgen, and thyroid pathways, EPA will make the decisions without seeking additional EDSP Tier 1 data. In contrast, if EPA determines that additional data are needed to make the decisions, EPA will base the next steps and timing for those steps on the priority group in which the chemical belongs, as further discussed subsequently in this document.

To inform when and how EPA will use existing FIFRA data or OSRI to determine whether a pesticide has a potential endocrine effect under FFDCA section 408(p), EPA has prepared a science support paper (Ref. 1), which is available in the docket and briefly summarized in this strategy. That paper explains the data typically submitted to EPA that will meet EPA's needs for evaluating potential interaction with human estrogen, androgen, and thyroid pathways. EPA is separating its discussion of estrogen and androgen data from thyroid data because the data on estrogen and androgen are often generated together and separate from thyroid data. As discussed further subsequently in this document, EPA plans to reevaluate its approach to assessing any additional thyroid data needs in the coming years.

a. Human Estrogen and Androgen Data

EPA created the two-tier EDSP system in 1998 as one way to screen and prioritize testing for the thousands of chemicals that required screening. The goal was to limit the more expensive and lengthier Tier 2 testing by using Tier 1 screening to eliminate Tier 2 testing requirements for chemicals that had no potential to affect the human endocrine system. Since 1998, however, EPA has obtained additional data for many pesticide active ingredients through registration or registration review, because those data are also important to evaluate whether a pesticide meets the FIFRA registration standard. Specifically, in 1998, EPA updated its guidelines for the two-generation reproductive study (OCSPP 850.3800). Soon after this update, EPA required the updated study to be submitted for all new registrations of conventional pesticide active ingredients. In addition, in some cases EPA may have also received the updated study for pesticides registered before the guideline update. The updated reproductive study is the same as what EPA would have required through Tier 2 testing to determine effects on human estrogen and androgen pathways, as explained in the science support paper (Ref. 1). Similarly, for some newer pesticide active ingredients, EPA has received a rodent EOGRT study instead of an updated two-generation reproductive study. The EOGRT study provides the same estrogen and androgen data as the updated reproductive study, and thus EPA also considers the EOGRT study as a validated alternative to satisfy the Tier 2 and FIFRA data needs (Ref. 1). There may also be OSRI (such as a study submitted to meet other countries' regulatory requirements) that might meet the data needs that the Tier 2 mammalian study is designed to fulfill.

Further, if EPA has adequate Tier 2 data, it does not expect that Tier 1 data are needed to inform FFDCA section 408(p)(6) decisions for human estrogen and androgen effects and FIFRA unreasonable adverse effects determinations. EPA recognized this relationship between EDSP Tier 1 and Tier 2 data in the 1998 **Federal Register** Notice (Ref. 12) with the conceptual framework for the EDSP, which states that ''the outcome of Tier 2 is designed to be conclusive in relation to the outcome of Tier 1 and any other prior information. Thus, a negative outcome in Tier 2 will supersede a positive outcome in Tier 1.'' Consistent with this statement, when EPA has either an updated two-generation reproductive or EOGRT study, only in exceptional situations would the Agency need to consider OSRI or require more data (*e.g.,* Tier 1 data) to assess for interaction with the estrogen or androgen pathway. For example, if the outcome of a two-generation reproductive study is ambiguous or inconclusive for one or more endocrine endpoints, EPA may consider whether OSRI addresses the

ambiguity or inconclusiveness. This strategy clarifies that when EPA concludes that the two-generation reproductive study, EOGRT study, or OSRI are adequate to assess a conventional pesticide active ingredient for interaction with the estrogen or androgen pathway, it will explicitly make that determination as part of a FIFRA assessment and the accompanying registration or registration review decision. In those situations, EPA will not need or require EDSP Tier 1 data under FIFRA or FFDCA section 408(p)(5).

Based on this analysis, for new pesticide active ingredient registrations, EPA will continue to require the updated two-generation reproductive study, the alternative EOGRT study, or equivalent data. Applications for new conventional pesticide active ingredients that are not accompanied by either study or equivalent data will be deemed incomplete and unacceptable for further review.

For conventional active ingredients in registration review, EPA will first determine whether an updated reproductive or EOGRT study is available and adequate to assess for interaction with the estrogen and androgen pathways. Among the approximately 460 conventional active ingredient cases currently in registration review, EPA has received acceptable updated two-generation reproductive or EOGRT studies for approximately 90 (20%) cases. This is only an estimate based on EPA's initial analysis and will change over time.

For the remaining conventional registration review cases without the updated two-generation reproductive or EOGRT study, EPA's approach will depend on which of three groups the chemical belongs to, as discussed in strategy three. To help implement these next steps, EPA will use its Endocrine Disruptor Science Policy Council (EDSPOC), established in 2022 to review hazard and exposure data and to recommend whether to exempt a pesticide under FFDCA section 408(p)(4). The EDSPOC will recommend whether additional Tier 2 data are needed based on its review of comments and data submitted in response to this document, future DCIs for endocrine data, and all existing data for pesticides for which the Agency lacks either an updated two-generation reproductive or EOGRT study. This issue is discussed in the science support paper (Ref. 1).

b. Human Thyroid Data

Unlike the estrogen and androgen pathways, a Tier 2 assay for thyroid was not established at the time of the EDSP's creation in 1998. At the time, only the Tier 1 rat pubertal assays provided thyroid evaluation in the EDSP battery. In 2005, EPA released its ''Guidance for Thyroid Assays in Pregnant Animals, Fetuses and Postnatal Animals, and Adult Animals'' (Ref. 13), which was used to develop studies to evaluate lifestage sensitivity to thyroid effects. This includes the EOGRT study that the OECD adopted in 2011 and the comparative thyroid assay (CTA). Both studies evaluate the same endpoints as the Tier 1 rat pubertal assays for adult animals, while providing additional information on thyroid toxicity at various stages of an animal's life. If a registrant has submitted an acceptable EOGRT study with a thyroid evaluation or a CTA, EPA does not expect to need Tier 1 or other data to inform its FFDCA section 408(p)(6) decision for thyroid effects, unless the Agency identifies an issue that warrants additional lifestage information.

EPA recognizes that studies such as the EOGRT and CTA are animal and resource intensive, and certain endpoint data may be difficult to obtain (*e.g.,* advanced techniques necessary for small blood volumes particularly in young animals, limited number of laboratories capable of properly conducting studies). As a result, EPA does not require either of these studies for all pesticide active ingredients unless data indicate such a need. Currently, EPA evaluates all available thyroid data during registration or registration review to assess whether evidence exists that a chemical may cause adverse thyroid effects and determine whether additional thyroid information is needed. This includes data from several studies required under FIFRA (*e.g.,* subchronic, chronic, and carcinogenicity) for conventional pesticide active ingredients that evaluate potential thyroid toxicity. Measurements in these studies typically include thyroid organ weights and histopathology (*e.g.,* colloid amount, follicular cell height and shape) that can detect changes associated with thyroid hormone perturbations. For some of these conventional pesticide active ingredients, registrants also submit optional thyroid hormone data to EPA to provide additional characterization of potential thyroid toxicity. Additionally, EPA may also consider data from EDSP Tier 1 rat pubertal assays or OSRI that provide thyroid evaluation. These data are predominantly obtained from guideline studies in rats, which are recognized as a sensitive animal model for humans, as discussed in the science support paper (Ref. 9). Thus, a lack of thyroid toxicity in these rat studies provides a strong basis for concluding a lack of concern for thyroid toxicity in humans and thus a sufficient basis for FIFRA and FFDCA section 408(p)(6) findings. This strategy clarifies that if EPA finds no evidence of thyroid toxicity, then it will conclude that no further data are needed at that time under FIFRA and FFDCA section 408(p) to assess the conventional pesticide active ingredient for thyroid toxicity. The registration and registration review documents will explain that conclusion.

In contrast, if EPA determines that there is evidence of thyroid toxicity, EPA will refer the case to the Hazard and Science Policy Council (HASPOC), an internal peer review council that addresses whether additional data may be necessary to evaluate the potential of an active ingredient to interact with the thyroid pathway. HASPOC takes a weight-of-evidence approach to determine whether additional thyroid information is needed considering data from multiple lines of evidence, such as physical-chemical properties, toxicity of the chemical and any structurally related chemicals, exposure from the registered use pattern, and estimated risks. HASPOC has predominantly considered the need for a CTA to obtain lifestage specific thyroid measurements, including thyroid hormones. Depending on the available data, however, EPA may seek additional thyroid data for screening the chemical before requiring lifestage information. If the HASPOC concludes that no further data are needed at that time under FIFRA and FFDCA section 408(p) to assess the conventional pesticide active ingredient for thyroid effects, the EPA registration or registration review documents will explain that conclusion. If substantial new information is raised in the future calling into question these FIFRA and FFDCA findings, EPA can address the issue at that time, as appropriate to the circumstances.

EPA believes that there may be existing studies with thyroid measurements, such as EDSP Tier 1 rat pubertal assays or EOGRT studies, that EPA had not yet specifically requested. Additionally, although thyroid hormone and organ weight measures are not required as part of the EPA rat subchronic toxicity test guidelines (OCSPP 870.3050, 870.3100), registrants may submit existing or future studies that follow the OECD guidelines to support pesticide registrations. In 2018, the OECD updated its guidelines for the 28-day and 90-day rat subchronic studies (TGs 407 and 408 (Refs. 14 and 15, respectively)) to measure thyroid hormones and organ weight, in addition

to the previously required thyroid histopathology evaluations in those guidelines, to detect perturbations to the thyroid pathway. EPA anticipates that as more pesticide applications are submitted consistent with the OECD guidelines, EPA will receive additional thyroid-related data, which will be consistent with the data obtained from the Tier 1 rat pubertal assays.

As of 2023, most new conventional pesticide active ingredient registration submissions that EPA receives have not followed the voluntary 2018 OECD guidelines for the subchronic rodent oral toxicity studies. One reason is that EPA regulations allow registrants, consistent with the OECD agreement on Mutual Acceptance of Data, to decide whether to follow the EPA or the OECD guidelines for the subchronic rodent oral toxicity studies. A second reason is that registrants typically perform these types of studies many years before they submit a registration application package to EPA. The Agency expects within the next few years to begin receiving more FIFRA new pesticide active ingredient applications with studies that follow the 2018 OECD guidelines for subchronic rodent oral toxicity studies that will contain these additional thyroid-related measures.

EPA is actively considering potential revisions to its current framework for thyroid data needs, including scientific advancements and potential to require additional thyroid measures. As described in the EDSP white paper on NAMs (Ref. 4), EPA has ongoing research to develop high-throughput screening assays for thyroid-relevant targets, and models to predict thyroid-related apical outcomes (*e.g.,* growth, reproduction). Further, EPA is collaborating in international efforts to advance NAMs for thyroid effects. EPA needs additional research and peer review before it can include these NAMs in the EDSP. Thus, EPA expects to convene a FIFRA Scientific Advisory Panel (SAP) (anticipated in 2025) to obtain external peer review on potential revisions to the thyroid framework and may alter its approach after the FIFRA SAP review.

c. Where Endocrine Data Are Inadequate or Absent

Strategy two pertains to situations where EPA can clearly use existing endocrine data, but in some situations further analysis of available data will lead EPA to determine that data gaps exist. For example, EPA estimates approximately 317 conventional pesticide cases in registration review that lack an updated, post-1998 two-generation reproductive or EOGRT study. Compared to the updated guideline reproductive study that provides Tier 2 test data (Ref. 7), the pre-1998 study likely did not evaluate all the endocrine-related endpoints that were added to the test guideline in 1998. As a result, for these pesticides, EPA will need to assess the results of the pre-1998 study along with any OSRI to determine the need for additional data on the potential for estrogen and androgen effects. What constitutes additional data will depend on the extent of missing information as described in more detail in strategy three. In general, EPA will seek Tier 1 data or OSRI to augment the data obtained from the pre-1998 reproductive study. Although both FIFRA section 3(c) and FFDCA section 408(p) provide authority for EPA to obtain any additional needed endocrine data, EPA already has an established FIFRA process under section 3(c) to obtain data, so the Agency will generally use this process rather than the FFDCA process.

d. Other Potential Uses of Tier 1 Data Unrelated to the EDSP

Thus far, the discussion of Tier 1 data has been limited to whether EPA needs those data when it has adequate Tier 2 data or OSRI to assess potential effects on the human endocrine system. This is a result of the structure of the two-tier EDSP that EPA developed in 1998. More generally, however, the data listed in EDSP Tier 1 may be developed independently of the EDSP and, thus, may also inform aspects of risk assessment unrelated to FFDCA section 408(p). One potential role is to inform the required FFDCA cumulative effects analysis of whether a substance ''may have an effect that is cumulative to the effect of a pesticide chemical.'' To the extent such Tier 1 data has already been submitted (or is submitted) to EPA for purposes of the EDSP, EPA may find that data useful for informing other aspects of risk assessment. If EPA needs similar data in those or other situations, it can obtain them under FIFRA or provisions of the FFDCA unrelated to the EDSP, although it would not be called ''Tier 1 data'' per se. Because this document covers only the initial rebuilding of the EDSP, it does not address potential uses of that type of data for non-EDSP uses.

To summarize, the key parts of strategy two are as follows:

- For human estrogen and androgen effects, if EPA has an adequate updated two-generation or EOGRT study to support a new conventional pesticide active ingredient application or a currently registered conventional pesticide active ingredient in registration review, then it will likely conclude that it has sufficient data to inform its FIFRA and its FFDCA section 408(p)(6) decisions for potential human estrogen and androgen effects. In those case, EPA will not seek Tier 1 data to complete those decisions.
- Consistent with current practice, new conventional pesticide active ingredient applications will be deemed incomplete if EPA has neither an adequate updated two-generation or EOGRT study, or equivalent data. Those applications will not proceed through the registration process.
- For currently registered conventional pesticide active ingredients, strategy three explains how EPA will prioritize these pesticides to determine whether and what additional data it needs. In general, EPA will prioritize an active ingredient that lacks an adequate updated two-generation or EOGRT study (which will likely be the case for pesticides registered before 1998), if EPA determines available data are inadequate or insufficient to address interaction on the estrogen and androgen pathway.
- For human thyroid effects, if EPA has an acceptable CTA or EOGRT study with thyroid evaluations, then it will likely have sufficient thyroid toxicity data to inform its FIFRA and FFDCA 408(p)(6) decisions for potential human thyroid effects, and EPA will not seek Tier 1 data to support those decisions. When neither of these studies are available, EPA will continue with its current approach of evaluating the available data for each pesticide active ingredient. If no evidence exists of thyroid-related toxicity or if HASPOC has not recommended requiring additional data (*e.g.,* CTA) based on the weight-of-the evidence evaluation, then EPA will include in its FIFRA assessments and accompanying registration or registration review decision an explanation for why the available data are sufficient to inform its FIFRA and its FFDCA section 408(p)(6) decisions for thyroid. In these cases, EPA will not need Tier 1 data for thyroid. If HASPOC recommends additional thyroid data, OPP's regulatory divisions will review the recommendation during the registration or registration review process for the pesticide to determine whether or when to issue a DCI for the additional needed thyroid data. EPA may alter its approach to determining additional thyroid data needs following the FIFRA SAP review (anticipated in 2025) of potential revisions to its thyroid framework.

4. Strategy Three: Through Registration Review, Phase in Any New Data Requirements To Address Potential Human Estrogen, Androgen, and Thyroid Effects for Registered Conventional Pesticide Active Ingredients, Starting with Priority Chemicals

EPA's longstanding goal is for its registration review final decisions to include decisions under FFDCA section 408(p) for potential human estrogen, androgen, and thyroid effects. To continue fulfilling this goal, EPA has created a framework for conventional pesticides awaiting human endocrine decisions that prioritizes obtaining new data based on whether EPA already has data for the pesticide and, if so, whether the data indicate a potential for endocrine disruption. Depending on the answers to these questions, EPA has assigned each conventional active ingredient in registration review into one of three groups. For example, Group 1, which consists of 30 cases, is the highest priority for potential data collection.

Where possible, EPA's goal is to incorporate any data requirements for additional estrogen, androgen, and thyroid data into the start of registration review cases, as EPA does for other potential human health effects. Where the current registration review case is farther along in registration review, EPA will address any additional endocrine data needs by issuing a DCI, as appropriate, in later stages of registration review for a chemical.

The number of registration review cases presented in this section is an approximation and subject to change. Readers should not focus on the number of cases for exactness and instead use them to gain a general understanding of the number of cases currently in registration review that are priorities for further human endocrine screening and decisions. In the future, EPA plans to revise the registration review website to include updates of the number of cases presented in this section.

a. How EPA Prioritized Conventional Active Ingredients Undergoing Registration Review for Obtaining Additional Estrogen-Androgen Data

EPA has developed the framework that EPA will be using to determine which conventional pesticides in registration review require additional estrogen and androgen data for human health effects and how the Agency will prioritize obtaining additional data through DCIs (as discussed in strategy two, EPA will continue its current approach for thyroid). The framework represents EPA's initial approach to organize and prioritize the large number of registration review pesticides for any additional estrogen and androgen data and regulatory decisions, and may evolve as EPA gains experience implementing it. See Figure 1. in Ref. 2 for a diagram of the framework used for prioritizing the 403 conventional pesticide cases currently in registration review for which an FFDCA section 406(p)(6) determination is needed.

EPA has 459 conventional pesticide cases currently in registration review that have neither a registration review final decision nor an FFDCA section 408(p)(6) decision. These cases cover pesticides registered before October 2007 (with a current registration review deadline of October 2026) and some pesticides registered after this date. There are seven cases for which EPA has exempted the pesticide active ingredient from testing under FFDCA section 408(p)(4), and 49 cases from List 1 that EPA is addressing separate from this framework (see List 1 decision memo (Ref. 3)). That leaves 403 cases currently in registration review for further consideration of whether and when to require additional endocrine data. A pesticide registration review case is comprised of one or multiple pesticide active ingredients depending on the case. Many conventional pesticide cases have only one active ingredient.

Table 2 includes estimates of the number of conventional pesticide cases currently in registration review for which an FFDCA section 406(p)(6) determination is needed. EPA is addressing List 1 pesticides separately in the List 1 decision memo (Ref. 3).

TABLE 2—CATEGORIZATION OF THE 403 CONVENTIONAL PESTICIDE CASES CURRENTLY IN REGISTRATION REVIEW FOR WHICH AN FFDCA SECTION 406(p)(6) DETERMINATION IS NEEDED

Description	Number of cases *
No further testing for estrogen or androgen	86
Cases with updated 2-gen. repro. study	82
Cases with EOGRT study	4
May need further estrogen or androgen data:	317
Group 1 cases	30
Group 2 cases	126
Group 3 cases	161

* Numbers as of 8/25/2023.

As previously stated and further explained in the science support paper, either an updated two-generation reproductive or EOGRT study will generally provide sufficient data on potential estrogen and androgen effects in humans. The Agency has data from at least one of these studies for 86 of the 403 cases (82 cases with the updated reproductive study and 4 cases with the EOGRT study) (Ref. 2).

, and EPA expects to make FFDCA section 408(p)(6) decisions for these human endocrine effects as part of registration review for these pesticides without seeking further estrogen or androgen data.

For the remaining 317 cases without either study, EPA then determined whether it has data on the estrogen receptor and androgen receptor from the ToxCast Pathway Models. The ToxCast program, which generates high throughput data for chemicals of interest to EPA, has produced endocrine screening data for over 1,800 chemicals to inform the estrogen receptor and androgen receptor ToxCast Pathway Models. For 191 of the 317 cases, EPA has ToxCast Pathway Model scores for the estrogen receptor, androgen receptor, or both. The ToxCast Pathway Model scores for 30 of these 191 cases show bioactivity that may provide evidence for a potential effect on estrogen, androgen, or both, indicating the need for additional data to evaluate the potential to interact with the estrogen, androgen, or both pathways (the remaining 161 of the 317 cases without positive ToxCast data are discussed later in this section). EPA is seeking through this notice any Tier 1 data, OSRI, or explanation of how existing data address the ToxCast

Pathway Model scores, in order to determine whether there is actually a potential for an estrogen-androgen effect for these 30 cases. During the public comment period, EPA will initiate the process for issuing DCIs for these cases by spring 2024. Because the cases show the potential for endocrine activity, EPA considers them the highest priority for obtaining additional data and will refer to them as ''Group 1'' cases.

For the remaining 126 of 317 cases, ToxCast Pathway Model scores were not available for the estrogen receptor or androgen receptor. These chemicals are also high priorities for obtaining data, but not as high as Group 1 cases because data currently exist that demonstrate potential activity in the ToxCast models for the Group 1 cases. EPA considers these 126 cases ''Group 2'' for assessment and potential data collection. While the Agency prioritizes Group 1 cases, it will refine the Group 2 cases as follows. First, EPA will determine whether any of the active ingredients for those cases are exempt from further testing under FFDCA section 408(p)(4) because the Agency has determined that an active ingredient ''is anticipated not to produce any effect in humans similar to an effect produced by a naturally occurring estrogen.'' If so, EPA will exempt the active ingredient and explain its decision. Second, for the remaining cases, EPA will search for any existing estrogen or androgen data and evaluate its potential as OSRI. EPA will then determine whether further testing is needed for each of the remaining cases to make an FFDCA section 408(p) determination.

Among the 191 cases with ToxCast data, there are 161 cases that show no activity for either estrogen or androgen receptors. EPA has assigned these pesticides a lower priority for obtaining additional data, given current data suggest no potential for estrogen or androgen activity, and is referring to these 161 cases as ''Group 3.'' In the docket is a document titled, ''List of Conventional Registration Review Chemicals for Which an FFDCA Section 408(p)(6) Determination is Needed,'' that lists the pesticide cases that fall within each group, accounting for all 403 registration review cases discussed in this strategy (Ref. 2).

b. How EPA Will Obtain Additional Data and Integrate the New Data Into Registration Review

i. For Group 1 Cases: 30 Cases Without an Updated Two-Generation Reproductive or EOGRT Study but for Which ToxCast Data Show Activity for Estrogen, Androgen, or Both

For the 30 Group 1 cases, EPA will seek additional data to better understand the positive findings in the ToxCast data for estrogen, androgen, or both. Specifically, for each pesticide, EPA is seeking through this notice any Tier 1 data, OSRI, or explanation of how existing data address the existing ToxCast Pathway Model scores. During this public comment period, EPA will begin the process for issuing DCIs for these 30 cases with the goal to begin issuing them in spring 2024. The DCIs will cover all the Tier 1 data relevant to mammals, except the assays for which the ToxCast Pathway Model scores may serve as alternatives (*i.e.,* estrogen receptor binding *in vitro* assay, estrogen receptor transcriptional activation *in vitro* assay, *in vivo* uterotrophic assay, and androgen receptor binding *in vitro* assay). Thus, as part of a DCI, EPA will require data from the following five Tier 1 assays to complete screening for estrogen and androgen effects in humans: Steroidogenesis, aromatase, Hershberger, female rat pubertal, and male rat pubertal (see Table 3). In lieu of all five Tier 1 assays, EPA expects to allow a registrant, in response to a DCI, to submit an updated two-generation reproductive or EOGRT study, or equivalent data, which will generally provide conclusive data for potential estrogen and androgen effects in humans. The DCIs will be based on the Pesticide Data Call-Ins Information Collection Request (EPA No. 2288.04).

TABLE 3—ADDITIONAL EDSP TIER 1 DATA EPA EXPECTS TO REQUEST

Assay name	Estrogen pathway	Androgen pathway	Thyroid pathway
In vitro Assays			
OCSPP 890.1550—Steroidogenesis (Human Cell Line—H295R)	■	■	
OCSPP 890.1200—Aromatase (Human Recombinant)	■		
In vivo Assays			
OCSPP 890.1400—Hershberger (Rat)		■	
OCSPP 890.1450—Pubertal Development and Thyroid Function in Intact Juvenile/Peripubertal Female Rats	■		■
OCSPP 890.1500—Pubertal Development and Thyroid Function in Intact Juvenile/Peripubertal Male Rats		■	■

As EPA receives data for the Group 1 cases through public comments and any DCIs, it will determine the most efficient way to review the data and integrate them into the registration review process so that the Agency can issue its FIFRA and FFDCA section 408(p) findings for potential human estrogen, androgen, and thyroid effects. EPA must consider multiple factors when developing this timeline, including efficiencies in batching similar chemicals, the timing of when the Agency will receive and review data for other EDSP priority pesticides, the length of time needed to generate the data, the deadlines to complete other aspects of registration review for a pesticide, and the timeframe for amending pesticide labels to reflect any needed updated mitigation measures. EPA expects to release a more detailed timeline in 2024.

ii. For Group 2 Cases: 126 Cases Without Updated Two-Generation Reproductive or EOGRT Study, and No ToxCast Pathway Model Scores

EPA is not initiating the process for issuing DCIs for Group 2 cases at this time because the Agency's resources are currently limited to obtaining and reviewing additional data for the Group 1 cases. The more immediate focus on Group 1 cases will also allow EPA to apply any lessons learned in collecting and reviewing data for Group 1 to Group 2 cases. Although EPA does not yet have

a precise timeframe for issuing FIFRA DCIs for these cases, it expects to begin drafting them in 2025.

In the meantime, the Agency will make some progress on Group 2 cases in two ways. One is to consider any endocrine data or OSRI that registrants of these pesticides submit to EPA. As with Group 1 cases, EPA is particularly interested in any existing Tier 1 or Tier 2 data that the Agency is unaware of, endocrine data submitted to support distribution and use of the pesticide in other countries, or data from well-conducted studies addressing the pesticide active ingredient's endocrine effects. Although EPA cannot yet commit to reviewing these data within a specific timeframe, the Agency believes it may be useful to, at a minimum, gain a better understanding of the breadth and depth of available data for these pesticides before issuing DCIs. Thus, as with the Group 1 cases, EPA encourages registrants of Group 2 pesticides to identify and submit any relevant endocrine data that have not been submitted to EPA or any explanations for why further testing should not be required.

Second, given the large number of pesticides in the Group 2 list, EPA will identify the pesticides within this group that are higher priorities for endocrine testing. EPA will use comments, data, and explanations submitted, as well as the tools for prioritization described in its January 2023 EDSP NAMs white paper (Ref. 4), to determine which Group 2 pesticides will receive DCIs first. EPA will also use these same data and tools to determine whether to exempt any pesticides on the list from further testing under FFDCA section 408(p)(4) using its current approach to exemptions. In 2024, EPA will provide more information on its timeline for Group 2 chemicals.

iii. For Group 3: All Remaining Conventional Registration Review Cases Not in Group 1 or Group 2

As explained earlier, a main goal of rebuilding the EDSP is to incorporate the FFDCA section 408(p) obligations and commitments into the FIFRA process, including the registration review of existing pesticides. EPA will thus begin phasing into registration review those obligations and commitments for the 161 Group 3 cases. By phasing Group 3 cases into the existing registration review schedule, EPA may also need to shift where a case currently stands in registration review.

Most Group 3 cases (approximately 154 out of 161 cases) have active ingredients that were registered before October 2007 and have a current registration review deadline of October 2026. Typically, EPA issues DCIs before the draft risk assessment (DRA) phase of registration review. The pre-2007 cases, however, are generally past the DRA phase, often by several years. EPA will thus likely address its endocrine data needs as part of its continuous work plan (CWP) for these cases. Like a preliminary work plan (PWP), a CWP will provide an overview of the registration review case status, list registrations, and provide other pertinent data or information. As a continuation of an existing registration review case, the CWP will explain any new developments that EPA knows about a case, including any newly identified data or other information needed for a final registration review decision. Thus, EPA currently plans to prioritize the Group 3 cases and use the CWP to notify the public of when additional endocrine data are needed for each case and then issue a DCI to obtain the necessary data before completing a final decision for registration review. Consistent with existing EPA policy, a final decision will include an FFDCA section 406(p)(6) decision for human estrogen, androgen, and thyroid.

For the approximately seven other Group 3 cases with active ingredients registered after October 2007, EPA will determine whether to address its endocrine data needs through a CWP or a PWP. EPA will use the latter approach when it can integrate endocrine data needs into the registration review process from the outset, such as for cases without a PWP yet. Thus, for these cases, EPA will likely address the endocrine data needs before it does so for many Group 2 case, because the Group 3 case happens to be at an early enough stage of registration review where EPA can incorporate those data needs into the normal review process.

V. References

The following is a listing of the documents that are specifically referenced in this document. The docket includes these documents and other information considered by EPA, including documents that are referenced within the documents that are included in the docket, even if the referenced document is not physically located in the docket. For assistance in locating these other documents, please consult the technical person listed under **FOR FURTHER INFORMATION CONTACT**.

1. US EPA. Use of Existing Mammalian Data to Address Data Needs and Decisions for Endocrine Disruptor Screening Program (EDSP) for Humans under FFDC Section 408(p). October 2023.
2. US EPA. List of Conventional Registration Review Chemicals for Which an FFDCA Section 408(p)(6) Determination is Needed. October 2023.
3. US EPA. Status of Endocrine Disruptor Screening Program (EDSP) List 1 Screening Conclusions. October 2023.
4. US EPA. Availability of New Approach Methodologies (NAMs) in the Endocrine Disruptor Screening Program (EDSP). December 12, 2022. *https://www.regulations.gov/document/EPA-HQ-OPP-2021-0756-0002*.
4. US EPA Office of Inspector General (OIG). EPA's Endocrine Disruptor Screening Program Has Made Limited Progress in Assessing Pesticides. Report No. 21–E–0186. Report Type: Audit. July 28, 2021. *https://www.epaoig.gov/reports/audit/epas-endocrine-disruptor-screening-program-has-made-limited-progress-assessing*.
5. The United States District Court for the Northern District of California. Case No. 22-cv-9030. Filed December 20, 2022.
6. US EPA. Health Effects Test Guidelines: OPPTS 870.3800 Reproduction and Fertility Effects [EPA 712–C–98–208]. August 1, 1998. *https://www.regulations.gov/document/EPA-HQ-OPPT-2009-0156-0018*.
6. Organisation for Economic Co-operation and Development (OECD). OECD Guideline for the Testing of Chemicals, Extended One-Generation Reproductive Toxicity Study. OECD/OCDE 443. Adopted: June 25, 2018. *https://www.oecd-ilibrary.org/docserver/9789264185371-en.pdf?expires=1695671098&id=id&accname=guest&checksum=F8B12F13B2F19A2731C51FA392B78716*.
7. US EPA. Exemption of Citric Acid from the Requirements of the Endocrine Disruptor Screening Program. January 19, 2023. *https://www.regulations.gov/document/EPA-HQ-OPP-2020-0558-0008*.
8. US EPA. Fipronil: Draft Human Health Risk Assessment for Registration Review. March 20, 2020. *https://www.regulations.gov/document/EPA-HQ-OPP-2011-0448-0076*.
9. US EPA. EPA's Workplan and Progress Toward Better Protections for Endangered Species. EPA website. *https://www.epa.gov/endangered-species/epas-workplan-and-progress-toward-better-protections-endangered-species*.
10. US EPA. Endocrine Disruptor Screening Program; Proposed Statement of Policy. **Federal Register**. 63 FR 71542, December 28, 1998 (FRL–6052–9). *https://www.epa.gov/sites/default/files/2015-08/documents/122898frnotice.pdf*.
11. US EPA. Guidance for Thyroid Assays in Pregnant Animals, Fetuses and Postnatal Animals, and Adult Animals. October 24, 2005. *https://www.epa.gov/sites/default/files/2015-06/documents/thyroid_guidance_assay.pdf*.

12. OECD. OECD Guidelines for the Testing of Chemicals, Repeated Dose 28-Day Oral Toxicity Study in Rodents. OECD/OCDE 407. Adopted: October 3, 2008. *https://www.oecd-ilibrary.org/docserver/9789264070684-en.pdf?expires=1695669052&id=id&accname=guest&checksum=B2CCC35058D14B03AFA5C29EBB5D1CE5.*
13. OECD. OECD Guideline for the Testing of Chemicals, Repeated Dose 90-Day Oral Toxicity Study In Rodents. OECD/OCDE 408 Adopted: June 25, 2018. *https://www.oecd-ilibrary.org/docserver/9789264070707-en.pdf?expires=1695668998&id=id&accname=guest&checksum=19E7679541E3927AE5066BBB8CFA0F54.*

VI. Paperwork Reduction Act (PRA)

The strategies outlined in this document describe information collection activities that do not create any new paperwork burdens that require additional approval by OMB under the PRA, 44 U.S.C. 3501 *et seq.* The information collection activities associated with pesticide registration are already approved by OMB under OMB Control No. 2070–0226, entitled ''Consolidated Pesticide Registration Submission Portal'' (EPA ICR No. 2624.01). Information collection activities associated with data call-in activities, including the generation of data for registration review, are approved under OMB Control No. 2070–0174, entitled ''Pesticides Data Call-In Program Information Collection Request'' (EPA ICR No. 2288.06).

Authority: 7 U.S.C. 136 *et seq.* and 21 U.S.C. 346a.

Dated: October 20, 2023.

Michal Freedhoff,

Assistant Administrator, Office of Chemical Safety and Pollution Prevention.

[FR Doc. 2023–23721 Filed 10–26–23; 8:45 am]

BILLING CODE 6560–50–P

FEDERAL ELECTION COMMISSION

Sunshine Act Meetings

TIME AND DATE: Wednesday, November 1, 2023 at 10:30 a.m. and its continuation at the conclusion of the open meeting on November 2, 2023.

PLACE: 1050 First Street NE, Washington, DC and virtual (This meeting will be a hybrid meeting).

STATUS: This meeting will be closed to the public.

MATTERS TO BE CONSIDERED:

Compliance matters pursuant to 52 U.S.C. 30109.

Matters relating to internal personnel decisions or internal rules and practices. Information for which disclosure would constitute an unwarranted invasion of privacy. Investigatory records compiled for law enforcement purposes and production would disclose investigative techniques.

Information the premature disclosure of which would be likely to have a considerable adverse effect on the implementation of a proposed Commission action.

Matters concerning participation in civil actions or proceedings or arbitration.

* * * * *

CONTACT PERSON FOR MORE INFORMATION: Judith Ingram, Press Officer, Telephone: (202) 694–1220.

(Authority: Government in the Sunshine Act, 5 U.S.C. 552b)

Dated: October 25, 2023.

Laura E. Sinram,

Secretary and Clerk of the Commission.

[FR Doc. 2023–23907 Filed 10–25–23; 4:15 pm]

BILLING CODE 6715–01–P

FEDERAL ELECTION COMMISSION

Sunshine Act Meetings

TIME AND DATE: Thursday, November 2, 2023 at 10:30 a.m.

PLACE: Hybrid meeting: 1050 First Street NE Washington, DC (12th floor) and virtual. *Note:* For those attending the meeting in person, current COVID–19 safety protocols for visitors, which are based on the CDC COVID–19 hospital admission level in Washington, DC, will be updated on the Commission's contact page by the Monday before the meeting. See the contact page at *https://www.fec.gov/contact/.* If you would like to virtually access the meeting, see the instructions below.

STATUS: This meeting will be open to the public, subject to the above-referenced guidance regarding the COVID–19 hospital admission level and corresponding health and safety procedures. To access the meeting virtually, go to the Commission's website *www.fec.gov* and click on the banner to be taken to the meeting page.

MATTERS TO BE CONSIDERED:

Proposed Directive Regarding Investigations Conducted by the Office of General Counsel
Proposed Final Audit Report on Steve Daines for Montana (A21–04)
Draft Advisory Opinion 2023–06: Texas Majority PAC
Management and Administrative Matters

CONTACT PERSON FOR MORE INFORMATION: Judith Ingram, Press Officer, Telephone: (202) 694–1220.

Individuals who plan to attend in person and who require special assistance, such as sign language interpretation or other reasonable accommodations, should contact Laura E. Sinram, Secretary and Clerk, at (202) 694–1040 or *secretary@fec.gov,* at least 72 hours prior to the meeting date.

(Authority: Government in the Sunshine Act, 5 U.S.C. 552b)

Laura E. Sinram,

Secretary and Clerk of the Commission.

[FR Doc. 2023–23930 Filed 10–25–23; 4:15 pm]

BILLING CODE 6715–01–P

GENERAL SERVICES ADMINISTRATION

[Notice–PBS–2023–06; Docket No. 2023–0002; Sequence No. 26]

Notice of Availability for a Draft Supplemental Environmental Impact Statement and Floodplain Assessment and Statement of Findings for the International Falls Land Port of Entry Modernization and Expansion Project in International Falls, Minnesota

AGENCY: Public Buildings Service (PBS), General Services Administration (GSA).

ACTION: Notice of Availability (NOA); Announcement of public hearing.

SUMMARY: This notice announces the availability of the Draft Supplemental Environmental Impact Statement (SEIS), which examines potential environmental impacts from the modernization and expansion of the International Falls Land Port of Entry (LPOE) in International Falls, Minnesota. The existing International Falls LPOE is owned and managed by GSA and is operated by the U.S. Department of Homeland Security's Customs and Border Protection (CBP). The Draft SEIS describes the purpose and need for the project; alternatives considered; the existing environment that could be affected; the potential impacts resulting from each of the alternatives; and proposed best management practices and/or mitigation measures. The Draft SEIS also includes the Draft Finding of No Practicable Alternative (FONPA), which provides a floodplain assessment and statement of findings as a result of construction in a floodplain at the International Falls LPOE.

DATES:

Public Comment Period—Interested parties are invited to provide comments on the Draft SEIS and Floodplain Assessment and Statement of Findings. The Public Comment Period begins with