Status of Endocrine Disruptor Screening Program (EDSP) List 1 Screening Conclusions

October 2023

Introduction

Pursuant to section 408(p) of Federal Food, Drug, and Cosmetics Act (FFDCA), EPA introduced the Endocrine Disrupter Screening Program (EDSP) in 1998, which includes the use of a two-tiered screening framework. The purpose of Tier 1 screening is to identify chemicals that have potential biological activity ("bioactivity") in the estrogen, androgen, or thyroid (E, A, or T) hormone pathways using a battery of assays. Tier 1 screening data are subjected to a weight-of-evidence (WoE) analysis where an assessment is made on the need for Tier 2 or additional testing[1]. The purpose of Tier 2 testing is to identify and establish a dose-response relationship for any adverse endocrine (E, A, or T) effects.

The first group of chemicals to be evaluated, referred to as List 1, was finalized using the approach described in the September 2005 notice and considers comments received in response to the June 2007 draft list. The list, announced in the 2009 Federal Register Notice (https://www.regulations.gov/document/EPA-HQ-OPPT-2004-0109-0080), includes pesticide chemicals (active and inert ingredients) that the Agency decided should be tested first, based on exposure potential. As described in the 2009 Federal Register Notice, six chemicals were removed from the original draft list of 73 chemicals based on additional exposure information. Subsequently, an additional 15 of these chemicals were canceled or discontinued by the pesticide registrant and no longer in use; therefore, these chemicals were also removed from the list.

After receiving data in response to required testing, the remaining 52 List 1 pesticide chemicals (50 active ingredients and 2 inert ingredients, acetone and isophorone) were subjected to EDSP Tier 1 screening (Appendix), which includes a battery of five *in vitro* screens and six *in vivo* screens. EPA scientists (composed of experts within the Office of Chemical Safety and Pollution Prevention (OCSPP) with consultations with experts in the Office of Research and Development) performed WoE analyses of the potential interaction with the E, A, and/or T signaling pathways for humans and wildlife using results of the Tier 1 battery and other scientifically relevant information (OSRI) to determine the need for additional testing for each List 1 pesticide chemical. This document provides an overall summary of the WoE conclusions for the List 1 pesticide chemicals for human E, A, and T and any subsequent updates based on further evaluation by EPA's Hazard and Science Policy Council (HASPOC). HASPOC is an interdivisional forum within the Office of Pesticide Programs (OPP) created to address science policy, hazard data waivers, and complex risk issues, and in this case to make recommendations on thyroid-related assessments and data needs.

This document concludes EPA's FFDCA section 408(p) review relating to the potential for effects to the *human* E, A, or T pathways for all 52 List 1 chemicals. In each of these cases, EPA has determined that for all List 1 chemicals except dimethyl tetrachlorophthalate (DCPA), the available data either show no E, A, or T activity or activity at dose levels that are higher than the

1 Weight-of-Evidence: Evaluating Results of EDSP Tier 1 Screening to Identify the Need for Tier 2 Testing. https://www.regulations.gov/document/EPA-HQ-OPPT-2010-0877-0021

regulated dose level in the human health risk assessment, and thus EPA has determined that use of these chemicals under the current regulations are protective of public health, as contemplated by FFDCA section 408(p)(6).

Additionally, this document provides a summary of testing recommended for wildlife following the Tier 1 WoE evaluation for some List 1 chemicals. As discussed in the Federal Register Notice for Endocrine Disruptor Screening Program; Near-Term Strategies for Implementation, EPA is prioritizing data and assessments on potential impacts to the human E, A, or T systems; however, EPA will be addressing at a future date issues relating to data and assessments on the potential for endocrine effects on wildlife for the List 1 chemicals where Tier 1 WoE memos recommend requiring additional data[2].

Initial Conclusions of Tier 1 Weight-of-Evidence Analyses for Human Estrogen, Androgen, or Thyroid Endpoints for List 1 Pesticide Chemicals

Starting in 2015, EPA released WoE analyses for each List 1 pesticide chemical using results of the Tier 1 battery and OSRI, including general toxicity data and open literature studies of sufficient quality. The details of each Tier 1 WoE analysis, conclusions regarding the potential to interact with E, A, and/or T pathways in humans, and testing recommendations are captured in the chemical-specific documents for all List 1 chemicals (hyperlinked in the Appendix).

Of the 52 chemicals on List 1, EPA recommended additional testing for human A or T endpoints for 5 chemicals. Specifically, additional testing to evaluate interaction with the androgen pathway was recommended for cypermethrin. For the remaining 4 chemicals (linuron, metribuzin, DCPA, and dimethoate), a comparative thyroid assay (CTA) was recommended to address concerns of potential interaction with the thyroid pathway. In the case of DCPA, a data call-in (DCI) under section 3 of the Federal, Insecticide, Fungicide, and Rodenticide Act (FIFRA) (GDCI-078701-1140) for a CTA was already issued by the Agency in 2013 and the Tier 1 WoE conclusion confirmed the need for this study.

Updates on Tier 1 Weight-of-Evidence Testing Recommendations for Human Androgen and Thyroid Endpoints for Five List 1 Chemicals

Following the completion of the Tier 1 WoE analyses, the HASPOC reconsidered the test recommendations for 4 of the 5 chemicals (Table 1) in 2017 and 2018. The HASPOC uses a WoE on the matters it addresses, including its approach in making recommendations to require additional studies, considering both hazard and exposure information. This approach considers multiple lines of evidence, such as the physical-chemical properties of the chemical, the available toxicity data for the chemical and structurally related chemicals, the chemical's use

[2] In addition to List 1, a second list of chemicals (referred to as List 2) was identified for Tier 1 screening under the EDSP in response to direction in a fiscal year 2010 House Appropriations Committee report and issued the 2013 Federal Register Notice. 78 FR 35922 (June 14, 2013). Although some of the chemicals on List 2 are addressed in the registration review plan announced in strategy 3 of the notice, "Endocrine Disruptor Screening Program (EDSP); Near-Term Strategies for Implementation," the status of EPA's approach to evaluating other List 2 chemicals will be addressed in future updates.

pattern and current risks, and any other pertinent data available (e.g., pharmacokinetic data) that could be used to characterize the potential risk from use of the chemical. Thus, HASPOC recommendations to require additional studies are informed by the totality of the data in a WoE analysis to ascertain if such data would lead to different risk management decisions.

HASPOC has utilized this WoE approach for over a decade to provide transparent and robust support for its recommendations. Furthermore, it has provided a consistent approach across chemicals for EPA to evaluate whether additional data will materially influence regulatory decisions. In particular, a more consistent approach has been applied in recent years when there is evidence of thyroid toxicity in a toxicological database. In those cases, the HASPOC is consulted to determine whether additional thyroid information, typically a CTA, is needed.

Table 1. Updates on Active Ingredients with Tier 1 WoE Memos Recommending Additional Data

Chemical	EDSP Tier 1 WoE Testing Recommendation	HASPOC Recommendation	HASPOC Memo Reference	Data Status
DCPA	CTA recommended. EDSP conclusion confirmed earlier need for CTA; DCI issued prior to EDSP review (GDCI-078701-1140)	NA	NA	Acceptable CTA study (MRID 51957801) submitted. https://www.regulations.gov/document/EPA-HQ-OPP-2011-0374-0080
Metribuzin	CTA recommended	CTA recommended	TXR 0057809; K. Yozzo, 11/28/2018	Acceptable CTA study (MRID 51670401) submitted. https://www.regulations.gov/document/EPA-HQ-OPP-2012-0487-0035
Dimethoate	CTA recommended	CTA not recommended	TXR 0057807; K. Yozzo, 12/3/2018	NA
Linuron	CTA recommended	CTA not recommended	TXR 0056555; A. Wray, 10/25/2017	NA
Cypermethrin	Recommended additional data to address androgen findings	No additional androgen-related data recommended	TXR 0047816; J. Camp, 12/18/2018	NA

For DCPA, in 2013, prior to issuance of the 2015 Tier 1 WoE memo, OPP issued a FIFRA DCI requiring the registrant to submit a CTA study. Following EPA's 2022 issuance of a Notice of Intent to Suspend the registration under FIFRA Section 3(c)(2)(B) for failure to submit that CTA study and other data, the DCPA registrant submitted an acceptable CTA study fulfilling that

portion of the DCI,[3] though the technical product registration has since been suspended for failing to submit other required data. Results from the CTA have been incorporated into selected endpoints and points of departure (PODs) used in the most recent occupational and residential exposure assessment for Registration Review (D. Carter; 18-MAY-2023; D467110)[4].

For the remaining 4 chemicals that were initially recommended for additional testing for the human A or T endpoints, new information, such as re-evaluation of critical data or updated use patterns and risk estimates, were considered in the HASPOC WoE evaluations. A summary of such information and re-evaluations for these 4 remaining chemicals is provided below and a table summarizing the outcomes for all 52 chemicals can be found in the Appendix to this document.

For metribuzin, the EDSP Tier 1 WoE review resulted in a recommendation for a CTA. In 2018, the HASPOC confirmed the need for the CTA (K. Yozzo; 28-NOV-2018; TXR# 0057809), and in 2021, the registrant for metribuzin submitted an acceptable study[5] to address the CTA testing need for this chemical. EPA found the effects observed in this study to be at dose levels above the current PODs for human health risk assessment, and thus current PODs are protective of effects on the thyroid.

Dimethoate is a member of the organophosphate (OP) class of pesticides. OPs have an established neurotoxic mode of action/adverse outcome pathway (MOA/AOP), where the initiating event involves inhibition of the enzyme acetylcholinesterase (AChE) leading to accumulation of acetylcholine and ultimately to neurotoxicity in the central and/or peripheral nervous system. AChE inhibition is the most sensitive endpoint in the toxicology database and used for human health risk assessment endpoints. In the EDSP WoE analysis, thyroid effects in the two-generation reproduction toxicity and rat carcinogenicity studies were described. The CTA was largely recommended for dimethoate due to increased thyroid weights noted in adult females at the lowest dose tested in the two-generation reproduction toxicity study (0.2 mg/kg/day), which was similar to the current POD for human health risk assessment that is based on AChE inhibition (0.22 mg/kg/day). However, this change in thyroid weight was not considered adverse given the lack of thyroid weight changes at higher doses and lack of corroborating histopathological findings at any dose level. The HASPOC recommended that a CTA not be required given the thyroid weight changes in the reproduction toxicity study were not considered adverse, as well as use of the most sensitive effect (AChE inhibition) for risk assessment endpoints that protects for other effects seen at much higher doses. Further, the current PODs are at least 35X lower than the thyroid effects observed in the rat carcinogenicity study, and thus a CTA is not expected to provide a more sensitive endpoint for risk assessment purposes (K. Yozzo; 3-DEC-2018; TXR 0057807).

For linuron, the EDSP WoE analysis resulted in a recommendation for a CTA primarily based on thyroid hormonal findings in adult animals in several OSRI studies. HASPOC was consulted

[3] https://www.regulations.gov/document/EPA-HQ-OPP-2011-0374-0080
[4] https://www.regulations.gov/document/EPA-HQ-OPP-2011-0374-0081
[5] https://www.regulations.gov/document/EPA-HQ-OPP-2012-0487-0035

after the registrant submitted a waiver request for the CTA, which argued that the dose levels resulting in decreased thyroid hormone levels were sufficiently above the dose levels that caused adverse hematological effects in dogs, which are the basis for current risk assessments endpoints and PODs for linuron. This waiver request included analysis of thyroid hormones using benchmark dose (BMD) modeling that was considered conservative. The HASPOC recommended that a CTA not be required because the results from the BMD analyses demonstrated the current POD would be protective of potential thyroid hormonal changes in the young, the current POD would also be protective of the increased quantitative sensitivity observed in the two-generation reproduction toxicity study, and chronic dietary risk estimates were not of concern (A. Wray; 25-OCT-2017; TXR 0056555).

Lastly, for cypermethrin, the EDSP WoE analysis resulted in a recommendation for additional data to address androgen findings due to concerns that the POD for human health risk assessment may not be protective of male reproductive effects observed in two literature studies published by the same laboratory (Hu et al., 2013; Li et al., 2013). These studies were reevaluated by the Health Effects Division (HED) with consultation from an Office of Research and Development (ORD) pathologist, which determined that the effects observed at the lowest doses in these literature studies were not considered toxicologically adverse due to the lack of a clear dose response in Hu et al. (2013) and the limited specificity for a pathological effect to be considered as the basis for the LOAEL in Li et al. (2013). The HASPOC was then consulted on the need for an androgen study taking into consideration the reevaluation of these literature studies. The HASPOC recommended that an androgen study not be required considering all available hazard and exposure information, including the lack of evidence of androgen effects in the guideline studies (including the two-generation reproduction toxicity study), the current PODs are protective of androgen effects observed in the literature studies, negligible chronic dietary risk, lack of any activity against the androgen receptor within the ToxCAST database[6], and the fact that an androgen study would not be expected to provide a lower POD for human health risk assessment (J. Camp; 18-DEC-2018; TXR# 0057816).

Summary of Additional Testing Recommendations for Wildlife for List 1 Chemicals

This document has focused on the status of testing recommendations for human health because, as mentioned previously, EPA is prioritizing data and assessments on potential impacts to the human E, A, or T systems at this time. However, the Tier 1 WoE evaluations also assessed the potential for List 1 chemicals to interact with the E, A, or T pathways for wildlife and provided recommendations on whether additional testing was warranted. For the 52 List 1 chemicals, EPA recommended additional testing for 17 chemicals. For the remaining 35 chemicals (33 active ingredients and 2 inert ingredients), EPA determined that the available data are sufficient for FFDCA section 408(p) assessment and review for potential effects to the E, A, or T pathways for

[6] 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 NAMs computational models. For more information, see https://www.epa.gov/chemical-research/toxicity-forecasting

wildlife. Therefore, there were no recommendations for additional testing for these chemicals in the Tier 1 WoE memos for these chemicals. Additional details can be found in the Appendix.

Conclusions

Taking into account the Tier 1 WoE memoranda and data discussed in those documents, HASPOC conclusions, and additional submitted data, EPA has determined that the available data are, at this time, sufficient to assess the potential for all List 1 chemical effects to human E, A, or T pathways for FFDCA section 408(p) purposes. In addition, for all List 1 chemicals except DCPA, the available data either show no E, A, or T activity or activity at dose levels that are higher than the regulated dose level in the human health risk assessment, and thus EPA has determined that use of these chemicals under the current regulations are protective of public health, as required by FFDCA section 408(p)(6). For DCPA, taking into account all data available, the Agency issued a revised occupational risk assessment identifying risks to human thyroid pathways for occupational users and is currently in discussions with the registrant concerning potential mitigation actions. The Agency will pursue any necessary steps to address the risks identified.

During the List 1 WoE analyses, no additional testing for wildlife was recommended for 35 chemicals. Thus, in each of these 35 cases, EPA has determined that the available data are sufficient for FFDCA section 408(p) assessment for potential effects to the E, A, or T pathways for both humans and wildlife. For the remaining 17, these recommendations will be further addressed in subsequent updates on implementation of the EDSP.

Appendix

Summary of Tier 1 WoE Review for All EDSP List 1 Pesticide Chemicals.

Chemical Name	CAS Number	EDSP Tier 1 WoE Conclusions	Links to EDSP Tier 1 Screening Determinations/WoE Assessments	Tier 2 Recommended for Humans	Tier 2 Recommended for Wildlife
2,4-D	94-75-7	No convincing evidence of potential interaction with estrogen, androgen or thyroid pathways	2,4-D EDSP Weight of Evidence Conclusions on the Tier 1 Screening Assays (PDF)	None	None
Abamectin	71751-41-2	No convincing evidence of potential interaction with estrogen, androgen or thyroid pathways	Abamectin EDSP Weight of Evidence Conclusions on the Tier 1 Screening Assays (PDF)	None	None
Acephate	30560-19-1	No convincing evidence of potential interaction with estrogen, androgen or thyroid pathways	Acephate EDSP Weight of Evidence Conclusions on the Tier 1 Screening Assays (PDF)	None	None
Acetone	67-64-1	No convincing evidence of potential interaction with estrogen, androgen or thyroid pathways	Acetone EDSP Weight of Evidence Conclusions on the Tier 1 Screening Assays (PDF)	None	None
Atrazine	1912-24-9	Evidence for potential interaction with the estrogen and androgen pathway. Chlorotriazines, including simazine, function through a neuroendocrine MOA that suppresses the surge of luteinizing hormone which may result in downstream effects on estrogen and androgen signaling pathways. No convincing evidence of potential interaction with the thyroid pathway in mammals or wildlife. EDSP Tier 2 testing is not recommended at this time because it is not expected to impact current EPA-established regulatory endpoints for human health or ecological risk assessment.	Atrazine EDSP Weight of Evidence Conclusions on the Tier 1 Screening Assays (PDF)	None	None

Chemical Name	CAS Number	EDSP Tier 1 WoE Conclusions	Links to EDSP Tier 1 Screening Determinations/WoE Assessments	Tier 2 Recommended for Humans	Tier 2 Recommended for Wildlife
Benfluralin	1861-40-1	Available data suggests that the antiestrogenic, anti-androgenic and anti-thyroid effects observed in the mammalian in vivo Tier 1 assays may result from liver enzyme induction and subsequent increased hormone clearance. However, there is no convincing evidence for an interaction with estrogen, androgen or thyroid pathways in wildlife. EDSP Tier 2 testing is not recommended at this time because it is not expected to impact current EPA-established regulatory endpoints for human health or ecological risk assessment.	Benfluralin EDSP Weight of Evidence Conclusions on the Tier 1 Screening Assays (PDF)	None	None
Bifenthrin	82657-04-3	No convincing evidence of potential interaction with estrogen, androgen or thyroid pathways	Bifenthrin EDSP Weight of Evidence Conclusions on the Tier 1 Screening Assays (PDF))	None	None
Captan	133-06-2	No convincing evidence of potential interaction with estrogen, androgen or thyroid pathways	Captan EDSP Weight of Evidence Conclusions on the Tier 1 Screening Assays (PDF)	None	None
Carbaryl	63-25-2	No convincing evidence for interaction with the estrogen or thyroid pathways, in mammals or wildlife. There is also no convincing evidence for interaction with the androgen pathway in mammals. Evidence suggests potential interaction with the androgen pathway in fish.	Carbaryl EDSP Weight of Evidence Conclusions on the Tier 1 Screening Assays (PDF)	None	MEOGRT
Carbofuran (Note: only import tolerances remain)	1563-66-2	No evidence of potential interaction with the estrogen or androgen pathways. There is no convincing evidence of thyroid interaction in mammals. There is evidence of potential interaction with the thyroid pathway in the AMA. However, at present, all U.S.	Carbofuran EDSP Weight of Evidence Conclusions on the Tier 1 Screening Assays (PDF)	None	None

Chemical Name	CAS Number	EDSP Tier 1 WoE Conclusions	Links to EDSP Tier 1 Screening Determinations/WoE Assessments	Tier 2 Recommended for Humans	Tier 2 Recommended for Wildlife
		uses/registrations have been canceled and only import tolerances remain for carbofuran.			
Chlorothalonil	1897-45-6	No convincing evidence of potential interaction with the estrogen or androgen pathways in mammals or wildlife, and no thyroid effects in mammals. Results of the AMA suggest a potential interaction with the thyroid pathway in amphibians	Chlorothalonil EDSP Weight of Evidence Conclusions on the Tier 1 Screening Assays (PDF)	None	LAGDA
Chlorpyrifos	2921-88-2	No convincing evidence of potential interaction with estrogen, androgen or thyroid pathways	Chlorpyrifos EDSP Weight of Evidence Conclusions on the Tier 1 Screening Assays (PDF)	None	None
Cyfluthrin	68359-37-5	No convincing evidence of potential interaction with estrogen, androgen or thyroid pathways	Cyfluthrin EDSP Weight of Evidence Conclusions on the Tier 1 Screening Assays (PDF)	None	None
Cypermethrin	52315-07-8	There was no convincing evidence for potential interaction with the estrogen or thyroid pathways. There was convincing evidence for potential interaction with the androgen pathway	Cypermethrin EDSP Weight of Evidence Conclusions on the Tier 1 Screening Assays (PDF)	Androgen study in adult male mammals.	MEOGRT
DCPA	1861-32-1	There was no convincing evidence for potential interaction with estrogen or androgen pathways. The was convincing evidence of an interaction with the thyroid pathway	DCPA EDSP Weight of Evidence Conclusions on the Tier 1 Screening Assays (PDF)	CTA	LAGDA
Diazinon	333-41-5	No convincing evidence of potential interaction with estrogen, androgen or thyroid pathways	Diazinon EDSP Weight of Evidence Conclusions on the Tier 1 Screening Assays (PDF)	None	None
Dichlobenil	1194-65-6	There is no convincing evidence for interaction with the estrogen or thyroid pathways. There is evidence for potential for interaction with the androgen pathway. Mammalian EDSP Tier 2 testing is not recommended for dichlobenil since additional testing will	Dichlobenil EDSP Weight of Evidence Conclusions on the Tier 1 Screening Assays (PDF)	None	MEOGRT

Chemical Name	CAS Number	EDSP Tier 1 WoE Conclusions	Links to EDSP Tier 1 Screening Determinations/WoE Assessments	Tier 2 Recommended for Humans	Tier 2 Recommended for Wildlife
		not impact the regulatory endpoints used for human health risk assessments. EDSP Tier 2, Medaka Extended One Generation Reproduction Test (MEOGRT) is recommended due to the potential interaction with the androgen pathway and the effects observed in the FSTRA			
Dimethoate	60-51-5	There was no convincing evidence of potential interaction with the androgen signaling pathway in mammals or wildlife. There was evidence of potential interaction with the thyroid pathway. The finding in the thyroid pathway in the AMA does not impact the ecological risk assessment	Dimethoate EDSP Weight of Evidence Conclusions on the Tier 1 Screening Assays (PDF)	CTA	None
EPTC	759-94-4	No convincing evidence of potential interaction with estrogen, androgen or thyroid pathways	EPTC EDSP Weight of Evidence Conclusions on the Tier 1 Screening Assays (PDF)	None	None
Esfenvalerate	66230-04-4	No convincing evidence for an interaction with the estrogen androgen pathway in mammals or wildlife. There is no convincing evidence of thyroid interactions in mammals. No conclusion can be made for potential thyroid interaction in non-mammalian species. Based on weight of evidence conclusions, mammalian or wildlife EDSP Tier 2 testing is not recommended	Esfenvalerate EDSP Weight of Evidence Conclusions on the Tier 1 Screening Assays (PDF)	None	None
Ethoprop	13194-48-4	No convincing evidence for potential interaction with the estrogen or androgen-pathway for mammals and wildlife. Ethoprop appears to interact with the thyroid pathway only in mammals and the interaction is seen only at doses that caused severe cholinesterase inhibition.	Ethoprop EDSP Weight of Evidence Conclusions on the Tier 1 Screening Assays (PDF)	None	None

Chemical Name	CAS Number	EDSP Tier 1 WoE Conclusions	Links to EDSP Tier 1 Screening Determinations/WoE Assessments	Tier 2 Recommended for Humans	Tier 2 Recommended for Wildlife
Fenbutatin oxide	13356-08-6	No convincing evidence of potential interaction with estrogen, androgen or thyroid pathways	Fenbutatin oxide EDSP Weight of Evidence Conclusions on the Tier 1 Screening Assays (PDF)	None	None
Flutolanil	66332-96-5	No convincing evidence of potential interaction with estrogen, androgen or thyroid pathways in mammals. Potential interactions with estrogen and androgen pathways were observed in fish. There was no convincing evidence of interaction with the thyroid pathway in wildlife.	Flutolanil EDSP Weight of Evidence Conclusions on the Tier 1 Screening Assays (PDF)	None	MEOGRT
Folpet	133-07-3	No convincing evidence for potential interaction of folpet with the estrogen pathway in mammals. Potential estrogenic effects were observed in Fish. No androgen-related effects were seen in any of the mammalian studies. No convincing evidence of thyroid activity was observed in mammals or wildlife.	Folpet EDSP Weight of Evidence Conclusions on the Tier 1 Screening Assays (PDF)	None	MOEGRT
Gardona (cis-isomer)/ Tetrachlorvinphos	22248-79-9	No convincing evidence of potential interaction with estrogen or androgen pathways in mammals or wildlife. There was evidence for potential interaction with the thyroid pathway in mammals; however, additional testing will not impact current EPA established regulatory point of departure or endpoint for human health risk assessments. No convincing evidence of thyroid interactions in wildlife	Gardona (cis-isomer)/ Tetrachlorvinphos EDSP Weight of Evidence Conclusions on the Tier 1 Screening Assays (PDF)	None	None
Glyphosate	1071-83-6	No convincing evidence of potential interaction with estrogen, androgen or thyroid pathways	Glyphosate EDSP Weight of Evidence Conclusions on the Tier 1 Screening Assays (PDF)	None	None
Imidacloprid	138261-41-3	No convincing evidence of potential interaction with estrogen, androgen or thyroid pathways	Imidacloprid EDSP Weight of Evidence Conclusions on the Tier 1 Screening Assays (PDF)	None	None

Chemical Name	CAS Number	EDSP Tier 1 WoE Conclusions	Links to EDSP Tier 1 Screening Determinations/WoE Assessments	Tier 2 Recommended for Humans	Tier 2 Recommended for Wildlife
Iprodione	36734-19-7	There appears to be a potential for iprodione to alter steriodogenesis, which may affect the estrogen and androgen pathways in mammals and wildlife. Mammalian EDSP Tier 2 testing is not recommended since additional testing is not expected to impact EPA's current regulatory point of departures and endpoints for human health risk assessments. Tier 2 data in fish are recommended. There is no convincing evidence of an interaction with the thyroid pathway in mammals or wildlife.	Iprodione EDSP Weight of Evidence Conclusions on the Tier 1 Screening Assays (PDF)	None	MOEGRT
Isophorone	78-59-1	No convincing evidence of potential interaction with estrogen, androgen or thyroid pathways	Isophorone EDSP Weight of Evidence Conclusions on the Tier 1 Screening Assays (PDF)	None	None
Linuron	330-55-2	No convincing evidence of potential interaction with estrogen pathway. For the androgen pathway, linuron appears to act as an anti-androgen both in vitro and in vivo. Tier 2 testing for androgen activity is not recommended since additional testing is not expected to impact EPA's current regulatory point of departures and endpoints for human health risk assessments. Given the potential for androgen-related effects in fish, the EDSP Tier 2 MEGORT is recommended. For the thyroid pathway, there is evidence of potential interaction in mammals and additional thyroid testing is recommended.	Linuron EDSP Weight of Evidence Conclusions on the Tier 1 Screening Assays (PDF)	CTA	MEOGRT and LAGDA
Malathion	121-75-5	No convincing evidence of potential interaction with estrogen, androgen or thyroid pathways	Malathion EDSP Weight of Evidence Conclusions on the Tier 1 Screening Assays (PDF)	None	None

Chemical Name	CAS Number	EDSP Tier 1 WoE Conclusions	Links to EDSP Tier 1 Screening Determinations/WoE Assessments	Tier 2 Recommended for Humans	Tier 2 Recommended for Wildlife
Metalaxyl	57837-19-1	No evidence of potential interaction with the estrogen, androgen or thyroid pathways in mammals. There is a potential for interaction with the estrogen and androgen pathway in fish. Existing Part 158 avian reproduction studies data are considered sufficient for evaluating potential reproductive effects to birds. No evidence of potential thyroid interactions in amphibians.	Metalaxyl EDSP Weight of Evidence Conclusions on the Tier 1 Screening Assays (PDF)	None	MOEGRT
Methomyl	16752-77-5	No convincing evidence of potential interaction with estrogen, androgen or thyroid pathways	Methomyl EDSP Weight of Evidence Conclusions on the Tier 1 Screening Assays (PDF)	None	None
Metolachlor	51218-45-2	There is no convincing evidence of an interaction with estrogen or androgen pathways. Thyroid effects were observed in mammals; however, mammalian Tier 2 testing is not recommended since additional testing is not expected to impact EPA's current regulatory point of departures and endpoints for human health risk assessments.	Metolachlor EDSP Weight of Evidence Conclusions on the Tier 1 Screening Assays (PDF)	None	None
Metribuzin	21087-64-9	No convincing evidence of potential interaction with estrogen and androgen pathways. Evidence supporting a potential interaction with the thyroid pathway was observed in Tier 1 and OSRI in adult animals.	Metribuzin EDSP Weight of Evidence Conclusions on the Tier 1 Screening Assays (PDF)	CTA	LAGDA
MGK 264	113-48-4	Evidence of potential interaction of MGK 264 with the estrogen and thyroid pathways in mammals but not in fish or amphibians. There was no evidence of potential interaction with the androgen pathway either in mammals or fish. Mammalian EDSP Tier 2 testing is not recommended for MGK 264 since additional testing is not expected to	MGK 264 EDSP Weight of Evidence Conclusions on the Tier 1 Screening Assays (PDF)	None	None

Chemical Name	CAS Number	EDSP Tier 1 WoE Conclusions	Links to EDSP Tier 1 Screening Determinations/WoE Assessments	Tier 2 Recommended for Humans	Tier 2 Recommended for Wildlife
		impact EPA's current regulatory point of departures and endpoints for human health risk assessments.			
Myclobutanil	88671-89-0	Myclobutanil potentially alters steroidogenesis which may affect estrogen and androgen pathways in fish. Mammalian EDSP Tier 2 testing is not recommended for myclobutanil since additional testing is unlikely to impact the current EPA established regulatory endpoints for human risk assessments. Myclobutanil is not likely to interact with the thyroid pathway.	Myclobutanil EDSP Weight of Evidence Conclusions on the Tier 1 Screening Assays (PDF)	None	MOEGRT
Norflurazon	27314-13-2	No convincing evidence for a potential interaction with the estrogen or androgen pathways for mammals or wildlife. Thyroid effects were observed in mammals; however, mammalian Tier 2 testing is not recommended since additional testing is not expected to impact EPA's current regulatory point of departures and endpoints for human health risk assessments.	Norflurazon EDSP Weight of Evidence Conclusions on the Tier 1 Screening Assays (PDF)	None	None
O-phenylphenol	90-43-7	No convincing evidence of potential interaction with the estrogen, androgen or thyroid pathways in mammals. There is evidence of potential interaction with the estrogen pathway in fish. No convincing evidence of potential interactions of androgen or thyroid pathways in wildlife.	O-phenylphenol EDSP Weight of Evidence Conclusions on the Tier 1 Screening Assays (PDF)	None	MEOGRT
Oxamyl	23135-22-0	No convincing evidence of potential interaction with estrogen, androgen or thyroid pathways	Oxamyl EDSP Weight of Evidence Conclusions on the Tier 1 Screening Assays (PDF)	None	None
PCNB	82-68-8	No evidence of potential interaction of PCNB with the estrogen pathway in the mammals. However, PCNB may	PCNB EDSP Weight of Evidence Conclusions on the Tier 1 Screening Assays (PDF)	None	MEOGRT

Chemical Name	CAS Number	EDSP Tier 1 WoE Conclusions	Links to EDSP Tier 1 Screening Determinations/WoE Assessments	Tier 2 Recommended for Humans	Tier 2 Recommended for Wildlife
		potentially interact with the estrogen pathway in wildlife. No convincing evidence of potential interaction of androgen pathway with the mammals or wildlife. There is evidence of potential interaction of PCNB with the thyroid pathway in mammals, but not wildlife. Mammalian EDSP Tier 2 testing is not recommended since additional testing is not expected to impact EPA's current regulatory point of departures and endpoints for human health risk assessments. Tier 2 testing in fish is recommended based on the concentration where responses were observed in the FSTRA.			
Permethrin	52645-53-1	No convincing evidence of potential interaction with the estrogen or thyroid pathways in mammals or wildlife. There is evidence for potential interaction with the androgen pathway in mammals, but not wildlife. Mammalian Tier 2 testing is not recommended since additional testing is not expected to impact EPA's current regulatory point of departures and endpoints for human health risk assessments.	Permethrin EDSP Weight of Evidence Conclusions on the Tier 1 Screening Assays (PDF)	None	None
Phosmet	732-11-6	No convincing evidence for a potential interaction with the estrogen or androgen pathway in mammals or wildlife. The available data indicate a potential interaction with the thyroid pathway in mammals, but not amphibians. mammalian EDSP Tier 2 testing is not recommended since additional testing is not expected to impact EPA's current regulatory point of departures and	Phosmet EDSP Weight of Evidence Conclusions on the Tier 1 Screening Assays (PDF)	None	None

Chemical Name	CAS Number	EDSP Tier 1 WoE Conclusions	Links to EDSP Tier 1 Screening Determinations/WoE Assessments	Tier 2 Recommended for Humans	Tier 2 Recommended for Wildlife
		endpoints for human health risk assessments.			
Piperonyl butoxide	51-03-6	No convincing evidence of potential interaction with estrogen, androgen or thyroid pathways	Piperonyl butoxide EDSP Weight of Evidence Conclusions on the Tier 1 Screening Assays (PDF)	None	None
Propargite	2312-35-8	No convincing evidence of potential interaction with the estrogen or androgen pathways in mammals and wildlife. There was evidence for potential interaction with the thyroid pathway. Mammalian EDSP Tier 2 testing is not recommended for propargite since additional testing is not expected to impact EPA's current regulatory point of departures and endpoints for human health risk assessments. Ecological effect studies with amphibians are not available to add to the understanding of potential adverse effects to amphibians.	Propargite EDSP Weight of Evidence Conclusions on the Tier 1 Screening Assays (PDF)	None	LAGDA
Propiconazole	60207-90-1	Potential to inhibit aromatase and steroidogenesis. However, there was no convincing evidence of estrogen-related or androgen effects in the mammalian studies. In fish, however, there were effects on estrogen- and androgen-related endpoints that could potentially be attributed to altered steroidogenesis. There was no interaction with the thyroid pathway either in mammals or wildlife.	Propiconazole EDSP Weight of Evidence Conclusions on the Tier 1 Screening Assays (PDF)	None	MOEGRT
Propyzamide	23950-58-5	No convincing evidence of potential to interact with the estrogen pathway in mammals or wildlife. There is potential evidence of interaction with the androgen pathway (mammals and wildlife) and thyroid pathway (mammals only). Tier 2 testing is not recommended	Propyzamide EDSP Weight of Evidence Conclusions on the Tier 1 Screening Assays (PDF)	None	None

Chemical Name	CAS Number	EDSP Tier 1 WoE Conclusions	Links to EDSP Tier 1 Screening Determinations/WoE Assessments	Tier 2 Recommended for Humans	Tier 2 Recommended for Wildlife
		since additional testing is not expected to impact EPA's current regulatory point of departures and endpoints for human health risk assessments or impact ecological risk assessments.			
Pyriproxyfen	95737-68-1	No convincing evidence for potential interaction with the estrogen pathway in mammals or wildlife. In mammals, there was limited evidence of potential interaction with the androgen and thyroid pathways. The evidence suggests potential interaction with the androgen pathway in fish. There is no convincing evidence of potential interaction with the thyroid pathway in amphibians. Tier 2 testing is not recommended since additional testing is not expected to impact EPA's current regulatory point of departures and endpoints for human health risk assessments or impact ecological risk assessments.	Pyriproxyfen EDSP Weight of Evidence Conclusions on the Tier 1 Screening Assays (PDF)	None	None
Simazine	122-34-9	Evidence for potential interaction with the estrogen and androgen pathway. Chlorotriazines, including simazine, function through a neuroendocrine MOA that suppresses the surge of luteinizing hormone which may result in downstream effects on estrogen and androgen signaling pathways. No convincing evidence of potential interaction with the thyroid pathway in mammals or wildlife. EDSP Tier 2 testing is not recommended at this time because it is not expected to impact current EPA-established regulatory endpoints for human health or ecological risk assessment.	Simazine EDSP Weight of Evidence Conclusions on the Tier 1 Screening Assays (PDF)	None	None

Chemical Name	CAS Number	EDSP Tier 1 WoE Conclusions	Links to EDSP Tier 1 Screening Determinations/WoE Assessments	Tier 2 Recommended for Humans	Tier 2 Recommended for Wildlife
Tebuconazole	107534-96-3	Tebuconazole showed potential to alter the steroidogenesis pathway which may result in endocrine-related effects in the estrogen and androgen pathways. There was no convincing evidence of an interaction with the thyroid pathway either in mammals or wildlife. Based on weight of evidence considerations, mammalian EDSP Tier 2 testing is not recommended for tebuconazole since additional testing will not impact the current EPA established regulatory endpoints for human health risk assessments. Since the reproductive effects observed in the FSTRA and Fish Sexual Development Test occur at concentrations similar or below the current NOAEC, additional information on potential reproductive effects is recommended.	Tebuconazole EDSP Weight of Evidence Conclusions on the Tier 1 Screening Assays (PDF)	None	MEOGRT
Triadimefon	43121-43-3	No convincing evidence of potential interaction with estrogen, androgen or thyroid pathways	Triadimefon EDSP Weight of Evidence Conclusions on the Tier 1 Screening Assays (PDF)	None	None
Trifluralin	1582-09-8	No convincing evidence of potential interaction with the estrogen or androgen pathways. Thyroid effects were observed in the mammalian in vivo studies, but not wildlife. Mammalian EDSP Tier 2 testing is not recommended for trifluralin since additional testing is unlikely to impact the current EPA established regulatory endpoints for human risk assessments.	Trifluralin EDSP Weight of Evidence Conclusions on the Tier 1 Screening Assays (PDF)	None	None