Acephate

Proposed Interim Registration Review Decision
Case Number 0042

April 2024

Approved by: _____

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I. INTRODUCTION

This document is the Environmental Protection Agency's (EPA or the Agency) Proposed Interim Registration Review Decision (PID) for acephate (PC Code 103301, case 0042). Acephate is an organophosphate (OP) insecticide registered for use on a variety of agricultural crops, commercial and on-farm seed treatments, for use in outdoor non-agricultural settings (building foundations/perimeters, non-residential lawns/ornamentals, golf courses, non-crop areas, sod farms, and as ant mount treatment on residential lawns/ornamentals), for indoor treatment of commercial/industrial buildings, and for use in greenhouses on ornamental plants. Acephate was first registered in 1973. The Agency completed a reregistration eligibility decision (RED) for acephate in 2006.

The Federal Insecticide, Fungicide, Rodenticide Act (FIFRA)[1] mandates a periodic review of existing pesticide registrations every 15 years, referred to as registration review.[2] During registration review, the Agency ultimately determines whether a currently registered pesticide continues to meet FIFRA's registration standard.[3] Where appropriate, the Agency may issue an Interim Registration Review Decision (ID) before completing a final registration review decision.[4] However, issuance of an ID is not a decision on whether a pesticide's registrations continue to satisfy the FIFRA standard for registration.[5] Rather, the ID may include mitigation measures and changes to labeling that EPA has determined would address risks of concern, identify data or information needed to complete registration review, and include schedules for submitting such data, conducting the new risk assessment, and completing the registration review.[6] The Agency is issuing this PID for acephate to identify risk mitigations that EPA has determined would address risks of concern for acephate, as presented in Section IV and Appendices A and B.

EPA has not yet fully evaluated acephate's effects on federally threatened and endangered (listed) species or designated critical habitats. However, consistent with its obligations under the Endangered Species Act (ESA)[7], EPA expects to complete effects determinations and any necessary consultation with the U.S. Fish and Wildlife Service and the National Marine Fisheries

[1] Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), 7 U.S.C. §§ 136–136w-8.
[2] For more information on the registration review program, see http://www.epa.gov/pesticide-reevaluation.
[3] FIFRA § 3(g), 7 U.S.C. § 136a(g); 40 C.F.R. § 155.57; *see also* FIFRA § 3(c)(5).
[4] 40 C.F.R. §§ 155.56, 155.58. Consistent with 40 C.F.R. § 155.58, EPA must first issue and take comment on a PID before issuing an ID.
[5] At the end of the registration review process, EPA will decide whether a pesticide registration "continues to satisfy the FIFRA standard for registration." 40 C.F.R. §§ 155.40(a), 155.57; FIFRA § 3(g), 7 U.S.C. § 136a(g); *see also* FIFRA § 3(c)(5), 7 U.S.C. § 136a(c)(5) (FIFRA registration standard); FIFRA § 2(bb), 7 U.S.C. § 136(bb) (defining "unreasonable adverse effects on the environment" as encompassing both "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" [FIFRA's risk-benefit standard] and "a human dietary risk from residues that result from a use of a pesticide in or on any food inconsistent with the [FFDCA safety standard]"). This document is not a "registration review decision" within the meaning of FIFRA Section 3(g) and 40 C.F.R. § 155.57.
[6] 40 C.F.R. § 155.56.
[7] Endangered Species Act (ESA) § 7, 16 U.S.C. § 1536.

Service (the Services) before completing the acephate registration review and issuing a final registration review decision. Under a settlement in *Center for Biological Diversity, et. al., v. United States Environmental Protection Agency, et al.*, No. 3:11 cv 0293 (N.D .Cal.), EPA committed to complete a final biological evaluation for potential effects of eight active ingredients on ESA-listed endangered and threatened species and designated critical habitat including acephate by September 30, 2027. For more information on EPA's ESA obligations during registration review, see Appendix C.

EPA continues to work with the Services to improve the consultation process for pesticides in registration review. In April 2022, EPA released its ESA Workplan, which outlines strategies and actions for the Agency to meet its ESA obligations for FIFRA actions.[8] Consistent with the ESA Workplan, EPA is focused on steps it will take during registration review to reduce exposure for listed species as it moves toward fulfilling its ESA obligations and making final registration review decisions. In November 2022, EPA released its first ESA Workplan Update.[9] As part of this update, EPA announced that, going forward, EPA may include a variety of FIFRA Interim Ecological Mitigation (IEM) measures in its registration review decisions that seek to reduce exposures for non-target organisms based on its FIFRA ecological risk assessment(s). EPA expects that this mitigation may also reduce pesticide exposures for listed species.

While these mitigation measures may not satisfy EPA's ESA obligations, EPA has determined that early mitigation may shorten the consultation process and improve protections for listed species from currently registered pesticide products. EPA also believes that the FIFRA IEM measures that the Agency is proposing for Acephate in this PID (Section IV.B) would fulfill EPA's obligations under Section 711 of the Consolidated Appropriations Act, PL-117-328 (Dec. 29, 2022). Among other things, Section 711 requires EPA to "include, where applicable, measures to reduce the effect of the applicable pesticide on" listed species and designated critical habitats in any ID noticed in the Federal Register between December 29, 2022 and October 1, 2026 for which EPA has not "made effects determinations or completed any necessary consultation under [ESA Section 7(a)(2)]."

Before completing registration review, EPA will also include a determination on its obligations for acephate under the endocrine disruptor screening program per section 408(p) of the Federal Food, Drug, and Cosmetic Act (FFDCA).[10] For more information on the endocrine disruptor screening for the acephate registration review, see Appendix D.

This document is organized in five sections:

- *Introduction* (summarizing the registration review milestones and responding to public comments);

[8] *Balancing Wildlife Protections and Responsible Pesticide Use* (Apr. 2022), https://www.epa.gov/system/files/documents/2022-04/balancing-wildlife-protection-and-responsible-pesticide-use_final.pdf.
Docket Number EPA-HQ-OPP-2008-0915
[10] Federal Food, Drug, and Cosmetic Act (FFDCA) § 408(p), 21 U.S.C. § 346a(p).

- *Use and Usage* (discussing how acephate may legally be used and where acephate is actually used);
- *Scientific Assessments* (summarizing EPA's risk and benefits assessments, updating or revising previous risk assessments, and discussing risk characterization);
- *Proposed Interim Registration Review Decision* (presenting EPA's proposed interim decision, regulatory rationale, and any mitigation measures to address risks of concern); and
- *Next Steps and Timeline* (discussing how and when EPA intends to complete registration review).

A. Summary of Acephate Registration Review

On March 18, 2009, the Agency formally initiated registration review for acephate with the opening of the registration review docket for the case.[11] The following summary highlights the docket opening and other significant milestones that have occurred thus far during the registration review of acephate:

- March 2009 – EPA posted the *Acephate Summary Document Registration Review: Initial Docket March 2009*, *Acephate. Human Health Assessment Scoping Document in Support of Registration Review* (January 8, 2009), and *Registration Review – Preliminary Problem Formulation for the Ecological Risk Assessment of Acephate* (January 5, 2009) to the public docket for a 60-day public comment period.

- September 2009 – EPA posted the *Acephate Final Work Plan for Registration Review* (FWP) (August 26, 2009) to the public docket. The Agency received two comments on the PWP, which did not change the schedule, risk assessment needs, or anticipated data requirements. The FWP identified both ecological and human health data needs for acephate, along with data on methamidophos, a degradate of acephate.

- November 2010 – EPA issued a generic data call-in (GDCI) for acephate to obtain data needed to conduct the registration review risk assessments (GDCI-103301-917). All required data were not fulfilled or waived, but the Agency was able to perform risk analysis without these data.

- June 2015 – The Agency completed its weight of evidence review of the Tier I assays required under the Endocrine Disruptor Screening Program (EDSP). Acephate was not recommended for additional endocrine testing.

[11] 40 C.F.R. § 155.50

- May 2018 – EPA posted *Revised Draft Human Health Risk Assessment (DRA) in support of Registration Review* (2018 HH DRA) and *Preliminary Ecological Risk Assessment for Registration Review of Acephate* (2017 Eco DRA) for a 60-day public comment period. The Agency received 12 comments during the comment period. The Agency has summarized and responded to these comments in Section I.B., below. The comments did not change the risk assessments or registration review timeline for acephate.

- August 2023 – EPA posted the *Second Revised Draft Human Health Risk Assessment (DRA) in Support of Registration Review* (2023 HH DRA) and *Acephate Refined Drinking Water Assessment for Registration Review, July 21, 2023* (2023 DWA). In addition, the following documents were also posted to the registration review docket for acephate:

    - Acephate: Second Revised Draft Human Health Risk Assessment (DRA) in Support of Registration Review, August 24, 2023.
    - Acephate. Second Dietary Exposure and Risk Assessments in Support of Registration Review, August 22, 2023.
    - Acephate. Second Revised Occupational and Residential Exposure Assessment for Registration Review, August 22, 2023.
    - Evaluation of the Developmental Neurotoxicity Potential of Acephate/Methamidophos to Inform the FQPA Safety Factor, August 24, 2023.
    - Acephate Refined Drinking Water Assessment for Registration Review, July 21, 2023.
    - Approach for Evaluating Developmental Neurotoxicity Potential for the Organophosphate Pesticides, April 10, 2023.
    - Acephate: Tier II Review of Human Incidents and Epidemiology for the Draft Risk Assessment, July 28, 2023.
    - Acephate (103301) National and State Summary Use and Usage Matrix (SUUM), Revised August 15, 2023.
    - Acephate (103301) National and State Summary Use and Usage Matrix (SUUM), April 4, 2022.
    - Updated Acephate (103301) Screening Level Usage Analysis (SLUA), January 28, 2021.
    - Non-Agricultural Usage Data for Acephate (103301), October 28, 2016.
    - Data Evaluation Record (DER) Addendum No. 1 to MRID 49092101, July 25, 2023.

- April 2024 – EPA completed the PID for acephate and made it available in the public docket for a 60-day public comment period. Comments on the 2023 HH DRA and 2023 DWA will be accepted during this comment period. Along with the PID, EPA posted the following documents to the public docket:
    - *Overview of the Usage of Acephate and Pest Management Benefits for Tobacco, Peanut, Mint, and Cranberry Production (PC# 103301)*, April 4, 2024.
    - *Assessment of the Usage and Pest Management Benefits of Acephate (PC# 103301) for Soybean Production*, April 11, 2024.

- *Assessment of the Usage and Pest Management Benefits of Acephate, an Organophosphate Insecticide, on Cotton (PC# 103301)*, April 10, 2024.
- *Usage and Pest Management Benefits of Acephate, an Organophosphate Insecticide, in Vegetable, Bean, and Seed Crops (PC# 103301)*, April 8, 2024.
- *Usage and Pest Management Benefits of Acephate, an Organophosphate Insecticide, in Non-Food Agricultural and Non-Agricultural Use Sites (PC# 103301)*, April 22, 2024.

B. Summary of Public Comments on the Draft Risk Assessments and Agency Responses

The 60-day public-comment period for the acephate 2017 Eco RA and 2018 HH DRA was open from May 24, 2018 to July 23, 2018, subsequently extended 30 days (to August 22, 2018) and later extended another 30 days (to September 21, 2018). The Agency received 16 public comments. Comments were submitted by: the Acephate Task Force, Arizona Farm Bureau Federation, Arizona Pest Management Center, Arysta LifeScience North America, Center for Biological Diversity, Creative Sales Incorporated, Georgia Farm Bureau, Mississippi Agricultural Consultants Association, National Cotton States Arthropod Pest Management Working Group, Oregon State University Integrated Plant Protection Center, United States Department of Agriculture Office of Pest Management Policy, and the University of Tennessee West Tennessee Research and Education Center. The National Cotton Council submitted three comments. There was also an anonymous comment unrelated to the registration review of acephate. The Agency has summarized and responded to all substantive comments and comments of a broader regulatory nature below. The Agency thanks all commenters for participating and has considered all comments in developing this PID.

Comments Submitted by Arysta LifeScience North America, LLC (Docket ID: EPA-HQ-OPP-2008-0915-0043)

Comment: Arysta commented on EPA's assumptions and methodologies in the 2017 DWA and 2018 HH DRA for acephate. Specifically, Arysta commented that EPA's use of 100X inter- and intra-species safety factor (SF) is not supported by the data. Arysta noted that acephate displays a steady state of acetylcholinesterase (AChE) inhibition after repeat exposure; that toxicokinetic studies show no significant difference between rats and humans; that an *in vitro* study on rats shows lower brain inhibition concentration which should be protective of humans; that data cited from a 2005 Joint FAO/WHO meeting on pesticide residues (JMPR) document[12] for dogs and monkeys *in vivo* indicate brain and erythrocyte are nearly equal at any given dose, and that a 28-day repeat-dose study in humans all suggest the SF for humans could be 10X. Additionally, Arysta suggested the EPA's assumption of 100% conversion of acephate to methamidophos to calculate estimated drinking water concentrations (EDWCs) is overly conservative as is EPA's dietary assessment at the 99.9th percentile.

[12] JMPR (2005). Pesticide Residues in Food. Joint FAO/WHO meeting on pesticide residues. Document 142. http://apps.who.int/pesticide-residues-jmpr-database/Document/142

EPA Response: The most recent acephate draft risk assessment from 2023 (R. Louden, 24-AUG-2023, D463758) reduced the Food Quality Protection Act (FQPA) safety factor (SF) to 1X based on a weight-of-evidence approach, but keeps the interspecies and intraspecies uncertainty factors (Ufs) at 10X for each (total UF of 100X). Since then, EPA has released a memorandum titled *Use of In Vitro Data to Determine Data Derived Extrapolation Factors (DDEFs) for Human Health Risk Assessment for Select Organophosphates (OPs)* (R. Louden, 12-DEC-2023, D468397)[13] which allows for the reduction of the pharmacodynamic (PD) portion of the interspecies UF for certain OPs that were considered to have reliable *in vitro* data to support the reduction. *In vitro* data was submitted for methamidophos, but not for acephate. Therefore, the Agency was unable to reduce the PD portion of the interspecies UF for acephate. In regard to the World Health Organization (WHO) Joint Meeting on Pesticide residues (JMPR) reducing their overall safety factor for humans from 100X to 10X, EPA has not made a similar finding based on current information available to the Agency. EPA will consider whether the interspecies UF may be reduced in future assessments as additional data are provided.

The updated dietary assessment for acephate assessed exposure at the 99.9th percentile. EPA has historically regulated at the 99.9th percentile of exposure when the dietary assessment is highly refined and incorporates PDP monitoring data. Dietary exposure is also calculated at the 95th and 99th percentiles and presented in the dietary assessment for further characterization of dietary risks. In the most recent analysis and in the 2023 DWA *Acephate Refined Drinking Water Assessment for Registration Review* (July 2023), EPA did not assume 100% conversion to methamidophos.

Comments Submitted by Acephate Task Force (Docket ID: EPA-HQ-OPP-2008-0915-0042)

Comment: The Acephate Task Force (ATF) commented on the EPA's revised occupational and residential exposure assessment, preliminary ecological risk assessment, preliminary drinking water exposure assessment, acute and steady state dietary exposure and risk assessment and revised draft human health risk assessment. In general, the ATF comments focused on factors, methods, and inputs used in the Agency's 2018 HH DRA. ATF highlighted new data and other information for the Agency to consider revising its risk estimates. The ATF also provided comment on the ecological assessments of various taxa, noting conservative assumptions in the Agency's assessment.

EPA Response: The ATF comments covered a wide array of issues, which are summarized and responded to in detail in, ACEPHATE: Response to Comments on the Draft Human Health Risk Assessment for Registration Review, and in Acephate – Response to Public Comments Submitted for Preliminary Drinking Water Assessment and Draft Ecological Risk Assessment for Registration Review of Acephate (available in docket).

[13] Document available in the Acephate Registration Review Docket EPA-HQ-OPP-2008-0915 (https://www.regulations.gov/docket/EPA-HQ-OPP-2008-0915)

The Agency highlights that since the 2018 HH DRA, high quality mechanistic data have become available as a result of an international effort to develop new approach methodologies (NAMs) for developmental neurotoxicity (DNT). The results from the DNT NAM battery for each OP compound tested indicated that potential neurodevelopmental outcomes are not occurring via the same pathway(s) and, therefore, organophosphates (OPs) should not be evaluated as a group for neurodevelopmental outcomes. As a result, DNT potential to inform the FQPA SF determination will be evaluated on a chemical-by-chemical basis for each OP considering multiple lines of evidence; for further information, please see *Approach for Evaluating Developmental Neurotoxicity Potential for the Organophosphate Pesticides* in the docket. For acephate and methamidophos, no true positive results were observed in the DNT battery using human or rat cells lines. There was also a lack of DNT effects observed in the *in vivo* guideline DNT studies for both acephate and methamidophos, and a lack of adverse effects in the toxicological studies available in the literature. Additionally, an updated review of the human incidents and epidemiology concluded that there was insufficient epidemiological evidence of a clear or causal relationship between acephate or methamidophos exposure and DNT outcomes in children. As a result, AChE inhibition continues to be the most sensitive and health-protective endpoint for human health risk assessment and is therefore protective of any potential downstream neurodevelopmental effects. Subsequently, the FQPA SF was reduced to 1X in the 2023 acephate DRA. Details on the evaluation of the DNT potential of acephate and methamidophos to inform the FQPA SF, and the WOE used to support the reduction of the FQPA SF to 1X can be found in the revised 2023 acephate DRA and associated documents.

Even though, as ATF points out, typically the steady state point of departure (POD) would be expected to be lower than the acute POD, for acephate, steady-state inhibition occurs almost immediately as evidenced by similar benchmark dose (BMD) values across single and repeat dose studies. Therefore, the POD based on brain AChE inhibition in post-natal day-11 male pups from the comparative cholinesterase assay (CCA) study is the most protective and appropriate value for both acute and steady-state scenarios.

The approach for deriving the toxicity-adjustment factors (TAFs) remained the same in the 2023 acephate DRA, because refined dietary risks are still exceeding for drinking water alone. EPA will look into potential refinements to the TAFs in future risk assessments. While a reduction of the methamidophos dermal TAF would be expected to result in a general improvement of risk estimates, acephate-only risk estimates (without consideration of methamidophos or any respective TAF) continue to result in MOEs of concern (<LOC) for several residential post-application scenarios.

After the release of the 2018 acephate ORE assessment, the occupational handler spreadsheet was updated several times (June 2018, March 2020, and most recently in May 2021)[14] to incorporate the most recent changes to the occupational pesticide handler unit exposure

[14] https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/occupational-pesticide-handler-exposure-data

surrogate reference table. EPA has updated the occupational exposure and risk estimates to show the impacts of the most recent unit exposures in the 2023 acephate HH DRA.

Comments Submitted by National Cotton Council (Docket ID: EPA-HQ-OPP-2008-0915-0040)

Comment: The National Cotton Council (NCC) provided information on the value of cotton, stating that loss of acephate products would reduce producer's ability to control plant bug pests across the cotton belt. NCC indicated concerns with changes to the point of departure (POD) and related toxicity adjustment factors (TAF) for the degradate methamidophos. NCC urged the Agency to further refine its risk assessments. NCC provided information on modern cotton growing/harvesting methods to help improve exposure estimates. NCC provided EPA with information on use and usage of acephate. NCC questions the Agency's use of an additional 10X SF. NCC discussed common pest issues and the expected impact of loss of acephate on producers.

EPA Response: EPA appreciates the information on the benefits of the use of acephate; please see *Assessment of the Usage and Pest Management Benefits of Acephate, an Organophosphate Insecticide, on Cotton (PC# 103301)* available in the public docket. EPA also addressed the information provided by NCC on modern cotton growing/harvesting methods; please see *Acephate. Second Revised Occupational and Residential Exposure Assessment for Registration Review*, available in the public docket. EPA also appreciates additional information relating to cotton harvest practice and anticipates future conversations with the NCC to better understand and evaluate cotton harvest exposures and risk.

As explained in further detail in the Agency's response to the ATF comment, the FQPA SF has been reduced to 1X for acephate/methamidophos in the 2023 HH DRA, and in the 2023 DWA EPA does not assume 100% conversion of acephate to methamidophos in drinking water.

Comments Submitted by United States Department of Agriculture Office of Pest Management Policy (Docket ID: EPA-HQ-OPP-2008-0915-0036)

Comment: The United States Department of Agriculture Office of Pest Management Policy (USDA OPMP) agreed with the Agency's use of cotton for its screening-level drinking-water assessment. USDA requested that EPA consider additional geographic characterization and additional refinements in determining surface water estimated environmental concentrations (EECs), noting the lack of detections of acephate and methamidophos in surface water monitoring data and the relatively short-lived nature of acephate and methamidophos in the environment. USDA OPMP also noted application rates used in EPA's assessments and other exposure assumptions used in the 2017 Eco DRA do not reflect actual usage, and asked EPA to consider working with acephate registrants on label updates that better reflect actual usage. USDA provided additional comments on the Eco DRA related to likelihood of exposure at the estimated levels. USDA also provided usage and benefit data for tobacco, cotton, lettuce, celery, cauliflower, and other crops.

EPA Response: The Agency thanks USDA for these data, and also appreciates the information on the benefits of acephate and other organophosphates, *Information on Critical and High Benefit Uses for Three Organophosphate Insecticides: Malathion, Acephate, and Dimethoate,* provided by USDA on September 14, 2023, and on usage characterization and potential risk mitigation options for acephate, *Acephate Usage Characterization and Potential Risk Mitigation Options for Agricultural Applications,* provided on November 21, 2023, in response to an EPA request. This information from USDA was provided outside of the formal comment period and is available in the docket. Information provided by USDA was considered in the development of this PID. EPA used information on usage and pest management in assessing the benefits of the use of acephate. EPA utilized reduced rates in the 2023 DRA refinements and is open to further discussion of acephate application rates. At the time of the 2017 DWA, monitoring data for surface water detections of acephate and methamidophos were not available. The 2023 revised DWA included an updated review of monitoring data. In surface water, 2,676 detections of acephate were reported across a number of states, and 581 detections of methamidophos were reported within California and New Jersey. For additional information on these monitoring data, please refer to *Acephate Refined Drinking Water Assessment for Registration Review, July 21, 2023*. EPA anticipates future conversations with USDA after the publication of this PID.

Comments Submitted by Center for Biological Diversity (Docket ID: EPA-HQ-OPP-2008-0915-0029)

Comment: The Center for Biological Diversity's (CBD) comments focus on the EPA's duty to consult with the Services on the registration review of acephate in accordance with the Endangered Species Act (ESA). The CBD comments mention various aspects of the risk assessment process, specifically use of the best available data, including all necessary data and studies, particularly to develop listed species risk assessments, and evaluation of effects on listed species and their designated critical habitat. CBD also expressed concern regarding the rigor of the Agency's preliminary determinations regarding the effects of acephate on listed species and their designated critical habitat for the acephate registration review. In addition, CBD expressed concern about effects on pollinators and other beneficial insects, effects on human health or environmental safety concerning endocrine disruption, and any additive, cumulative or synergistic effects of the use of the pesticide.

EPA Response: EPA has reviewed CBD's comments and is addressing many of the concerns regarding listed species as part of its ongoing collaborative work with the Services and USDA to improve the consultation process for listed species for pesticides in accordance with the Endangered Species Act (ESA) § 7. See Appendix C of this document for more information on EPA's progress. As to acephate specifically, and noted in the introduction to this document, EPA and CBD (along with others) settled a lawsuit that involved this pesticide. EPA committed to issuing a final biological evaluation no later than September 30, 2027. Additionally, EPA stated in its ESA Workplan (discussed in Appendix C to this document) its goal of finalizing a biological evaluation by 2026. In either case, EPA will take public comment on a draft biological evaluation before finalizing the assessment.

The EPA will address concerns specific to acephate particularly with regard to pollinators, ESA, and endocrine disruption, in connection with the development of its final registration review decision for this pesticide. See Endocrine Disruptor Screening Program in Appendix D of this document for more information regarding endocrine disruption. The EPA is currently developing an agency policy on how to consider claims of synergy being made by registrants in their patents. On September 9, 2019, the EPA released an interim process for public comment, available at regulations.gov in docket EPA-HQ-OPP-2017-0433. After the Agency has received and considered public comment on the proposed policy, and once that policy has been finalized, the EPA will consider its implications on the EPA's final decision for acephate.

Comments Submitted by Stephanie Smallhouse, President, Arizona Farm Bureau Federation (Docket ID: EPA-HQ-OPP-2008-0915-0035), Arizona Pest Management Center (Docket ID: EPA-HQ-OPP-2008-0915-0037), Brian Wolfe, Creative Sales Incorporated (Docket ID: EPA-HQ-OPP-2008-0915-0038), Georgia Farm Bureau (Docket ID: EPA-HQ-OPP-2008-0915-0031), Katie Murray, Oregon State University Integrated Plant Protection Center (Docket ID: EPA-HQ-OPP-2008-0915-0033), Mississippi Agricultural Consultants Association (Docket ID: EPA-HQ-OPP-2008-0915-0039), National Cotton States Arthropod Pest Management Working Group (Docket ID: EPA-HQ-OPP-2008-0915-0041), Steve Hensley, National Cotton Council (Docket ID: EPA-HQ-OPP-2008-0915-0034 and EPA-HQ-OPP-2008-0915-0028), and West Tennessee Research and Education Center, The University of Tennessee (Docket ID: EPA-HQ-OPP-2008-0915-0032)

Comments: These commenters provided information about acephate use and importance in integrated pest management for various crops, also noting few incidents attributed to acephate in agriculture.

EPA Response: EPA thanks the commenters for providing this information. EPA recognizes the efforts of extension and education centers in contributing to the Agency's efforts to better understand the use and benefits of acephate. EPA considered the information on usage and pest management in assessing the benefits and use of acephate. Regarding the number of incidents attributed to acephate in agriculture, the 2023 revised human health risk assessment includes a summary of EPA's detailed review of reported incidents. Human incident data is one line of evidence evaluated by EPA in the risk assessment process, and it can assist in characterizing risk. However, EPA relies on the totality of the information presented in its risk assessments for the purpose of making risk management decisions.

II. USE AND USAGE

Acephate is an organophosphate insecticide registered for use on both agricultural (food and non-food) and non-agricultural use sites. Methamidophos, a degradate of acephate, was previously registered as a stand-alone active ingredient (apart from acephate) but has since been cancelled in 2009.

Agricultural (food) Use Sites

Agricultural (food) uses of acephate are dry beans, fresh lima beans, Brussels sprouts, cauliflower, celery, cotton, cranberries, lettuce (head type), peanuts, mint (peppermint and spearmint), bell peppers, non-bell peppers, soybeans, and tobacco.

Acephate agricultural products are formulated as: soluble concentrate, water dispersible granules, pelleted/tableted, flowable concentrate, and as a wettable powder, dry flowable, soluble concentrate, granular, and wettable powders.

Dependent on use site, acephate products may be applied by ground (broadcast, spot, or in-furrow [to cotton]) or aerial application equipment. Acephate may also be applied as a seed treatment on cotton and peanuts.

Non-Food Agricultural and Non-Agricultural Use Sites

Acephate is registered for use on various non-food agricultural crops. Acephate may be applied to non-food trees: forestry, shelter belts, rangeland trees, tree farms/plantations (including Christmas trees), and seed orchards/plantations. Acephate may be used on southern pine seed orchards for use in Florida, Georgia, North Carolina, and Virginia only. Acephate is also registered under a Special Location Needs (SLN) label for use on kenaf (in North Carolina only). Acephate is registered for use on non-bearing fruit and nut trees and vines as seedlings, nursery stock, and non-bearing orchards (within the field). Acephate is also registered for use on succulent green beans (also known as snap, bush, pole, string) grown for seed.

Acephate Special Local Needs registrations are available for use on carrots grown for seed (in Idaho, Oregon, and Washington only), alfalfa grown for seed (in California, Idaho, Oregon, Washington, and Wyoming only), radish grown for seed (in Washington only), and parsley grown for seed (in Oregon only).

Turf uses of acephate are ornamental turf (golf courses, schools, lawns, parks, athletic fields, etc.), around commercial (including airports, cemeteries, etc.), industrial, recreational (including parks, and playgrounds, etc.) areas, residential lawns, and sod farms. Acephate is registered for use on residential, landscape, and nursery grown ornamental plants (flowering plants, trees, shrubs, etc.). Nursery grown ornamental plants include ornamentals grown in greenhouses, lathhouses, shade houses, outdoor, or container grown nursery stock. Acephate is allowed for residential/consumer use on turfgrass (for fire/harvester ant control) and outdoor residential use on ornamental plants.

Indoor non-food commercial uses of acephate include treatment of boats, eating establishments, food processing plants/storage/distribution areas, hospitals, hotels/motels, warehouses and storage areas, stores, locker rooms, lavatories, garbage rooms, meat processing plants, floor drains to sewer entries/vestibules, baseboards, around sinks and/or

other appliances, etc. Labels currently include language stating that products are not for indoor residential use.

Acephate is also registered for use on non-agricultural areas (such as rights-of-ways, field borders, ditch banks, fence rows, roadsides, wasteland [non-food or feed producing] areas, etc).

Registered formulations of acephate for use on non-food agricultural and non-agricultural use sites include dust, water soluble packets, granules, water dispersible granules, pellets, as a soluble concentrate, wettable powder, emulsifiable concentrate, dry flowable, pelleted/tableted, impregnated materials, ready to use solution, and as a pressurized liquid (as an aerosol fogger).

Registered acephate non-food agricultural and non-agricultural product applications may be made by ground equipment (broadcast or spot treatments) or by aerial equipment. Aerial application is prohibited in turf. Additional application methods for use on ornamental plants, other than ground or aerial equipment, includes the application of acephate as a paint on slurry to bark, tree injection, basal soil injection, and aerosol can/fogger (in commercial greenhouses only). Additional application methods for use on turf and ornamental plants include mound treatment or drench (for fire ant control). Additionally, when applying acephate to trees, including non-bearing fruit and nut trees and vines as seedlings, nursery stock, and non-bearing orchards, applicators may also apply by tree injection or airblast.

At indoor non-agricultural use sites, acephate can be applied as a spot, crack or crevice treatment. Acephate can also be applied via a paintbrush onto window screens, frames, eaves, wood shutters, entryways, patios, garages, carports, etc.

Agricultural Usage

Nationally, across all surveyed agricultural crops except celery and Brussels sprouts, users reported applying about 3.9 million pounds of acephate (lbs a.i.) to approximately 7.6 million total acres treated (TAT) annually from 2017 to 2021. Within celery and Brussels sprouts, about 10,000 lbs a.i. were applied (2017-2021) and 3,600 lbs a.i. were applied (2015- 2019) respectively.

Relatively high percent crop treated (PCT) were reported from 2017-2021 for celery (32 PCT), tobacco (29 PCT), cotton (28 PCT), lettuce (12 PCT), and peanuts (10 PCT). About 5% of cauliflower and peppers (bell and non-bell) were treated with acephate between 2017-2021. Reported usage for dry beans was low nationally (≤2.5 PCT) from 2017-2021. A PCT of 6 was reported on fresh lima beans, implying that growers apply acephate more often to fresh lima beans as compared to other beans. The sum of all vegetable crops accounts for less than 2% of acephate lbs applied and less than 1% of all acephate TAT.

Cotton and soybean together accounted for approximately 94% of total pounds applied and 96% of total acres treated with acephate (2017-2021). Less than 2% of soybean acres were

treated with acephate nationally from 2017-2021. The percent of soybeans acres grown that are treated with acephate was low for all regions in the U.S. (≤2%) except within the Mid-South, which was reported at 19 PCT. Nationally, the annual average PCT of all cotton acres treated with acephate was about 28% but growers in the Midsouth and Southeast regions applied acephate to a higher proportion of acres grown (59 and 35 PCT, respectively).

Nationally representative usage data for cranberry and mint are not collected by available data sources.

Seed Treatment Usage

Seed treatment data available to the Agency can be utilized qualitatively as an indicator of positive usage, though at this time, it is not possible to estimate the geographic extent of the seed treatment usage or provide robust quantitative estimates of usage. Qualitative estimates of seed treatment usage can be informative to compare relatively large differences within or across active ingredients over time for specific crops.

Acephate seed treatment usage was reported on cotton over the five most recent years of available data (2017-2021). From 2017-2021, acephate was one of the market leading insecticide seed treatments in terms of acres planted with insecticide-treated cotton seed.

Seed treatment insecticides were surveyed for use on peanuts from 2017-2021; however, no usage was reported, suggesting acephate is not widely used as a seed treatment on peanuts.

Non-Food Agricultural and Non-Agricultural Usage

Usage on Seed Crops

The Agency does not have usage information for carrots grown for seed (in Idaho, Oregon, and Washington only), alfalfa grown for seed (in California, Idaho, Oregon, Washington, and Wyoming only), radish grown for seed (in Washington only), and on parsley grown for seed (in Oregon only). The absence of such information should not be interpreted as lack of usage.

Usage on Non-Bearing Fruit and Nut Trees and Vines

Acephate is registered for use on non-bearing fruit and nut trees and vines as seedlings, nursery stock, or non-bearing orchards (within the field). Recent acephate usage was reported on non-bearing apples, raisin grapes, table grapes, tangerines, pistachios, lemons, oranges, grapefruit, table grapes, almonds, and walnuts. Additional non-bearing use sites were surveyed for usage, though no acephate usage was reported.

Usage on Turf and Ornamental Plants

In 2021, about 86,000 lbs of acephate was reported as applied to golf courses. Lawn care operators and landscape contractors, both of whom install and maintain turf and ornamentals within residential, commercial, industrial, institutional and government areas, reported applying 170,000 lbs of acephate. About 8,200 lbs of acephate were reported as applied to parks in 2021. In 2021, little to no acephate usage was reported as applied to school areas, within nurseries and greenhouses, on sod farms, or within cemeteries. In the U.S. consumer market (use by general consumers on lawns, gardens, and household plants), on average, about 825,000 lbs of acephate were reported as applied by consumers on lawns and gardens in 2019 and 2022.

Usage on Indoor and perimeter commercial uses

In 2021, acephate usage was reported as applied by pest management professionals within and around the exterior of commercial and residential establishments for flea, ant, cockroach, and other insect control. In total, about 51,000 lbs of acephate were used across all insect types for control by pest management professionals in 2021. Acephate was reported as applied within food handling establishments, institutional kitchens, food processing plants, and food warehouses as well in 2021.

Usage on rights-of-ways and other non-food agricultural and non-agricultural areas

Usage data surveys indicated that there was likely very little usage of acephate within railroads, roadways, or among electric utilities and pipelines in 2016 and 2019.

In 2016 and 2019, forestry and rangeland trees were surveyed for insecticide usage; no usage was reported in either year, indicating there is likely very little usage of acephate within these sectors.

EPA does not have usage data for acephate for use on shelter belts, tree farms/plantations (including Christmas trees), and seed orchards/plantations. The Agency also does not have specific usage information for southern pine seed orchards in Florida, Georgia, North Carolina, and Virginia at this time. The absence of such data should not be interpreted as lack of usage.

The Agency does not have usage data for acephate in kenaf at this time. The absence of such data should not be interpreted as lack of usage.

*For more details on the use and usage of acephate, see the following documents in the acephate registration review docket (*EPA-HQ-OPP-2008-0915*):*

- Overview of the Usage of Acephate and Pest Management Benefits for Tobacco, Peanut, Mint, and Cranberry Production (PC# 103301)
- Assessment of the Usage and Pest Management Benefits of Acephate (PC# 103301) for Soybean Production
- Assessment of the Usage and Pest Management Benefits of Acephate, an Organophosphate Insecticide, on Cotton (PC# 103301)

- Usage and Pest Management Benefits of Acephate, an Organophosphate Insecticide, in Vegetable, Bean, and Seed Crops (PC# 103301)
- Usage and Pest Management Benefits of Acephate, an Organophosphate Insecticide, in Non-Food Agricultural and Non-Agricultural Use Sites (PC# 103301)

III. SCIENTIFIC ASSESSMENTS

A. Human Health Risks

A summary of the Agency's 2023 human health risk assessment for acephate is presented below. The Agency used the most current science policies and risk assessment methodologies to prepare this risk assessment in support of the registration review of Acephate. For additional details on the 2023 HH DRA, see *Second Revised Draft Human Health Risk Assessment (DRA) in Support of Registration Review* in EPA's public docket (EPA-HQ-OPP-2008-0915).

1. Risk Summary and Characterization

The 2023 HH DRA incorporated several updates since the 2018 risk assessment. Key updates included an updated hazard evaluation for acephate and methamidophos that, using chemical-specific data across multiple lines of evidence (toxicology studies, epidemiological studies, and *in vitro* developmental neurotoxicity new approach methods [DNT NAMs] battery), showed little support for adverse neurodevelopmental outcomes particularly at doses eliciting significant acetylcholinesterase (AChE) inhibition. Therefore, AChE inhibition continues to be the most sensitive and health-protective endpoint for human health risk assessment, supporting the reduction of the FQPA SF to 1X. Methamidophos has been found to be a more potent AChE inhibitor than acephate. There have been no changes to the toxicity adjustment factors (TAFs) for methamidophos since the 2018 risk assessment.

Humans may be exposed to acephate and its degradate methamidophos in food and drinking water since acephate may be applied directly to growing crops, and applications may result in residues in food and residues reaching surface and ground sources of drinking water. The 2018 dietary risk assessment identified acute and steady state risk estimates of concern based upon estimated drinking water-only concentrations (EDWCs) that exceed 100% of the population-adjusted dose (PAD) at currently labeled application rates and uses (including agricultural and non-agricultural) for acephate, with dietary estimates well exceeding 10,000% of the PAD at the 99.9th percentile of exposure. Even when evaluating agricultural (crop) uses that have some of the lower acephate use application rates in the 2018 drinking water assessment (e.g., alfalfa, rights-of-way, peppers), uses still exceeded 100% of the PAD. Infants were the population subgroup with the highest risk estimate, at 2400% of the PAD, based on water-only exposure estimates.

The 2023 revised dietary assessment included risk analyses that incorporated updated and refined drinking water exposure analyses; see *Acephate Refined Drinking Water Assessment for Registration Review* (2023 DWA, available in docket). Given the significant exceedances of the

PAD for all labeled uses in the HH DRA, with drinking water as the driver of these risk estimates, and without a proposed subset of uses or label changes from the registrants to model, the Agency decided to focus the 2023 DWA on the two crops with the highest acephate usage (based on pounds applied and total acres treated of acephate): cotton and soybeans. Maximum labeled use rates for ground application scenarios for cotton and soybean were modeled. The 2023 HH DRA also includes further refined modeling in which percent cropped area (PCA) adjustment factors and state-level percent crop treated (PCT) data are incorporated. Acute and steady-state risk estimates for food-only dietary residues are below 100% of the PAD; however, all drinking water-only scenarios still exceeded 100% of the PAD for all population subgroups at the 99.9th percentile of exposure. The population subgroup having the highest risk estimate for the cotton only and cotton plus soybean (using PCA and PCT data) is infants at 120% of the PAD, where drinking water exposure is driving those risk estimates.

All handler activities are anticipated to be exposed to acephate only (i.e., not to its degradate, methamidophos, with the potential exception of seed treatment planting activities). Due to the degradation of acephate once applied, post-application exposures (both occupational and non-occupational) may result in exposure to the residues of both acephate and methamidophos. In the occupational and residential exposure assessment completed in 2017, the assessment identified residential post-application risk of concern to adults and children, bystander spray drift risk of concern, and occupational handler risks of concern for most scenarios. A revised occupational and residential risk assessment for acephate and methamidophos was completed in 2023. This assessment was updated with current exposure assumptions, the FQPA safety factor reduction, policy updates, and further evaluated products available for homeowner use. Overall, there continues to be risk estimates of concern for various occupational/residential handler and post-application exposures as well as non-occupational exposure scenarios resulting from spray drift.

A. Dietary (Food + Water) Risk

For acephate and methamidophos, AChE inhibition is the most sensitive endpoint in the toxicology database in multiple species, durations, lifestages, and routes. Clinical signs of neurotoxicity can be found throughout the database of toxicity studies at doses much higher than those causing inhibition of AChE. The point of departure (POD) was derived from the results of a comparative cholinesterase assay (CCA) rat study for the acute dietary (all populations), steady-state dietary (all populations), and incidental oral exposure scenarios. A lower limit on the benchmark dose of 0.272 mg/kg/day associated with brain AChE inhibition in male pups was selected as a suitable POD for oral exposure scenarios. The FQPA SF used in the 2018 human health risk assessment was reduced from 10X to 1X for infants, children, youth, and women of child-bearing age for all exposure scenarios in the revised assessment based on a WOE evaluation of DNT potential using chemical-specific data. The interspecies (10X) and intraspecies (10X) uncertainty factors were retained. As a result, a total uncertainty factor of 100X was applied for all dietary exposure scenarios, and the PADs used for all populations in

the acute and steady-state assessments increased by an order of magnitude from 0.0003 mg/kg/day to 0.003 mg/kg/day.

Acephate exhibits steady-state inhibition of AChE in a single day. Therefore, the acute and steady-state PODs are the same, and dietary risk (food and drinking water) estimates are presented as "acute and steady-state." The acute and steady-state dietary exposure assessment for acephate and methamidophos incorporated USDA's Pesticide Data Program (PDP) food monitoring data, percent crop treated estimates along with default empirical processing factors. DWAs were conducted in 2017 and 2023 as described in greater detail in section III.A.1 of this PID. Unlike the 2017 drinking water assessment, drinking water concentration estimates in the updated 2023 assessment do not assume 100% conversion of acephate to the more toxic degradate methamidophos.

Certain uses were not included in the DWA because their use patterns are not associated with movement to water, so little or no exposure is expected. No exposure is expected for indoor uses. Estimating exposure from tree injection is highly uncertain, but since both acephate and methamidophos degrade rapidly and it is unlikely any residues will be present after leaf fall and degradation, exposure through runoff is not expected to be significant.

In the 2023 revised dietary assessment, acute and steady-state dietary (food and drinking water) risk estimates for acephate were of concern for the general U.S. population and population subgroups for cotton only; however, food-only exposures are below 100% of the PAD. For the U.S. population, the acute and steady-state dietary (food only) risk estimate is 10% of the PAD. The population subgroup having the highest risk estimate is children 3-5 years of age at 19% of the PAD. When considering all registered uses as labeled and various drinking water refinements there were still dietary exceedances. Acute and steady state dietary risk estimates for drinking water alone exceeded 100% of the PAD at the 99.9th percentile as follows: unrefined cotton drinking water at 580% PAD, refined cotton drinking water at 120% PAD, and refined drinking water exposure reflecting a cotton-soybean rotation at 120% PAD. EDWCs for ornamentals resulted in dietary risk estimates of >10,000% of the PAD for the highest exposure subgroup (infants). For more details see the *Acephate: Second Revised Draft Human Health Risk Assessment (DRA) in Support of Registration Review* (Aug 2023), and the *Acephate Refined Drinking Water Assessment for Registration Review* (July 2023).

Acephate is classified as a Group C possible human carcinogen based on hepatocellular carcinomas in mice. A non-linear risk quantification approach adequately accounts for all chronic toxicity, including potential carcinogenicity, resultant from acephate exposure. Therefore, a separate quantitative cancer dietary assessment was not conducted.

B. Residential Handler Risks

An acephate product for treatment of fire ants (EPA Reg. No. 239-2632) allows for use on residential use sites (ant mound treatments on residential lawns and gardens). That label currently requires specific clothing and personal protective equipment (PPE) to be worn, which

are typically risk mitigation measures for occupational handlers. However, based upon the label, product size, and packaging, the Agency expects this product may be used by homeowners, and has therefore evaluated this product for this exposure pathway. Additionally, several incidents have been reported by residential handlers using this product, which also supports conducting a residential handler assessment. Residential handler exposure and risk estimates consider only acephate as any exposure would be limited to application during residential ant mound treatment activities. Most residential handler risk estimates are of concern. Garden and lawn/turf ant mound spot treatment with dust formulations using electric dusters, hand crank dusters, spoons, or shaker cans results in the lowest risk estimates of concern with a combined dermal and inhalation ARI of 0.19, and are the most likely representative uses, while plunger dusters and bulb dusters have combined ARIs of 2.3 (ARIs <1 are of concern).

C. Residential Post-Application Risks

Residential post-application exposure and risk estimates were calculated for the registered uses of acephate on ornamentals, golf courses, and in commercial/industrial buildings such as schools, hotels/motels, and hospitals. The residential post-application assessment considers both acephate and methamidophos residues. Post-application risk estimates of concern were identified for all uses on garden ornamentals, with dermal MOEs of 27 for adults and 40 for children 6 to < 11 years (level of concern (LOC) = 100). Post-application risk estimates for adults and children (6 to < 11, and 11 to < 16 years old) exposed to treated turf from golfing are not of concern (dermal MOEs range from 1,500 to 2,000).

Although applicable labels include language stating, “not for indoor residential use,” the lack of specificity in the descriptions of some indoor spot, crack and crevice treatment uses (i.e., hotels and hospitals) may result in indoor exposures comparable to those resulting from indoor residential uses, and were therefore assessed. Risks of concern were identified for uses in indoor environments. ARIs for indoor uses ranged from 0.071 to 0.82 (ARIs <1 indicate risks of concern).

D. *Bystander Risks*

A spray drift assessment was conducted which considered both acephate residues and residues of methamidophos. Risk estimates from indirect exposure to spray drift are not of concern at field edge (MOEs ≥ LOC of 100) for adults. However, incidental oral risk estimates from indirect exposure related to children (1 to < 2 years) were of concern (combined dermal and incidental oral MOEs < LOC of 100) at field edge with combined MOEs no longer of concern between 10 to 75 feet from field edge depending on use site and application rate.

Bystanders living and working near treated areas have the potential for exposure to acephate from volatilization. Acephate was detected in air monitoring data from California Department of Pesticide Regulation (CDPR) Air Monitoring Network (AMN) and California Air Resources Board (CARB) from 2002 to 2019. Based on this monitoring data there are no risks of concern

for steady-state bystander exposure with MOEs ranging from 8,100 to 21,000 (inhalation LOC = 30).

E. Aggregate Risks

In an aggregate assessment, EPA considers the combined pesticide exposures and risks from three major sources: food, drinking water, and residential exposures. The Agency sums the exposures from these sources and compares the aggregate risk to quantitative estimates of hazard. EPA considers the route and duration of exposure when assessing aggregate risks. Since risks of concern have been identified for dietary and residential routes of exposure, there is also aggregate risk of concern. A quantitative aggregate risk assessment was not conducted; combining those exposures would result in even greater risk estimates of concern for acephate.

F. Cumulative Risks

OPs such as acephate inhibit AChE leading to cholinergic neurotoxicity. This shared mode of action (MOA) is the basis for the OP common mechanism grouping per the Office of Pesticide Programs (OPP) Guidance for Identifying Pesticide Chemicals and Other Substances that have a Common Mechanism of Toxicity[15]. The 2002 and 2006 OP cumulative risk assessments (CRA) used brain AChE inhibition in female rats as the source of dose response data for the relative potency factors and PODs for each OP, including acephate. There were no risks of concern identified in the 2006 update of the OP CRA[16].

EPA is not making any findings regarding the potential cumulative risks of acephate and other OPs that share a common mechanism of toxicity in this document. EPA intends to make those conclusions collectively for all registered OPs after completing the individual OP assessments. As OPP assesses each OP during the Registration Review process, OPP will determine if there is any new information since the 2006 CRA was conducted that would affect the conclusions of the 2006 CRA. Should the Agency determine that new information (e.g., changes in use pattern, risks of concern) could potentially impact the CRA, the Agency will revisit the OP CRA after all the OPs in the class have been assessed.

G. Occupational Handler Risks

The Agency updated the occupational exposure risk assessment in 2023, incorporating updated hazard characterization, unit exposure values, and updated policies. Of the 228 occupational scenarios assessed, 76 presented risks of concern with ARIs ranging from 0.00022 to 2,000 (ARIs <1 are of concern). Inhalation exposures are driving most of the risk estimates. Respiratory PPE and/or engineering controls would alleviate some of the risk concerns. However, there are scenarios that continue to present risks of concern even at maximum levels of PPE.

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[15] https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/guidance-identifying-pesticide-chemicals-and-other

[16] https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/cumulative-assessment-risk-pesticides

The Agency identified risks of concern when using personal protective equipment (PPE) of double-layer clothing, gloves, and PF10 respirator for the following application methods and uses:

- Loading/applying granules for broadcast with belly grinder for landscaping trees/shrubs/bushes/plants/flowers (ARI = 0.95);
- Loading/applying granules for broadcast with cup equipment for greenhouse and nursery ornamentals/roses/cut flowers/container stock/trees/vegetables (ARI = 0.023)
- Loading/applying with ground directed spoon equipment for greenhouse and nursery ornamentals/roses/cute flowers/container stock/trees/vegetables (ARI = 0.0015)

Most of the acephate seed treatment occupational handler scenarios are of concern when assuming PPE of double-layer clothing plus gloves and PF10 respirator, with ARIs ranging from 0.031 to 1.8 (ARIs < 1 are of concern). Uses with identified risk of concern include:

- Cleaning equipment for commercial seed treatment on cotton (ARI 0.52)
- Cleaning equipment for on-farm seed treatment on cotton with solid (dry flowable) formulations (ARI of 0.47)

All the combined acephate and methamidophos loading/planting seed treatment occupational handler scenarios are of concern (i.e., ARIs < 1) when assuming PPE of double-layer clothing, gloves, and PF10 respirator, with ARIs ranging from 0.025 to 0.59. Uses with identified risk of concern include:

- Loading/planting cotton seed with commercial seed treatment (ARI = 0.59)
- Loading/planting peanut seed with commercial seed treatment (ARI = 0.24)
- Treating/planting peanut seed on-farm with liquid water-soluble packets (WSP) (ARI = 0.6)
- Treating/planting cotton seed on-farm with solid (dry flowable) formulations (ARI = 0.57)

EPA did not identify any risks of concern related to the use of acephate for tree injections.

h. Occupational Post-Application Risks

Current acephate agricultural use site products require a 24-hour restricted entry interval (REI). Risks were identified for occupational post-application dermal exposure on the day of application with MOEs ranging from 15 to 1,900 (LOC = 100). REIs of 12 hours to 28 days would be necessary to reach acceptable MOEs (i.e., MOEs ≥ LOC of 100) from exposure to the combined residues of acephate and methamidophos. REIs of 24 hours are long enough for MOEs to reach the LOC of 100 for many crops/activities. However, application methods and uses with identified risk of concern beyond 24 hours include:

- Floriculture hand-set irrigation (MOE = 38); no longer a risk of concern 2 days after treatment (DAT)
- Floriculture hand-harvesting (MOE = 38); no longer a risk of concern 5 DAT
- Nursery hand-set irrigation (MOE = 29); no longer a risk of concern 2 DAT
- Dry beans and peas scouting (MOE = 64); no longer a risk of concern 3 DAT
- Dry beans and peas hand-set irrigation (MOE = 64); no longer a risk of concern 2 DAT
- Celery hand-set irrigation (MOE = 37); no longer a risk of concern 6 DAT
- Leaf lettuce hand-set irrigation (MOE = 37); no longer a risk of concern 6 DAT
- Mint scouting (MOE = 64); no longer a risk of concern 3 DAT
- Mint hand-set irrigation (MOE = 37); no longer a risk of concern 6 DAT
- Peanut hand-set irrigation (MOE = 37); no longer a risk of concern 6 DAT
- Bell pepper tying/training (MOE = 64); no longer a risk of concern 3 DAT
- Soybean scouting (MOE = 64); no longer a risk of concern 3 DAT
- Tobacco hand-set irrigation (MOE = 47); no longer a risk of concern 8 DAT
- Cotton mechanical harvesting with tramper (MOE = 53); no longer a risk of concern 28 DAT

For seed treatment, a post-application inhalation exposure assessment was not conducted as exposure is expected to be negligible. It is expected that the exposure and risk estimates described above would be protective of any potential low-level post-application inhalation exposure that could result from these types of applications. Commercial applicators do not typically return to the treated areas after an indoor commercial pesticide application (sites such as warehouses, food handling establishments, and hotels, etc.). For these reasons an occupational post-application inhalation exposure assessment was not performed.

2. Human Incidents and Epidemiology

EPA reviewed acephate incidents reported to OPP's incident data system (IDS), sentinel event notification system for occupational risk (SENSOR) Pesticides Program of National Institute of Occupational Safety & Health (NIOSH) (2010-2017), National Pesticide Information Center (NPIC) (2018-2022) and California pesticide illness surveillance program (PISP) (2015-2018). EPA's latest search on July 28, 2023 showed 35 incidents reported to Main IDS, and 350 incidents reported to Aggregate IDS from January 1, 2018 to February 24, 2023. SENSOR-pesticides showed 70 incidents involving acephate from 2010 to 2017, NPIC showed 21 acephate incidents from 2018-2022, and PISP showed 21 acephate incidents from 2015-2018. The majority of acephate incidents were classified as low severity (91% in IDS, 64% in SENSOR, and 80% in NPIC). Residential exposures resulted in the most reported acephate incidents and included post-application exposures, contact with spills, product misuse, and ingestion (intentional and unintentional). The incident record, along with residential risk estimates, point to a need to address these uses. The Agency intends to monitor human incidents for acephate and will conduct additional analyses if necessary.

EPA also conducted a systematic review of the epidemiologic literature on acephate and methamidophos, using methods described in OPP's *Framework for Incorporating Human Epidemiologic & Incident Data in Risk Assessments for Pesticides*[17] and generally following the guidance provided by the National Toxicology Program/Office of Health Assessment and Translation (NTP/OHAT)[18]. This systematic literature review considered articles available in peer-reviewed literature databases (PubMed, PubMed Central, Scopus, and Science Direct) and a HED-maintained electronic library of published articles from the Agricultural Health Study (AHS)[19] that were published between 1980 and December 2022.

EPA concluded that while some individual epidemiology studies reported positive associations between acephate and methamidophos exposure and some adverse health outcomes, the overall evidence was mostly based on a small body of evidence (i.e., typically only one or two study populations per health outcome) that often had substantive limitations with respect to their study design, exposure assessment approach, and/or outcome assessment approach. As such, HED concluded there was insufficient epidemiologic evidence to suggest that a clear associative or causal relationship exists between acephate and methamidophos exposure and the carcinogenic and non-carcinogenic outcomes. The Agency will continue to monitor the epidemiology data and, if a concern is triggered, additional analysis will be conducted.

3. Tolerances

Although U.S. registrations of the insecticide methamidophos were cancelled and the tolerances to support uses of methamidophos (40 CFR 180.315) are expired, the Agency has identified that for any food uses of acephate that are determined to meet the safety standard, the tolerances of acephate and methamidophos included in the 40 CFR 180.108 should be updated to reflect current crop group definitions and rounding practices, remain separate, and be retained to maintain harmonization with Canada and Codex. For information on proposed tolerance actions for acephate, please see Section IV.D of this document.

The dry bean commodity definition includes cowpea, which has forage and hay commodities that are considered significant livestock feedstuffs. Crop field trials depicting residues of acephate in/on cowpea forage and hay have not been submitted. If the registrant wishes to support the use on cowpea, residue data measuring residues of acephate and methamidophos in/on cowpea forage and hay should be provided.

Separate tolerances for acephate and methamidophos were recommended for cotton gin byproducts and cotton undelinted seed (D446265, D. Drew, 09-MAR-2018). A 2001 Interim

[17] US EPA. December 28, 2016. Office of Pesticide Programs' Framework for Incorporating Human Epidemiologic & Incident Data in Risk Assessments for Pesticides. https://www3.epa.gov/pesticides/EPA-HQ-OPP-2008-0316-DRAFT-0075.pdf

[18] See *Handbook for Conducting a Literature-Based Health Assessment Using OHAT Approach for Systematic Review and Evidence Integration,* January 9, 2015. https://ntpniehs.nih.gov/ntp/ohat/pubs/handbookjan2015508.pdf

[19]Agricultural Health Study - Publications. Accessed 4/26/2022. https://aghealth.nih.gov/news/publicationshtml

Reregistration Eligibility Decision (IRED) identified the need for a magnitude of the residue study in cotton gin byproducts and a confined rotational crop study. These studies were received and reviewed (D446265, D. Drew, 09-MAR-2018). The submitted field trial data for acephate on cotton gin byproducts (MRID 45256201) were acceptable and suitable for recommending acephate and methamidophos tolerances for cotton gin byproducts. A tolerance for methamidophos on cotton seed is required to account for residues from acephate use. The highest residue of methamidophos in/on cotton seed is 0.05 ppm (F. Fort, D259659, 8/18/1999); therefore, a tolerance of 0.1 ppm for cotton undelinted seed is recommended.

Tolerances for residues of acephate on foods as a result of use in food handling establishments may be moved from 40 CFR 180.108(a)(2) to the table in 180.108(a)(1); the specific use instructions for food handling establishments should not be included in the tolerance definition and should be removed.

Revocation of the regional tolerance for acephate in/on macadamia nuts is recommended because this use is no longer registered as the Special Local Needs registration in HI for macadamia nuts was cancelled in 1987.

4. Human Health Data Needs

The human health database for acephate is considered complete for registration review. Crop field trials depicting residues of acephate in/on cowpea forage and hay have not been submitted. If the registrant wishes to support the use on cowpea, residue data depicting residues of acephate and methamidophos in/on cowpea forage and hay should be provided. However, please also refer to section IV.A.1. of this PID for information on the Agency's proposed mitigation for dietary and aggregate risks of concern.

B. Ecological Risks

The Agency has summarized the 2017 Eco DRA below. The Agency used the most current science policies and risk assessment methodologies to prepare a risk assessment in support of the registration review of acephate. For additional details on the 2017 Eco DRA, see *Preliminary Ecological Risk Assessment for Registration Review of Acephate* in EPA's public docket (EPA-HQ-OPP-2008-0915).

The EPA Is currently working with its federal partners and other stakeholders to improve the consultation process for listed species and their designated critical habitats. The Agency has not yet fully evaluated acephate's risks to listed species. However, EPA will complete its listed-species assessment and any necessary consultation with the Services before completing the acephate registration review. As noted earlier in this document, EPA and CBD (along with others) settled a lawsuit that involved acephate. EPA committed to issuing a final biological evaluation no later than September 30, 2027. Additionally, EPA stated in its ESA Workplan (discussed in Appendix C to this document) its goal of finalizing a biological evaluation by 2026.

In either case, EPA will take public comment on a draft biological evaluation before finalizing the assessment. See Appendix C for more details. As such, only potential risks for non-target species under FIFRA are described below.

1. Risk Summary and Characterization

a. Terrestrial Risks

Risk quotients (RQs) were compared against the Agency's LOCs to estimate potential risks, where the RQ is the ratio of exposure estimates compared to the toxicity endpoints. For acute and chronic risks to animals, the LOCs are 0.5 and 1.0, respectively, and for plants, the LOC is 1.0. RQs greater than the LOC represent potential risks of concern. EPA uses LOC exceedances as one line of evidence to describe the potential risks posed by a pesticide to non-target organisms. Because acephate degrades rapidly to methamidophos, and methamidophos is more toxic than acephate to most taxa, the terrestrial risk assessment is based on both acephate and methamidophos toxicity and exposure estimates. The Agency identified potential acute and chronic risks of concern to birds and mammals from all currently registered uses of acephate. The Agency also identified risks of concern to terrestrial invertebrates where exposure can be expected. There were no risks of concern identified to terrestrial plants.

Mammals

Acephate is moderately toxic and its degradate, methamidophos, is highly toxic to mammals on an acute oral exposure basis. The mammalian 3-generation reproductive no-observed-adverse-effect level (NOAEL) for methamidophos was 1.65 mg a.i./kg-body weight based on decreases in the number of sperm positive females giving birth. The highest RQs were for methamidophos and thus are referenced in the risk descriptions below. However, LOC exceedances were also identified for acephate for all assessed uses. All outdoor uses had acute and chronic risks of concern for mammals with RQs up to 12,800, except peppers (non-bell peppers) and celery/mint for certain seed feeding, fruit/pod feeding, and arthropod feeding species. Consumption of treated cotton and peanut seeds resulted in both acute and chronic risks of concern. For mammals, acute RQs from seed treatment ranged up to 15.8, with less than one seed needed to exceed the LOC for small (15 g) mammals, and 16 to 48 seeds for large (1000 g) mammals. Chronic RQs for mammals consuming treated seeds ranged up to 494 (cotton).

Birds, Reptiles, and Terrestrial-Phase Amphibians

Acephate is moderately toxic and its degradate, methamidophos, is very highly toxic to avian species on an acute oral and sub-acute dietary exposure basis. The avian reproduction study no-observable-adverse-effect-concentration (NOAEC) for methamidophos was 3 mg a.i./kg-diet based on reduction in egg thickness, viable embryos, embryo survival, and 14-day-old chick survival. The Agency identified acute and chronic risks of concern for all outdoor uses with RQs up to 36,500, except for peppers (non-bell peppers) and celery/mint for certain seed feeding, and fruit/pod feeding species. Both cotton and peanut seed treatments had RQ values which exceeded the acute risk LOC for small and medium birds feeding on seeds based on both

acephate and methamidophos modeling (with RQs as high as 122), and for all size classes when based on methamidophos modeling. Chronic RQs were exceeded for birds consuming treated seeds with RQs as high as 855. Risk was also estimated based on the number of treated seeds consumed based on methamidophos consumption. Less than half of one cotton seed or one fourth of one peanut seed would need to be consumed to exceed the LOC for small (20 g) birds, and 12 to 38 seeds for large (1000 g) birds.

Terrestrial Invertebrates

EPA relies on toxicity data for honey bees as a surrogate for terrestrial invertebrate species. Risk was calculated using both honey bee and other insect toxicity data. The full suite of Tier 1 pollinator studies has not yet been submitted for acephate or methamidophos; therefore, no adult acute oral, chronic toxicity data or larval toxicity data are available for honey bees. These data gaps represent significant uncertainties for the assessment of the impact of acephate on pollinators as sensitivity may vary according to life-stage and length of exposure (adult vs. larval and acute vs. chronic, respectively). For acephate toxicity the endpoint used to evaluate risk was from soybean looper larvae, and for methamidophos from Western spruce budworm larvae toxicity data. Acephate is classified as highly toxic to terrestrial invertebrates on an acute contact exposure basis. Based on the available data, EPA has determined that acephate uses may present risks of concern to honey bees. All assessed uses exceeded the acute LOC (LOC = 0.4). Using both the available acephate acute contact honey bee toxicity data, and the Spruce budworm methamidophos toxicity data, acute RQs ranged from 1 to 365 and 9 to 5760, respectively. Additional pollinator data are needed to fully characterize the risk to honey bees. Incidents with probable and highly probable causality, including bee kills, have been associated with acephate and/or methamidophos exposure to honey bees.

Terrestrial Plants

The only terrestrial plant LOC exceedances (LOC = 1.0) for acephate were from the ornamentals, roses, and non-residential building uses (RQ's from 1.3 to 2.8). Risk to plants in semi-aquatic areas could not be precluded based on a non-definitive endpoint. Due to a lack of toxicity information at the maximum application rates, the actual risk is uncertain, but cannot be precluded without data showing that the no-adverse-effects level is above the maximum application rate. Incidents involving damage to plants have been reported for acephate. All but one of the incidents involved damage to plants sprayed directly with the product rather than as a result of spray drift from a separate target area, as was the case for one reported incident since 2016.

b. Aquatic Risks

Because acephate degrades rapidly to methamidophos, and methamidophos is more toxic than acephate to most taxa, aquatic risk assessments are based on the assumption that acephate completely converts to methamidophos. Both exposure and toxicity estimates are derived for methamidophos. Exposures to acephate and methamidophos resulted in both acute and chronic risks of concern for aquatic invertebrates. Risk estimates minimally exceeded the

chronic LOC for fish, and available data did not show toxicity at the highest concentration tested for either vascular or non-vascular aquatic plants.

Freshwater Fish and Aquatic-Phase Amphibians

Acephate is considered practically non-toxic and methamidophos is slightly toxic to freshwater fish on an acute exposure basis. There were no acute risks (RQs ≤ 0.1; LOC = 0.5). There were no chronic acephate or methamidophos toxicity data available for freshwater fish with survival, growth, or reproductive endpoints; therefore, an acute to chronic ratio (ACR) was calculated using other organophosphate insecticide toxicity data as a surrogate. Chronic risk was estimated using the most sensitive acute 96-h LC50 for dichlorvos (a structurally similar organophosphate chemical) and the corresponding ACR for rainbow trout resulting in an estimated no observable adverse effect concentration (NOAEC) of 5.9 mg a.i./L for acephate and 0.17 mg a.i./L for methamidophos. The chronic risk LOC (LOC = 1) was exceeded for roses, ornamentals, and non-residential buildings with RQs of 1.1 to 5.3, respectively for freshwater fish.

Estuarine/Marine Fish

Acephate is slightly toxic and methamidophos is moderately toxic to estuarine/marine fish on an acute exposure basis. No acute risks of concern were identified (RQs ≤ 0.45; LOC = 0.5). There are no chronic data for estuarine/marine fish, so uncertainty for chronic risk exist for these taxa.

Freshwater Invertebrates

Acephate is moderately toxic and methamidophos is very highly toxic to freshwater invertebrates on an acute exposure basis. Chronic toxicity is based on reduction in average number of young with a lowest observed adverse effect concentration (LOAEC) of 0.375 mg a.i./L (NOAEC of 0.15 mg a.i./L). All assessed uses except cranberry, soybean, mint, tobacco, and rights-of-way had acute LOC exceedances with RQs ranging from 0.5 to 97. Chronic risks of concern (LOC = 1) were also identified for all uses except peppers (both bell and non-bell peppers), cranberry, mint, tobacco, rights-of-way, and alfalfa with RQs ranging from 1.0 to 247.

Estuarine/Marine Invertebrates

Acephate and methamidophos are moderately toxic to freshwater invertebrates on an acute exposure basis. Chronic toxicity is based on decreased dry weight with an LOAEC of 0.36 mg a.i./L (NOAEC of 0.174 mg a.i./L). Ornamentals, and non-residential buildings were the only acephate uses with acute risks of concern, with RQs ranging from 1.6 to 2.4. Roses, ornamentals, recreational lawns, and non-residential buildings were the only uses with chronic risks of concern with RQs ranging from 1.6 to 6.4.

Aquatic Vascular and Non-Vascular Plants

Methamidophos is more toxic to vascular and non-vascular aquatic plants than acephate, with EC50 values of 3.65 and 679 mg a.i./L for methamidophos compared to >1040 mg a.i./L for acephate, respectively. The no observable adverse effect concentration (NOAEC) of 1.42 mg a.i./L for methamidophos for aquatic vascular plants is based on frond yield, dry weight, and growth rate, and the NOAEC of 29.5 mg a.i./L for methamidophos for non-vascular aquatic plants is based on dry weight, growth rate and frond number yield. There were no risk concerns for aquatic vascular or non-vascular plants (RQs all <1).

2. Ecological Incidents

A review of the ecological incidents involving acephate and methamidophos was previously summarized, and a full list of incidents was included in the 2017 Eco DRA. The reported incidents from the 2017 Eco DRA were summarized from previous incident databases (i.e., the Ecological Incident Information System (EIIS, version 2.1), the 'Aggregate Incident Reports' (v. 1.0) database, and the Avian Monitoring Information System (AIMS)).

A more recent search of the incident data system (IDS) was completed on April 10, 2024 to identify any incidents that occurred since the 2017 Eco DRA. EPA noted five (5) additional incidents that have occurred since the 2017 Eco DRA, for a total of 45 reported for acephate. For methamidophos, there were no new additional incidents reported since the 2017 Eco DRA, with a total of 3 terrestrial plant incidents and 15 terrestrial animal incidents previously reported. All reported incidents for acephate, except three, were categorized as "Registered Use" or "Undetermined;" with the three being categorized as "Misuse." The aquatic incidents were classified as unlikely to probable for acephate causality. The plant incidents were classified as possibly or probably caused by acephate, with one incident classified as unlikely. The terrestrial incidents were classified as possibly or probably caused by acephate except for two incidents that were classified as highly probable. For methamidophos, the certainty index for the plant incidents was either unlikely or possible for methamidophos causality and these incidents were the result of either "Registered Use" or "Undetermined" use. Terrestrial animal incidents were either possible or probable for methamidophos causality except for one incident that was highly probable. The terrestrial incidents were the result of either "Registered" or "Unknown" uses, with one "Accidental Misuse" reported (with a certainty of probable). A third (*approximately* 12) of acephate-specific incidents reported and half (*approximately* 10) of methamidophos-specific incidents reported were honey bee kills; and were classified as possibly to highly probably cause by acephate and/or methamidophos.

Since the 2017 Eco DRA, the Aggregate Incident Reports database contained 1 additional minor fish and wildlife incident and 15 additional minor plant incidents for acephate (total of 12 minor fish and wildlife incidents and 468 minor plant incidents); and 349 additional domestic animal incidents for acephate (total of 1960 domestic animal incidents). No detailed information was available for these incidents. There were no methamidophos incidents reported in the aggregate database.

In summary, EPA notes that acephate and methamidophos incidents have been reported across a variety of taxa and support the conclusions of the risk assessment modeling that predict risks of concern across taxa based on the high toxicity of these chemicals. It should be noted that the lack of reported incidents should not be construed as the absence of incidents. The Agency intends to continue to monitor ecological incidents for acephate and will conduct additional analyses if necessary.

3. Ecological and Environmental Fate Data Needs

The environmental fate database for acephate is not considered complete. Environmental chemistry methods for soil and water (Guideline studies 835.6100 and 835.6200) are outstanding from DCI-GDCI-103301-917 which requested these studies for acephate and the degradate methamidophos. The Agency will continue to work with the registrant to fulfill this requirement, however, the absence of these data did not impact the Agency's assessment. The ecological effects database is also incomplete. As described below, data are needed to complete the Tier I, Tier II, and Tier III pollinator data sets. Uncertainties still exist regarding toxicity to terrestrial plants for the ornamental shrub and vine uses, but additional plant data are not requested at this time.

Pollinator Data Requirements for Acephate and Methamidophos
Given the existing pollinator data gaps and because methamidophos is more toxic than acephate across several taxa, pollinator data are being requested for parent acephate and the methamidophos degradate.

Tier 1

- Non-Guideline (OECD TG 213) Honey bee adult acute oral toxicity (TGAI)
- Non-Guideline (OECD TG 237) Honey bee larvae acute oral toxicity (TGAI)
- Non-Guideline (OECD TG 245) Honey bee adult chronic oral toxicity (TGAI)
- Non-Guideline (OECD GD 239 Honey bee larvae chronic oral toxicity (TGAI)

Tier 2[†]

- Non-Guideline Field trial of residues in pollen and nectar (TEP)
- Non-Guideline (OECD GD 75) Semi-field testing for pollinators (TEP)

Tier 3[†]

- 850.3040 Full-Field testing for pollinators (TEP)

[†] The need for higher-tier tests for pollinators will be determined based upon the results of lower tiered tests and/or other lines of evidence and the need for a refined pollinator risk assessment.

C. Endocrine Disruptor Screening Program (EDSP)

For information regarding acephate and the Endocrine Disruptor Screening Program, please see Appendix D.

D. Benefits Assessment

Acephate is used to control a variety of sucking and chewing insect pests and is classified by the Insecticide Resistance Action Committee (IRAC) as a Group 1B Mode of Action (MOA) insecticide. It is registered for use on both agricultural and non-agricultural uses sites, and it is a contact insecticide with systemic activity within plant tissues, providing protection against insects which feed on them for approximately 10 to 15 days after application. Additional details may be found in the supporting documents located in the acephate docket EPA-HQ-OPP-2008-0915. Following below are summaries of EPA's benefits findings for specific use settings, as based on these supporting documents.

Cotton

Acephate can be used in multiple ways in cotton production: as a seed treatment, a soil (in-furrow) treatment, and a foliar treatment. Seed, soil, and early season foliar applications generally target thrips; later season foliar applications more commonly target stink and plant bugs. Acephate has benefits as a seed treatment and in-furrow ground spray, where it provides a unique mode of action in early season control of thrips. Acephate is the only organophosphate available which can be used as a seed or in-furrow treatment against thrips. Identified effective chemical alternatives to acephate for thrip control as seed treatment include imidacloprid, either alone or in combination with thiodicarb; and identified alternatives for acephate as an in-furrow application for thrips include aldicarb and imidacloprid. These alternatives are at least as efficacious as acephate but are usually more expensive.

Acephate also has benefits as an early emergent foliar spray against thrips. Growers have several efficacious alternatives, including spinetoram, dicrotophos, and dimethoate. However, compared to acephate, the alternatives are either much more expensive (spinetoram) or have the potential to cause crop damage (dimethoate and dicrotophos) when mixed with herbicides. This can increase operational costs and limit application flexibility. Growers can also replace early season acephate treatments (seed, in-furrow, and foliar) to control thrips by planting a cotton variety that has been genetically modified to control thrips, but this may increase seed costs.

To control plant bugs and stink bugs, acephate is used in the later stages of cotton production from pinhead squaring to harvest. Acephate has benefits for late season control of plant bugs and stink bugs where alternatives to acephate can be slightly more expensive, though more effective. Identified chemical alternatives for late season control of plant bugs and stink bugs include dicrotophos, dicrotophos with bifenthrin, and sulfoxaflor (for plant bugs only).

When taken altogether, the Agency finds that acephate provides cost-effective control against key pests in cotton, and application flexibility (due to herbicide tank-mix compatibility) when also treating for early season weeds. In the absence of acephate, the Agency expects that cotton growers would be able to replace acephate with viable alternatives while incurring an increase of operational costs. Efficacious alternatives, both in the form of other pesticides and the availability of new varieties of genetically modified cotton that offers some control of plant bugs and thrips, provide growers with the tools to manage important cotton pests which are currently managed with acephate.

Soybean

Acephate is used on soybean almost exclusively within Arkansas, Louisiana, Mississippi, and Texas. This region, referred to here as the Mid-South, accounts for 8% of soybean acres harvested nationwide and creates about 8% of the national soybean gross revenue per year on average ($3 billion per year). Set in that context, acephate is a minor component of insect pest management programs in the nation's overall soybean production. However, in the Mid-South region, acephate is used on 19% of soybean acres grown. Within the Mid-South, more than half of acephate treated acres are reported to have applied acephate to soybeans aerially.

Soybean growers primarily use acephate (often tank mixed with bifenthrin, a pyrethroid) to control various stink bug species. While all these species can cause significant damage to soybean flowers and seed pods, the redbanded stink bug (RBSB) is the most important stink bug species targeted with acephate in the Mid-South region's soybeans because acephate appears to provide better control of RBSB than other pest control options and the RBSB can cause more damage than other relevant stink bugs. There are two alternatives similar in performance to acephate for the RBSB; one pyrethroid (bifenthrin, available as a stand-alone product and as a premix with another pyrethroid, zeta-cypermethrin) and a combination product which contains a neonicotinoid (thiamethoxam) and a pyrethroid (lambda-cyhalothrin). These offer levels of control that are similar but somewhat less than the level provided by acephate. Additionally, these alternatives are priced similarly to acephate. However, in the absence of acephate, the increased use of the remaining two MOAs (pyrethroid and neonicotinoid) would exacerbate resistance problems. This in turn would greatly increase crop damage by RBSB.

For non-RBSB stink bug control, there are alternative efficacious chemistries with cost profiles similar to acephate. Of these stink bugs, the green stink bug has the largest number of alternatives with efficacy equivalent or close to that of acephate; the brown stink bug has fewer of these. However, these alternatives have efficacy ratings that appear to be slightly less than acephate. Consequently, growers will need to apply these alternatives more frequently than acephate to achieve the same broad-spectrum stink bug control.

EPA concludes that acephate provides overall high benefits to soybean growers in the Mid-South because there are only a few viable alternatives able to target the RBSB but have less flexibility. These alternatives are all pyrethroids and neonicotinoids so that resistance problems

would be exacerbated due to the loss of an additional MOA (acephate) and the increased use of the remaining two MOAs (bifenthrin and thiamethoxam). In the few areas of the Mid-South with low RBSB pressure, there are lower benefits from acephate use because there are more recommended alternative MOAs that are effective and have similar costs. However, in the longer term, the unavailability of acephate will increase the likelihood of resistance development to pyrethroids and neonicotinoids, which may lead to significant economic impacts to southern U.S. soybean growers due to resistance development.

Vegetables, beans, and seed crops

In vegetable and seed crops, acephate is frequently recommended for use against piercing sucking insects including aphids, Lygus bugs, thrips, and various lepidopteran pests. One key benefit of acephate is its low cost compared to alternatives. Growers may experience elevated production costs in order to maintain the same level of insect pest control in the absence of acephate.

Acephate confers moderate benefits for celery production as an inexpensive control option for aphid outbreaks early in the season. Efficacious alternatives exist and are used by celery growers but are typically more expensive than acephate. The main benefit of acephate for aphid management in celery is likely for early season outbreaks, while more expensive alternatives are reserved for aphid management close to harvest to ensure a marketable crop. In the absence of acephate, celery growers may incur increased costs of insecticide applications to maintain adequate pest control for early season aphid outbreaks.

Acephate confers low to medium benefits for seed crops including alfalfa, carrot, radish, and parsley. Acephate is used in these crops to manage Lygus and/or aphids. The main benefits of acephate to these crops is its broad spectrum of efficacy against multiple key target pests, and as a resistance management tool. In carrot and radish seed production, acephate is one of only two active ingredients recommended for use against all key target pests, so it would likely need to be replaced by two or more chemistries which may be complicated and costly. In carrot, radish, and parsley seed, growers may have some difficulty maintaining a thorough resistance management program in the absence of acephate.

Acephate confers low benefits for lettuce, dry beans, fresh lima beans, succulent beans, succulent green beans grown for seed, pepper, cauliflower, and Brussels sprout production. This conclusion is based on the overall low precent crop treated in these sites and the availability of efficacious alternatives with a range of modes of action (some of which are less expensive per acre than acephate), for all major pests targeted by acephate in these crop sites.

Other crops: tobacco, peanut, mint, cranberry

Acephate confers high benefits for tobacco production, both on seedlings in float beds and post-transplant in the field. Acephate is the only synthetic insecticide registered for use on tobacco seedlings in greenhouses and is used to control aphids, thrips, flea beetles, and

cutworms in both indoor and outdoor float beds. Acephate is also the most frequently used insecticide for several pests (aphids, flea beetles, cutworms) post-transplant in the field, and growers frequently target more than one pest with a single application. Acephate's combination of a broad spectrum of activity, low cost, and short pre-harvest interval provide a unique set of characteristics that is unfulfilled by alternatives.

For peanut production, acephate confers high benefits, as it is the primary insecticide used for thrips post-emergence in the field through harvest. In the post-emergence crop stage, an average of 59% of acres treated for thrips are treated with acephate. Alternatives are either more expensive than acephate or are known to cause secondary pest outbreaks and may cause more issues for growers after being used.

Acephate confers medium benefits for mint production due to its efficacy against some of the most economically damaging pests of mint: redbacked cutworm and mint root borer. There are a limited number of effective insecticides available for redbacked cutworm, so growers may have difficulty adequately managing them and maintaining resistance management in the absence of acephate. Acephate is also recommended for several other mint pests which can co-occur in fields (aphids, weevils, loopers, cutworms, armyworms), so growers may use acephate to target more than one pest at each application. Therefore, growers may need to use more than one insecticide to replace acephate, maintain adequate pest control, and maintain resistance management, which could increase pest control costs and management complexity.

In Pacific Northwest cranberry production, acephate offers overall low benefits. Currently, alternative chemistries, along with cultural and biological measures are available to effectively control target pests in this use site.

Non-food agricultural and non-agricultural uses

The Agency assessed acephate usage, availability of chemical alternatives, pest management benefits, and impacts from potential loss of acephate in the following non-food agricultural and non-agricultural use sites: turf and ornamental plants (in both landscape and nursery settings), trees, kenaf (a fiber commodity), non-bearing fruit and nut trees and vine crops, miscellaneous landscapes (rights-of-ways, field borders, etc.), and indoor non-residential structures (e.g., eating establishments, food processing plants).

EPA concludes that acephate offers overall low benefits for turf and ornamental use sites. In these use settings, multiple alternatives are currently available to effectively control pests targeted by acephate, and stakeholders report a decreasing trend in acephate use. However, due to the vast diversity of ornamental commodities and surveyed use patterns, there might be certain pest/host plant scenarios where acephate might provide higher benefits.

Similarly, the Agency concluded that benefits of acephate as a pest management tool are generally low for insect control in and outside commercial and instructional structures and for

kenaf, which is a fiber and forage commodity that appears to have no production in the one state where acephate is registered (North Carolina), and very little U.S. production generally.

For insect pests of trees, EPA again concludes that acephate generally provides low pest management benefits because several effective alternatives are available for most insect pests. However, for a few pests (e.g., the cottony maple leaf scale), there may be very few alternatives to acephate. In that case, management of the pest will become either more complicated (if the alternative is more difficult to implement), resistance to alternatives in pest populations may become more likely to occur, or the pest may cause enough damage for the tree to be removed and/or replaced. That would add to the economic costs of a loss of acephate where such pests rise to high population levels.

IV. PROPOSED INTERIM REGISTRATION REVIEW DECISION

The Agency is issuing this PID in accordance with 40 C.F.R. §§ 155.56 and 155.58. Based on the Agency's review of acephate at this time in the registration review process, EPA is proposing certain changes to the affected registrations and their labeling. EPA proposes that the mitigations identified in Sections IV.A–B and Appendices A and B will address specific risks of concerns identified at this point in the ongoing registration review process.

At the end of the registration review process, EPA will decide whether each acephate registration "continues to satisfy the FIFRA standard for registration."[20] However, the mitigation proposed in this PID may not be sufficient for EPA to conclude that acephate registrations continue to satisfy the FIFRA standard for registration. EPA may determine that additional mitigations or other measures are necessary in subsequent interim decisions or in the final registration review decision. For acephate, in this PID, EPA has identified data on ecological effects that are needed to complete registration review and will issue a data call-in for that information, as discussed in Section IV.E.

The Agency has not made ESA effects determinations for acephate registrations. However, EPA proposes that the mitigation in this PID will reduce environmental exposure to acephate and may reduce effects on listed species whose range or critical habitat co-occur with the use of acephate.

Additionally, EPA has added FIFRA IEM measures in Section IV.B of this PID, which are intended to reduce effects to non-target organisms, including listed species. EPA also believes that the FIFRA IEM measures proposed in Section IV.B would fulfill EPA's obligations under Section 711 of the Consolidated Appropriations Act, PL-117-328 (Dec. 29, 2022). Section 711 requires EPA to

[20] 40 C.F.R. §§ 155.40(a), 155.57; 7 U.S.C. § 136a(g); *see also* 7 U.S.C. §§ 136a(c)(5) (FIFRA registration standard), 136(bb) (defining "unreasonable adverse effects on the environment" as encompassing both "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" [FIFRA's risk-benefit standard] and "a human dietary risk from residues that result from a use of a pesticide in or on any food inconsistent with the [FFDCA safety standard]"). This document is not a "registration review decision" within the meaning of FIFRA Section 3(g) and 40 C.F.R. § 155.57.

"include, where applicable, measures to reduce the effect of the applicable pesticide on" listed species and designated critical habitats in any ID noticed in the Federal Register between December 29, 2022 and October 1, 2026 for which EPA has not "made effects determinations or completed any necessary consultation under [ESA Section 7(a)(2)]." Section 711 also requires EPA to "take into account the input" of the Secretary of Agriculture and other members of the Interagency Working Group (IWG), established under FIFRA Section 3(c)(11), in developing such measures. EPA has taken into account input from USDA and other members of the IWG in developing the FIFRA IEM measures. EPA has previously requested public input on the FIFRA IEM measures described in this PID. The Agency will complete effects determinations and any necessary Endangered Species Act (ESA) Section 7 consultation with the Services before issuing a final registration review decision for acephate. For more information, see Appendix C.

A. Proposed Risk Mitigation and Regulatory Rationale

EPA evaluated the current registered uses of acephate and identified the following risks of concern:

1. Dietary risk driven by drinking water concentrations that even when highly refined is of concern.
2. Risks of concern and incidents involving residential handler and post-application exposures.
3. Risks of concern for occupational handlers that cannot be resolved with PPE for landscape/ornamental and seed treatment applications.
4. Risks of concern to terrestrial vertebrates.
5. Risks of concern to freshwater invertebrates.
6. Risks of concern and incidents involving honey bees.

Based on the currently registered uses of acephate, EPA cannot determine that there is a reasonable certainty that no harm would result from aggregate exposure, including all anticipated dietary (food and drinking water) exposures and residential exposures.

While the EPA has investigated retaining a subset of uses as described in section III.A.1. in this PID, EPA has not evaluated all possible subsets of uses. The purpose of focusing on this subset (cotton and soybeans) was to determine, whether or not the resulting reductions to estimated drinking water concentrations would sufficiently reduce dietary risk if these were the only uses permitted on the label. Given that the Agency was without registrant agreement on evaluating a specific subset of uses to retain, the subset of uses assessed for this PID were selected solely based on their high usage (pounds applied and total acres treated of acephate).

In section III.D. of this PID, EPA discussed its assessment of the benefits of acephate use and potential impacts should acephate no longer be available for use. EPA has identified overall high benefits to soybean growers in the Mid-South because there are only a few viable alternatives. However, EPA has identified efficacious alternatives for acephate use in cotton, both in the form of other pesticides and the availability of new varieties of genetically modified cotton as tools to manage important cotton pests.

The EPA requests commentors consider focusing comments on this PID to identify specific pest pressures in specific crops with few alternatives to acephate and particularly high impacts should acephate not be available as a tool. Additional information of this nature is critical if EPA is to conduct any further analysis of uses that could be maintained.

However, given the current registered uses of acephate, to address dietary and aggregate risks along with post-application risk from indoor uses, the Agency is proposing the cancellation of all uses of acephate that contribute to dietary and aggregate risk. Uses that do not contribute to dietary or residential exposure may be retained, as discussed below.

The proposed use cancelations would eliminate the exposure to acephate which is driving the risks to occupational handlers, terrestrial vertebrates, and aquatic invertebrates. However, EPA has identified a need for FIFRA IEM measures to reduce exposure to non-target terrestrial invertebrates, including listed species, at this time based on the use patterns that would remain after the proposed cancellations.

1. Use Cancellation

Because current uses of acephate pose dietary and aggregate risks inconsistent with the FFDCA safety standard, and also pose occupational handler risk and risk to non-target organisms, EPA is proposing to cancel all uses of acephate other than tree injection. This will eliminate all risks of concern, including dietary/drinking water risk, residential and occupational risks, and risks to non-target organisms.

The Agency is proposing to maintain current uses of acephate for tree injection – including applications to forestry, shelter belts, rangeland trees, tree farms/plantations (including Christmas trees), seed orchards/plantations, southern pine seed orchards, non-bearing fruit and nut trees and vines as seedlings, nursery stock, and non-bearing orchards – because this application method does not contribute to dietary or aggregate risk or pose any occupational, post-application risks of concern. The Agency did not assess this method of application for ecological risk, however, due to the fate properties of acephate and methamidophos, it is not expected to contribute significantly to runoff, and due to the route of exposure is not expected to pose significant risk to non-target organisms.

The standard for assessing aggregate risks such as these does not allow for risk-benefit balancing. However, the Agency has assessed the benefits of acephate for pest management (and resistance management), which is summarized in section III.B. of this document.

Under 40 CFR 155.53, the EPA includes a public participation process in its decision making. For acephate, EPA is soliciting public comment on alternate mitigation (including the feasibility of potential application rate reductions, reductions in the number of yearly applications, prohibitions on higher exposure application methods, and other mitigations) and on data-

supported regional and national information (regarding specific uses with high pest management benefits or unusual pest pressures) that may allow for certain registered uses of acephate to fall below the Agency's LOC for dietary and aggregate risk. After considering any comments on the PID, the Agency will issue an interim registration review decision that will include an explanation of any changes to the proposed decision and the Agency's response to significant comments.

B. FIFRA Interim Ecological Mitigation Measures

The ESA Workplan Update Appendix includes a menu of FIFRA IEM measures, some of which are included in this PID. EPA previously sought public comment on the full suite of FIFRA IEM measures, which is available in the ESA Workplan Docket (EPA-HQ-OPP-2022-0908-0002), at www.regulations.gov. EPA updated some of the FIFRA IEM measures after considering public comments on the ESA Workplan Update and additional EPA and interagency review of the mitigations. The FIFRA IEM measures proposed for acephate in this PID reflect these revisions.

EPA developed the FIFRA IEM measures to reduce exposure to non-target organisms, including listed species, based on the risks and benefits of acephate.[21] As outdoor use for tree injections are proposed to remain, EPA is proposing the following FIFRA IEM measures for acephate products for use in tree injection:

- Pollinator stewardship advisory label language
- Ecological incident reporting label language
- Bulletins Live! Two (BLT) labeling

Note that the FIFRA IEM language for the proposed remaining acephate tree injection uses have been slightly modified from the standard FIFRA IEM language, as the standard language was designed for more common agricultural applications. The proposed FIFRA IEM measures in this PID are not designed to fully address EPA's ESA obligations for acephate during registration review. Rather, they are initial steps under FIFRA that are designed to reduce exposure to all non-target organisms, including listed species, while EPA continues to work towards meeting its ESA obligations during registration review before issuing a final registration review decision. EPA may subsequently propose additional mitigation measures for acephate during registration review, such as mitigations developed as part of its various ESA initiatives.[22] Additional measures may also be necessary when EPA conducts effects determinations and, if necessary, consults with the Service(s) on acephate.

1. Pollinator Hazard Statement and Advisory Pollinator Stewardship Language

[22] https://www.epa.gov/endangered-species/implementing-epas-workplan-protect-endangered-and-threatened-species-pesticides

Acephate may be applied as a tree-injection on pollinator attractive trees. Pollinators may collect pollen even from wind pollinated tree species. Toxicity and incident data indicate risks of concern for honey bees, so the EPA is proposing a pollinator hazard statement.

The proposed pollinator hazard statement is as follows:
"This product is highly toxic to bees."

EPA is proposing the pollinator hazard statement above for products with labeled agricultural crop uses. The language is derived from language in EPA's Label Review Manual and should not have adverse impacts to the user.

EPA is also proposing to include advisory language for insect pollinators. This advisory language distills the most important information growers need to know to voluntarily reduce risk to insect pollinators. The language is intended to raise awareness of potential hazard to bees and other insect pollinators. Although this language is advisory, the goal is to promote best management practices that applicators may consider to reduce exposures to bees, particularly managed pollinators. This language is consistent with EPA's pollinator protection strategic plan.[23]

Best management practices describe ways to manage pesticide applications in order to protect non-target organisms and mitigate environmental impacts. The Agency is proposing the following labeling to highlight pollinator best management practices:

"Advisory Best Management Practices for Pollinator Protection

The following best management practices (BMPs) can help reduce risk to pollinators:

- Develop and maintaining clear communication with local beekeepers to help protect bees. To the extent possible, advise beekeepers within a 1-mile radius 48-hrs in advance of the application, and confirm hive locations before injection.
- Avoid applications when bees are actively foraging.
- Avoid applying pesticides to trees in bloom.
- Apply pesticides when fewer bees are foraging.
- Use Pollinator Protection Plans when they are available. These plans may be available from state lead agencies and promote communication between growers, landowners, farmers, beekeepers, pesticide users, and other pest management professionals to reduce exposure of bees and other pollinators to pesticides.
- Use integrated pest management to prevent or mitigate potential negative effects to pollinators and consider multiple pest management options before resorting to a pesticide application.

[23] https://www.epa.gov/pollinator-protection/pollinator-protection-strategic-plan

For additional resources on pollinator BMPs and Pollinator Protection Plans, visit https://www.epa.gov/pollinator-protection/find-best-management-practices-protect-pollinators ."

2. Ecological Incident Reporting Label Language

EPA has required ecological incident reporting language on some labels in the past, and ecological incident reporting has been included as a reasonable and prudent measure in Biological Opinions issued by the Services. The Agency anticipates the need to add incident reporting labeling as part of any necessary ESA consultation. EPA is proposing incident reporting labeling to provide consistent information to pesticide users on how to report ecological incidents and in order to expedite any ESA necessary consultation. The proposed incident reporting language is as follows:

"**REPORTING ECOLOGICAL INCIDENTS**: For guidance on reporting ecological incidents, including death, injury, or harm to plants and animals, including bees and other non-target insects, see EPA's Pesticide Incident Reporting website: https://www.epa.gov/pesticide-incidents or call (registrant phone number)."

3. Bulletins Live! Two Labeling

ESA mitigation can take the form of nationwide restrictions on the general pesticide product labeling or geographic-specific restrictions located in Endangered Species Protection Bulletins (hereafter referred to as Bulletins), which are extensions of the general labeling accessed through a website. EPA is using a web-based system, Bulletins Live! Two (BLT), to provide timely protections for listed species and to minimize pesticide product labeling changes.

EPA uses BLT when mitigation applies in a particular geographic region where listed species are present and, in some cases, during only certain times of the year. BLT simplifies compliance by offering a tool for users to identify where and when they are subject to the mitigation. When directed by product labeling, pesticide applicators are required to visit the BLT online database, and follow any mitigation specified in a Bulletin for the application area.

Acephate does not currently have any listed species bulletins. However, the Agency is proposing the following Bulletins language be added to all acephate product labels. This language instructs users to check the Bulletins Live! Two website in order to understand listed species use restrictions that may apply to them, if available. Including this language on product labels will help streamline implementation of any additional risk reduction measures that may be identified during any necessary ESA consultation.

The proposed BLT language is as follows:

"**ENDANGERED AND THREATENED SPECIES PROTECTION REQUIREMENTS**: Before using this product, you must obtain any applicable Endangered Species Protection Bulletins ('Bulletins') within six months prior to or on the day of application. To obtain Bulletins, go to Bulletins Live! Two (BLT) at https://www.epa.gov/pesticides/bulletins. When using this product, you must

follow all directions and restrictions contained in any applicable Bulletin(s) for the area where you are applying the product, including any restrictions on application timing if applicable. It is a violation of Federal law to use this product in a manner inconsistent with its labeling, including this labeling instruction to follow all directions and restrictions contained in any applicable Bulletin(s). For general questions or technical help, call 1-844-447-3813, or email ESPP@epa.gov."

Although the BLT system has been in place for many years, there may be applicators who are unfamiliar with this system. Using the online tool to determine if mitigation is required for a particular treatment area may be a new step that many users will need to take prior to an application. However, the Agency anticipates that over time and with wider implementation, BLT will become a familiar tool that is integrated into a user's planning process for pesticide applications. In February 2022, EPA released an improved version of BLT[24], which allows users to more easily find the information they need for a particular pesticide product. The Agency has also developed a tutorial[25] that explains how to use the online system. In addition, the general label language referring users to BLT provides a phone number and email address for those needing technical assistance.

EPA is currently working on several ESA strategies such as the Vulnerable Species Pilot[26] and the Herbicide Strategy[27] to expedite and streamline the ESA consultation process and provide protections for listed species. Pesticide Use Limitation Areas (PULAs) and the associated geographically specific mitigation (i.e., bulletins) are not yet available under these efforts. While the BLT language above is being proposed to be added on the pesticide label without being linked to PULAs or bulletins for acephate at this time, pesticide users should be aware that as various ESA pilot efforts are finalized, EPA expects to add new PULAs and new bulletins to BLT. Before new PULAs and bulletins are added in BLT, EPA will notify stakeholders and provide an opportunity for public comment. See Appendix C: Listed Species Assessments for more information.

C. Environmental Justice

EPA seeks to achieve environmental justice, the fair treatment and meaningful involvement of all people, regardless of race, color, national origin, or income, in the development, implementation, and enforcement of environmental laws, regulations, and policies. The Agency seeks information on any other groups or segments of the population who, as a result of their location, cultural practices, or other factors, may have atypical, unusually high exposure to acephate compared to the general population or who may otherwise be disproportionately affected by the use of acephate as a pesticide.

[25] https://www.epa.gov/endangered-species/bulletins-live-two-blt-tutorial
[26] https://www.regulations.gov/docket/EPA-HQ-OPP-2023-0327
[27] https://www.regulations.gov/docket/EPA-HQ-OPP-2023-0365

One community which may experience disproportionate exposure to pesticides is agricultural farmworkers. EPA has conducted assessments of risks to farmworkers who handle acephate or may be exposed to acephate when mixing, loading, applying, entering treated areas performing post-harvest and planting activities and has found risks of concern for acephate. EPA plans to eliminate these risks through the mitigation outlined in Section IV. A. EPA has also evaluated the risks to people living adjacent to treated fields, which may include many farmworker families, and has found risks of concern for acephate, such as non-occupational spray drift. This risk will be eliminated by the proposed mitigation.

D. Tolerance Actions

Typically, when pesticide food uses are cancelled, the Agency would take action to revoke the related tolerances since there would no longer be U.S. registrations for these uses. Should there be food-uses that can be reconsidered following the comment period on this PID, and should any food uses remain, the Agency plans to exercise its FFDCA authority to update the tolerance expression to appropriately cover the metabolites and degradates of acephate and to specify the residues to be measured for each retained commodity for enforcement purposes. EPA would amend the tolerance expression for such commodities to read as follows:

Acephate 40 C.F.R. § 180.108: Summary of Anticipated Tolerance Actions			
§180.108 (a) General (1) Tolerances are established for residues of the insecticide acephate, including its metabolites and degradates other than methamidophos, in or on the commodities in the following table. Compliance with the tolerance levels specified in this paragraph is to be determined by measuring only acephate, O,S-dimethyl N-acetylphosphoramidothioate, in or on the commodity.			
Commodity/Correct Commodity Definition	**Established Tolerance (PPM)**	**Anticipated Tolerance (PPM)**	**Comments**
All food and feed commodities (other than those covered by a higher tolerance as a result of use on growing crops) in food handling establishments	--	0.02	Moved from (b)
Brussels sprouts	3.0	3	OECD rounding class practice
Cauliflower	2.0	2	OECD rounding class practice
Cotton, gin byproducts	-	150	Recommended for in memo D. Drew, D446265, 09-MAR-2018
Cotton, hulls	1.0	1	OECD rounding class practice
Cotton, meal	1.0	1	OECD rounding class practice

Pepper, bell	-	4	Corrected commodity definition, OECD rounding class practice
Pepper	4.0	-	
Pepper, nonbell	-	4	Corrected commodity definition, OECD rounding class practice
Pepper	4.0	-	
Peppermint, fresh leaves	-	27	Corrected commodity definition
Peppermint, tops	27	-	
Spearmint, fresh leaves	-	27	Corrected commodity definition
Spearmint, tops	27	-	
Soybean, seed	1.0	1	OECD rounding class practice
Vegetable, legume, pulse, dried shelled, except soybean, subgroup 6-22E	-	3	Corrected commodity definition, OECD rounding class practice
Bean, dry, seed	3.0	-	
2) A tolerance of 0.02 ppm is established for residues of acephate, *O,S*-dimethyl acetyl phosphoramidothioate, including its metabolites and degradates other than methamidophos, in or on all food items (other than those already covered by a higher tolerance as a result of use on growing crops) in food handling establishments where food and food products are held, processed, prepared and served, including food service, manufacturing and processing establishments, such as restaurants, cafeterias, supermarkets, bakeries, breweries, dairies, meat slaughtering and packing plants, and canneries, where application of acephate shall be limited solely to spot and/or crack and crevice treatment (a coarse, low-pressure spray shall be used to avoid atomization or splashing of the spray for spot treatments; equipment capable of delivering a pin-stream of insecticide shall be used for crack and crevice treatments). Spray concentration shall be limited to a maximum of 1.0 percent active ingredient. Contamination of food or food-contact surfaces shall be avoided. Contamination of food or food-contact surfaces shall be avoided. Compliance with the tolerance levels specified in this paragraph is to be determined by measuring only acephate, O,S-dimethyl acetyl phosphoramidothioate, in or on the commodity.			
Food commodities (other than those covered by a higher tolerance as a result of use on growing crops) in food handling establishments	0.02	remove	Remove 180.108(a)(2) and add to the table in 180.108(a)(1); Remove specific use directions from tolerance definition.
(3) Tolerances are established for residues of methamidophos, including its metabolites and degradates, in or on the commodities in the following table as a result of the application of acephate. Compliance with the tolerance levels specified in this paragraph is to be determined by measuring only methamidophos, *O,S*-dimethyl phosphoramidothioate, in or on the commodity.			
Brussels sprouts	0.5	1	Harmonize with Canada
Cotton, gin byproducts	-	20	Recommended in memo D. Drew,

			D446265, 09-MAR-2018
Cotton, undelinted seed	-	0.1	Recommended for 0.2 ppm in memo D. Drew, D446265, 09-MAR-2018 for harmonization. No longer applicable for harmonization with Canada and Codex. Highest residue is 0.05 ppm in memo F. Fort, D259659, 18-AUG-1999.
Pepper, bell	-	1	Corrected commodity definition
Pepper	1	-	
Pepper, non-bell	-	1	Corrected commodity definition
Pepper	1	-	
Peppermint, fresh leaves	-	1	Corrected commodity definition
Peppermint, tops	1	-	
Spearmint, fresh leaves	-	1	Corrected commodity definition
Spearmint, tops	1	-	
Vegetable, legume, pulse, bean, dried shelled, except soybean, subgroup 6-22E	-	1	Corrected commodity definition
Bean, dry, seed	1	-	
(b) Section 18 emergency exemptions (c) Tolerances with regional registrations. A tolerance with a regional registration is established for residues of acephate, O,S-dimethyl acetyl phosphoramidothioate, including its metabolites and degradates other than methamidophos, in or on the commodity in the following table. Compliance with the tolerance level specified in this paragraph is to be determined by measuring only acephate, O,S-dimethyl acetyl phosphoramidothioate, in or on the commodity.			
Nut, macadamia	0.05	remove	Special Local Needs registration in HI for macadamia nuts was cancelled in 1987

E. Data Requirements

EPA intends to generate a data call-in for acephate and methamidophos for submission of Tier I, II, and III pollinator data as a separate action. These data would allow the Agency to conduct an assessment of pollinator and terrestrial invertebrate risk with greater certainty. Crop field trials depicting residues of acephate in/on cowpea forage and hay have not been submitted. If

the registrant wishes to support the use on cowpea, residue data depicting residues of acephate and methamidophos in/on cowpea forage and hay should be provided.

V. NEXT STEPS AND TIMELINE

A. Comment on this Proposed Interim Decision

A Federal Register Notice will announce the availability of the Acephate PID and open a 60-day comment period on this PID, as well as the 2023 updated HH DRA and DWA. The Agency may issue an ID after the close of this comment period if appropriate or may proceed to a final registration review decision for acephate without previously issuing an ID. However, a final registration review decision for acephate will only be made after EPA (1) completes effects determinations, and (2) meets EPA's ESA section 7 obligations (*e.g.*, initiates any necessary consultation with the Services, consistent with ESA section 7(a)(2)).

A. Implementation of Mitigation Measures if EPA Issues an ID

If EPA ultimately posts an ID for acephate to the public docket, then the acephate registrants will be expected to submit amended labels, include the label changes described in the Appendices to the ID, and requests for amendment of registrations within 60 days.

Appendix A: Summary of Proposed Mitigation for Acephate

Registration Review Case #: 0042
PC Code: 103301
Chemical Type: insecticide
Chemical Family: organophosphate
Mode of Action: cholinesterase inhibition

Affected Population(s)	Source of Exposure	Route of Exposure	Duration of Exposure	Potential Risk(s) of Concern	Proposed Mitigation	Comment
• General population • Residential handlers • Occupational Handlers • Post Application • Birds, mammals, terrestrial Invertebrates, Aquatic Invertebrates, terrestrial plants	• Water (dietary) • Contact • Spray drift • Runoff • Treated seed	• Ingestion • Dermal • Inhalation	• Acute • Sub-Chronic • Chronic	• Acute Toxicity • AChE inhibition • Neurotoxicity	• Cancel all use except tree injection	

Appendix B: Proposed Labeling Changes for Acephate Products

Description	Proposed Label Language for Acephate Products	Placement on Label
	Technical and Manufacturing Use Products	
Formulation restrictions	**"Only for formulation into products for application by tree injection"**	Directions for Use
Cancellation of Uses	Remove use on: o Alfalfa o Beans (dry) and Lima beans o Brussel sprouts o Cauliflower o Celery o Christmas trees (not including tree injection to non-bearing trees) o Citrus (not including tree injection to non-bearing trees) o Cotton and cottonseed o Cranberry o Deciduous fruit trees (not including tree injection to non-bearing trees) o Fire ant mounds o Grapes o Lettuce o Macadamia nuts (not including tree injection to non-bearing trees) o Mint including peppermint and spearmint o Non-bearing Trees (not including tree injection to non-bearing trees) o Nursery stock (not including tree injection to non-bearing trees) o Ornamental floral and foliage plants o Peanuts o Peppers (bell and non-bell) and sweet peppers o Residential and commercial premises o Rights-of-way o Indoor use on residential, institutional/commercial/industrial, greenhouse, recreation, refuse containers, restaurants, manufacturing plants, hotels, ships, and boats	

<table>
<tr><td></td><td>

Outdoor use on wasp nests, perimeter of structures, windows, entryways, patios, carports and garages
Sod
Pine trees (not including tree injection to non-bearing trees)
Shrubs
Soybeans
Succulent green beans grown for seed
Tobacco
Tree nuts (not including tree injection to non-bearing trees)
Turfgrass
Wasteland/non-crop undeveloped areas

</td><td></td></tr>
<tr><td></td><td>End Use Products</td><td></td></tr>
<tr><td></td><td>Note to registrant:

Include the name of the ACTIVE INGREDIENT in the first column
Include the word “GROUP” in the second column
Include the MODE/MECHANISM/SITE OF ACTION CODE in the third column (for fungicides this is the FRAC Code, and for insecticides this is the Primary Site of Action; for Herbicides this is MODE OF ACTION)
Include the type of pesticide in the fourth column.

<table>
<tr><td>ACEPHATE</td><td>GROUP ORGANO PHOSPHATE</td><td>MODE OF ACTION CODE 1B
as designated by IRAC</td><td>INSECTICIDE</td></tr>
</table>
</td><td>Front Panel, upper right quadrant.
All text should be black, bold face and all caps on a white background, except the mode of action code, which should be white, bold face and all caps on a black background; all text and columns should be surrounded by a black rectangle.</td></tr>
<tr><td>Pollinator Hazard Statement</td><td>“This product is highly toxic to bees”</td><td>Environmental Hazards under the Heading “POLLINATOR HAZARD STATEMENT”</td></tr>
<tr><td>Endangered Species Protection Requirements</td><td>“ENDANGERED AND THREATENED SPECIES PROTECTION REQUIREMENTS: Before using this product, you must obtain any applicable Endangered Species Protection Bulletins (‘Bulletins’) within six months prior to or on the day of application. To obtain Bulletins, go to Bulletins Live! Two (BLT) at https://www.epa.gov/pesticides/bulletins. When</td><td>Directions for Use, at the beginning under the heading</td></tr>
</table>

For all products, excluding those where exposure is negligible or there are no toxic effects expected across uses included on a product label (e.g., cattle ear tag, fly baits)	using this product, you must follow all directions and restrictions contained in any applicable Bulletin(s) for the area where you are applying the product, including any restrictions on application timing if applicable. It is a violation of Federal law to use this product in a manner inconsistent with its labeling, including this labeling instruction to follow all directions and restrictions contained in any applicable Bulletin(s). For general questions or technical help, call 1-844-447-3813, or email ESPP@epa.gov."	"ENDANGERED AND THREATENED SPECIES PROTECTION REQUIREMENTS"
Ecological Incidents Statement For all products with outdoor uses	"**REPORTING ECOLOGICAL INCIDENTS**: For guidance on reporting ecological incidents, including death, injury, or harm to plants and animals, including bees and other non-target insects, see EPA's Pesticide Incident Reporting website: https://www.epa.gov/pesticide-incidents or call (registrant phone number)".	Directions for Use, under the heading "REPORTING ECOLOGICAL INCIDENTS"
Resistance-management labeling statements for insecticides and acaricide	Include resistance management label language for insecticides/acaricides from PRN 2017-1 (https://www.epa.gov/pesticide-registration/pesticide-registration-notices-year). See section 3 (Scope) of the PRN to determine whether the resistance management measures outlined in the PRN apply to your product.	Directions for Use, prior to directions for specific crops
Advisory Best Management Practices for Pollinator Protection	**"Advisory Best Management Practices for Pollinator Protection** The following best management practices (BMPs) can help reduce risk to pollinators: • Develop and maintaining clear communication with local beekeepers to help protect bees. To the extent possible, advise beekeepers within a 1-mile radius 48-hrs in advance of the application, and confirm hive locations before injection. • Avoid applications when bees are actively foraging. • Avoid applying pesticides to trees in bloom. • Apply pesticides when fewer bees are foraging. • Use Pollinator Protection Plans when they are available. These plans may be available from state lead agencies and promote communication between growers, landowners, farmers, beekeepers, pesticide users, and other pest management professionals to reduce exposure of bees and other pollinators to pesticides. • Use integrated pest management to prevent or mitigate potential negative effects to pollinators and consider multiple pest management options before resorting to a pesticide application.	Directions for Use – Under the Advisory Best Management Practices header after Resistance Management section

Appendix C: Listed-Species Assessment

This Appendix provides general background about the Agency's assessment of the effects of pesticides on listed species and designated critical habitats under the Endangered Species Act (ESA).

Developing Approaches for ESA Assessments and Consultation for FIFRA Actions

In 2015, EPA, along with the Services—the U.S. Fish and Wildlife Service (FWS) and the National Marine Fisheries Service (NMFS)—and the United States Department of Agriculture (USDA) (referred to as "the agencies") released their joint Interim Approaches[28] for assessing the effects of pesticides to listed species. The agencies jointly developed these Interim Approaches in response to the 2013 National Academy of Sciences' recommendations that discussed specific scientific and technical issues related to the development of assessments of pesticides' effects to listed species. Since that time, the agencies have been continuing to work to improve the approaches for assessing effects to listed species. After receiving input from the Services and USDA on proposed revisions to the interim method and after consideration of public comments received, EPA released an updated *Revised Method for National Level Listed Species Biological Evaluations of Conventional Pesticides* ("Revised Method") in March 2020.[29]

The agencies also continue to work collaboratively through a FIFRA Interagency Working Group (IWG). The IWG was created under the 2018 Farm Bill to recommend improvements to the ESA section 7 consultation process for FIFRA actions and to increase opportunities for stakeholder input. This group is led by EPA and includes representatives from NMFS, FWS, USDA, and the Council on Environmental Quality (CEQ). The IWG outlines its recommendations and progress on implementing those recommendations in reports to Congress.[30]

Consultation on Chemicals in Registration Review

EPA initially conducted biological evaluations (BEs) using the interim method on three pilot chemicals representing the first nationwide pesticide consultations (final pilot BEs for chlorpyrifos, malathion, and diazinon were completed in January 2017). These initial pilot consultations were envisioned as the start of an iterative process. Later that year, NMFS issued a final biological opinion for these three pesticides. In 2019, EPA requested to reinitiate formal consultation with NMFS on malathion, chlorpyrifos and diazinon to consider new information that was not available when NMFS issued its 2017 biological opinion. EPA received a final

[28] https://www.epa.gov/endangered-species/interim-approaches-pesticide-endangered-species-act-assessments-based-nas-report.
[29] https://www.epa.gov/endangered-species/revised-method-national-level-listed-species-biological-evaluations-conventional.
[30] https://www.epa.gov/endangered-species/reports-congress-improving-consultation-process-under-endangered-species-act.

malathion biological opinion[31] from FWS in February 2022 and a final biological opinion from NMFS on malathion, chlorpyrifos and diazinon in June 2022.[32] In August 2023, the Agency implemented the FWS malathion biological opinion by issuing Endangered Species Protection Bulletins[33] and approving malathion label amendments[34] to incorporate measures to protect listed species. EPA plans to implement the NMFS biological opinion on malathion, chlorpyrifos and diazinon according to the 18-month timeframes specified in the biological opinion.

In 2020, EPA released draft BEs for the first two chemicals conducted using the 2020 Revised Method—carbaryl and methomyl. Subsequently, EPA has used the Revised Method to complete final BEs for carbaryl, methomyl, atrazine, simazine, glyphosate, clothianidin, imidacloprid, and thiamethoxam. EPA is currently in consultation with the Services on these active ingredients.

EPA's New Actives Policy and the 2022 Workplan

In January 2022, EPA announced a policy[35] to evaluate potential effects of new conventional pesticide active ingredients to listed species and their designated critical habitat and initiate consultation with the Services, as appropriate, before registering these new pesticides. Before the Agency registers new uses of pesticides for use on pesticide-tolerant crops, EPA will also continue to make effects determinations. If these determinations are likely to adversely affect determinations, the Agency will not register the use unless it can predict that registering the new use would not have a likelihood of jeopardizing listed species or adversely modifying their designated critical habitats. EPA will also initiate consultation with the Services as appropriate.

In April 2022, EPA released a comprehensive, long-term approach to meeting its ESA obligations, which is outlined in *Balancing Wildlife Protections and Responsible Pesticide Use*.[36] This workplan reflects the Agency's most comprehensive thinking to date on how to create a sustainable ESA-FIFRA program that focuses on meeting EPA's ESA obligations and improving protection for listed species while minimizing regulatory impacts to pesticide users and collaborating with other agencies and stakeholders on implementing the plan. Appendix A of the workplan noted that the current schedule for the expected draft and final biological evaluations for acephate will be in 2026. Additionally, as noted in the introduction section of this document, EPA recently settled a lawsuit with the Center for Biological Diversity and others that involves acephate. In the settlement EPA committed to issuing biological evaluations for certain pesticides, including acephate, no later than September 30, 2027. EPA will issue a draft biological evaluation for public comment before finalizing its biological evaluation.

[31] https://www.epa.gov/endangered-species/biological-opinions-available-public-comment-and-links-final-opinions.
[32] https://www.epa.gov/endangered-species/biological-opinions-available-public-comment-and-links-final-opinions.
[33] https://www.epa.gov/endangered-species/endangered-species-protection-bulletins
[34] https://www.regulations.gov/document/EPA-HQ-OPP-2009-0317-0154
[35] https://www.epa.gov/newsreleases/epa-announces-endangered-species-act-protection-policy-new-pesticides.
[36] https://www.epa.gov/endangered-species.

On November 16, 2022, EPA released the *ESA Workplan Update: Nontarget Species Mitigation for Registration Review and Other FIFRA Actions*.[37] As part of this update, EPA announced its plan to consider and include, as appropriate, a menu of FIFRA Interim Ecological Risk Mitigation intended to reduce off-target movement of pesticides through spray drift and runoff in its registration review and other FIFRA actions. These measures are intended to reduce risks to non-target organisms efficiently and consistently across pesticides with similar levels of risks and benefits. EPA expects that these mitigation measures may also reduce pesticide exposures to listed species.

The *ESA Workplan Update* also discussed additional efforts to expedite and streamline ESA consultation, including the Vulnerable Species Pilot, regional strategies (i.e., a Hawaii strategy), approaches for specific niche pesticide uses (e.g., mosquito adulticide applications), and programmatic approaches to consultation (e.g., the Herbicide Strategy).

In June 2023, EPA announced proposed mitigation for the Vulnerable Species Pilot, an implementation plan, and information on potential expansion of the pilot.[38] EPA also published interactive maps (StoryMaps) for the 27 pilot species to convey geospatial information about the location of the affected species and the location of draft pesticide application minimization and avoidance zones to protect these species.[39] Visit the public docket for more information about the Vulnerable Species Pilot (docket EPA-HQ-OPP-2023-0327 at www.regulations.gov).

In July 2023, EPA published the framework of the draft Herbicide Strategy[40] for public comment along with various supporting documents. For more information about the Herbicide Strategy, visit the public docket (docket EPA-HQ-OPP-2023-0365 at www.regulations.gov).

EPA continues to work on these pilot efforts and once finalized, expects to implement these through registration review and new active ingredient registration.

[37] https://www.epa.gov/system/files/documents/2022-11/esa-workplan-update.pdf.
[38] https://www.regulations.gov/document/EPA-HQ-OPP-2023-0327-0002
[39] View the StoryMaps for the 27 pilot species here:
https://storymaps.arcgis.com/collections/896d140363174c9d8ee78e4c471bd7fd
[40] https://www.regulations.gov/document/EPA-HQ-OPP-2023-0365-0009

Appendix D: Endocrine Disruptor Screening Program

The Federal Food Drug and Cosmetic Act (FFDCA) §408(p) requires EPA to develop a screening program to determine whether certain substances (including pesticide active and other ingredients) may have an effect in humans similar to an effect produced by a "naturally occurring estrogen, or other such endocrine effects as the Administrator may designate." (21 U.S.C. 346a(p)). In carrying out the Endocrine Disruptor Screening Program (EDSP), FFDCA section 408(p)(3) requires that EPA "provide for the testing of all pesticide chemicals," which includes "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) and 346a(p)(3)). 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." (21 U.S.C. 346a(p)(4)).

The EDSP initiatives developed by EPA in 1998 includes human and wildlife testing for estrogen, androgen, and thyroid pathway activity and employs a two-tiered approach. Tier 1 consists of a battery of 11 screening assays to identify the potential of a chemical substance to interact with the estrogen, androgen, or thyroid pathways. Tier 2 testing is designed to identify any adverse endocrine-related effects caused by the substance and establish a dose-response relationship for any adverse estrogen, androgen, or thyroid effect. If EPA finds, based on that data, that the pesticide has an adverse endocrine effect on humans, FFDCA § 408(p)(6) also requires EPA, "… as appropriate, [to] take action under such statutory authority as is available to the Administrator … as is necessary to ensure the protection of public health." (21 U.S.C. 346a(p)(6))[41].

Between October 2009 and February 2010, EPA issued Tier 1 test orders/data call-ins (DCIs) for its first list of chemicals ("List 1 chemicals") for EDSP screening and subsequently required submission of EDSP Tier 1 data for a refined list of these chemicals. EPA received data for 52 List 1 chemicals (50 pesticide active ingredients and 2 inert ingredients). EPA scientists performed weight-of-evidence (WoE) analyses of the submitted EDSP Tier 1 data and other scientifically relevant information (OSRI) for potential interaction with the estrogen, androgen, and/or thyroid signaling pathways for humans and wildlife.[42]

In addition, for FIFRA registration, registration review, and tolerance-related purposes, EPA collects and reviews numerous studies to assess potential adverse outcomes, including potential outcomes to endocrine systems, from exposure to pesticide active ingredients. Although EPA has been collecting and reviewing such data, EPA has not been explicit about how

[41] For additional details of the EDSP, please visit https://www.epa.gov/endocrine-disruption.
[42] Summarized in *Status of Endocrine Disruptor Screening Program (EDSP) List 1 Screening Conclusions*; EPA-HQ-OPP-2023-0474-0001; https://www.regulations.gov/document/EPA-HQ-OPP-2023-0474-0001

its review of required and submitted data for these purposes also informs EPA's obligations and commitments under FFDCA section 408(p). Consequently, on October 27, 2023, EPA issued a Federal Register Notice (FRN) providing clarity on the applicability of these data to FFDCA section 408(p) requirements and near-term strategies for EPA to further its compliance with FFDCA section 408(p). This FRN, entitled *Endocrine Disruptor Screening Program (EDSP): Near-Term Strategies for Implementation' Notice of Availability and Request for Comment* (88 FR 73841) is referred to here as EPA's EDSP Strategies Notice. EPA also published three documents supporting the strategies described in the Notice:

- *Use of Existing Mammalian Data to Address Data Needs and Decisions for Endocrine Disruptor Screening Program (EDSP) for Humans under FFDCA Section 408(p)*;
- *List of Conventional Registration Review Chemicals for Which an FFDCA Section 408(p)(6) Determination is Needed;* and,
- *Status of Endocrine Disruptor Screening Program (EDSP) List 1 Screening Conclusions* (referred to here as List 1 Screening Conclusions).

The EDSP Strategies Notice and the support documents are available on www.regulations.gov in docket number EPA-HQ-OPP-2023-0474. As explained in these documents, EPA is prioritizing its screening for potential impacts to the estrogen, androgen, and thyroid systems in humans, focusing first on conventional active ingredients. Although EPA voluntarily expanded the scope of the EDSP to screening for potential impacts to the estrogen, androgen, and thyroid systems in wildlife, EPA announced that it is not addressing this discretionary component of the EDSP at this time, considering its current focus on developing a comprehensive, long-term approach to meeting its Endangered Species Act obligations (See EPA's April 2022 ESA Workplan[43] and November 2022 ESA Workplan Update[44]). However, EPA notes that for 35 of the List 1 chemicals (33 active ingredients and 2 inert ingredients), Tier 1 WoE memoranda[45] indicate that available data were sufficient for FFDCA section 408(p) assessment and review for potential adverse effects to the estrogen, androgen, or thyroid pathways for wildlife. For the remaining 17 List 1 chemicals, Tier 1 WoE memoranda made recommendations for additional testing. EPA expects to further address these issues taking into account additional work being done in concert with researchers within the EPA's Office of Research and Development (ORD).

As discussed in EPA's EDSP Strategies Notice and supporting documents, EPA will be using all available data to determine whether additional data are needed to meet EPA's obligations and discretionary commitments under FFDCA section 408(p). For some conventional pesticide active ingredients, the toxicological databases may already provide sufficient evaluation of endocrine potential for estrogen, androgen, and/or thyroid pathways and EPA will generally not need to obtain any additional data to reevaluate those pathways, if in registration review, or to

[43] https://www.epa.gov/system/files/documents/2022-04/balancing-wildlife-protection-and-responsible-pesticide-use_final.pdf
[44] https://www.epa.gov/system/files/documents/2022-11/esa-workplan-update.pdf
[45] https://www.epa.gov/endocrine-disruption/endocrine-disruptor-screening-program-tier-1-screening-determinations-and

provide an initial evaluation for new active ingredient applications. For instance, EPA has endocrine-related data for numerous conventional pesticide active ingredients through either a two-generation reproduction toxicity study performed in accordance with the current guideline (referred to here as the updated two-generation reproduction toxicity study; OCSPP 870.3800 - Reproduction and Fertility Effects) or an extended one-generation reproductive toxicity (EOGRT) study (OECD Test Guideline 443 - Extended One-Generation Reproductive Toxicity Study). In these cases, EPA expects to make FFDCA 408(p)(6) decisions for humans without seeking further estrogen or androgen data. However, as also explained in the EPA's EDSP Strategies Notice, where these data do not exist, EPA will reevaluate the available data for the conventional active ingredient during registration review to determine what additional data, if any, might be needed to confirm EPA's assessment of the potential for impacts to estrogen, androgen, and/or thyroid pathways in humans. For more details on EPA's approach for assessing these endpoints, see EPA's EDSP Strategies Notice and related support documents.

Also described in the EPA's EDSP Strategies Notice is a framework that represents an initial approach by EPA to organize and prioritize the large number of conventional pesticides in registration review. For conventional pesticides with a two-generation reproduction toxicity study performed under a previous guideline (i.e., an updated two-generation reproduction toxicity study or an EOGRT is not available), EPA has used data from the Estrogen Receptor Pathway and/or Androgen Receptor Pathway Models to identify a group of chemicals with the highest priority for potential data collection (described in EPA's EDSP Strategies Notice as Group 1 active ingredients). For these cases, although EPA has not reevaluated the existing endocrine-related data, EPA has sought additional data and information in response to the issuance of EPA's EDSP Strategies Notice to better understand the positive findings in the ToxCast™ data for the Pathway Models and committed to issuing DCIs to require additional EDSP Tier 1 data to confirm the sufficiency of data to support EPA's assessment of potential adverse effects to the estrogen, androgen, and/or thyroid pathways in humans and to inform FFDCA 408(p) data decisions. For the remaining conventional pesticides (described in EPA's EDSP Strategies Notice as Group 2 and 3 conventional active ingredients), EPA committed to reevaluating the available data to determine what additional studies, if any, might be needed to confirm EPA's assessment of the potential for impacts to endocrine pathways in humans.

Acephate is on List 1. In 2015, EPA published the Tier 1 WoE analyses for acephate, and that evaluation determined that no further data to assess the potential for impacts on the estrogen, androgen, or thyroid pathways are needed for humans or wildlife[46]. Based on that evaluation, EPA has concluded at this time that the points of departure for human health risk assessment to evaluate the EPA-registered uses and established tolerances of acephate are protective of potential adverse estrogen, androgen, and thyroid effects in humans. There was no convincing evidence of potential interaction of acephate with the estrogen, androgen or thyroid pathways. Therefore, EPA has completed its FFDCA section 408(p)(6)-related commitments and obligations "to ensure the protection of public health" at this time.

[46] https://www.regulations.gov/document/EPA-HQ-OPP-2008-0915-0017