Jasmonates and Jasmolates

PC Codes 028100, 028000, 130819, 031135

Preliminary Work Plan
Case Number 6319, 6322, 6336, 6355

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I. Introduction

This document is the Environmental Protection Agency's (EPA or the Agency) Preliminary Work Plan (PWP) for jasmonates and jasmolates (Cases 6319, 6322, 6336, 6355) and is being issued pursuant to 40 CFR § 155.50. This case includes the active ingredients methyl jasmonate, prohydrojasmon (PDJ), *cis*-jasmone, and methyl-dihydrojasmolate (MDJ) (Case Nos. 6319, 6322, 6336, 6355), hereafter referred to as "jasmonates and jasmolates". The Agency is issuing a single PWP for all four active ingredients because they exhibit similar chemical structures and toxicological and ecological effects. This document explains what EPA's Office of Pesticide Programs (OPP) knows about jasmonates and jasmolates, highlights anticipated data and assessment needs, identifies types of information that would be especially useful to the Agency in conducting the review, and provides an anticipated timeline for completing the registration review process for jasmonates and jasmolates. As stated in 40 CFR § 155.50, the opening of this docket initiates the current cycle of registration review for jasmonates and jasmolates.

A registration review decision is the Agency's determination of whether a pesticide meets, or does not meet, the standard for registration in the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). FIFRA, as amended by the Food Quality Protection Act (FQPA) of 1996, mandates the continuous review of existing pesticides. All pesticides distributed or sold in the United States generally must be registered by the Agency based on scientific data showing that they will not cause unreasonable adverse effects to human health or to the environment when used as directed on product labeling. The registration review program is intended to ensure that, as the ability to assess and reduce risk evolves and as policies and practices change, all registered pesticides continue to meet the statutory standard of no unreasonable adverse effects. Changes in science, public policy, and pesticide use practices will occur over time. Through the registration review program, the Agency periodically re-evaluates pesticides to ensure that as these changes occur, products in the marketplace can continue to be used safely. Information on this program is provided at www.epa.gov/pesticide-reevaluation.

In 2006, the Agency implemented the registration review program pursuant to FIFRA § 3(g). The Agency will review each registered pesticide every 15 years to determine whether it continues to meet the FIFRA standard for registration. The regulations governing registration review are provided in 40 CFR part 155, subpart C. The public phase of registration review begins when the initial docket is opened for the case. The docket is the Agency's opportunity to inform the public what it knows about jasmonates and jasmolates and what additional risk analyses and data or information it believes are needed to make a registration review decision on jasmonates and jasmolates.

The Agency encourages all interested stakeholders to review the PWP and to provide comments and additional information that will help the Agency's decision-making process for jasmonates and jasmolates. Interested stakeholders could include the following: environmental nonprofit or interest groups; pesticide manufacturers; agricultural labor or commodity groups; commercial, institutional, residential, and other users of pesticides; or the general public. In addition to general areas on which persons may wish to comment, there are some areas identified in the PWP about which the Agency specifically seeks comments and information.

After reviewing and responding to comments and data received in the docket during this initial comment period, the Agency will develop and commit to a Final Work Plan (FWP) and anticipated schedule for the registration review of the jasmonates and jasmolates case. Additional information on

jasmonates and jasmolates can be found in the Agency's public docket (EPA-HQ-OPP-2024-0219) at www.regulations.gov.

This document is organized into five sections: the *Introduction*, which includes this summary and jasmonates and jasmolates case overview; *Use Information*, which describes how and why jasmonates and jasmolates are used and summarizes data on its use, and associated pesticide products; *Scientific Assessments*, which summarizes the Agency's risk assessments, any revisions, risk conclusions, and any anticipated data needs that will help the Agency's decision-making process for jasmonates and jasmolates; *Guidance for Commentors*, which highlights topics of special interest, additional information and data the Agency should consider prior to issuing a FWP; and, lastly, the *Next Steps* and *Timeline* which provides an anticipated timeline for the registration review process for jasmonates and jasmolates.

Jasmonates and Jasmolates Registration Review Case Overview

Pursuant to 40 CFR § 155.50, the Agency will initiate a pesticide's registration by establishing a docket for registration review of jasmonates and jasmolates (Case Nos. 6319, 6322, 6336, 6355) and opening it for public review.

This PWP marks the beginning of the current cycle of registration review for jasmonates and jasmolates, with the opening of public docket EPA-HQ-OPP-2024-0219 available at www.regulations.gov. The following list highlights significant events that have occurred during the current cycle of registration review for this case:

- September 2024 – The Agency is now publishing the *Jasmonates and Jasmolates Preliminary Work Plan* for a 60-day public comment period.

II. Use Information

The first pesticide product containing methyl jasmonate as an active ingredient was registered by the Agency in 2013. Currently, there are two registered products containing methyl jasmonate, one manufacturing-use product (MP) and one end-use product (EP), ranging from 0.037%-99.0% active ingredient. Methyl jasmonate is a biochemical pesticide active ingredient intended for use as a 'systemic acquired resistance' (SAR) inducer on a variety of agricultural crops. It is applied as a seed treatment. Methyl jasmonate is naturally occurring and elicits plant defense responses in vulnerable seedlings. It is the principal derivative of jasmonate, a hormone ubiquitous to most plants but particularly concentrated in jasmine and honeysuckle. Jasmonate are known to trigger plant responses to a variety of stresses. Methyl jasmonate, in particular, is known to bolster plant defenses against extreme temperature changes and attacks by insects, fungi and bacteria. Methyl jasmonate is present in most fruits, is already a regular part of the human diet, and has a safe history of dietary exposure (U.S. EPA 2013a).

The first pesticide product containing prohydrojasmon as an active ingredient was registered by the Agency in 2013. Currently, there are seven registered products containing prohydrojasmon, two manufacturing-use products and five end-use products, ranging from 1.875%-98.0% active ingredient. Prohydrojasmon is a synthetically made plant growth regulator that is structurally similar and functionally identical to jasmonic acid (JA), a naturally occurring plant regulator present in all vascular (higher) plants. The highest levels for JA are found in actively growing plant tissues such as leaves, flowers, and developing fruit, and thus JA has always been a natural component of diets containing

plant materials. The jasmonates, of which JA is a member, is a group of plant hormones involved in multiple stages of plant development and defense, including the ability to stimulate fruit ripening. As a pesticide, prohydrojasmon is used to stimulate fruit ripening in apples and grapes, and as a repellent (U.S. EPA 2013b).

The first pesticide product containing *cis*-jasmone as an active ingredient was registered by the Agency in 2019. Currently, there are two registered products containing *cis*-jasmone, one manufacturing-use product and one end-use product, ranging from 0.88%-93.0% active ingredient. *Cis*-jasmone, is an alpha, beta-unsaturated monocyclic ketone that is released naturally by plants as part of the jasmonic acid pathway which is induced during plant defense. As a pesticide, the substance is used to elicit plant defense mechanisms against nematodes. Concentrations of 0-114 ppm have been found in mint varieties, tea, and jasmine, and *cis*-jasmone has also been identified in bergamot, apricot, raspberry, cinnamon, and soybean. The chemical is a fragrance ingredient used in cosmetics such as perfume, body lotion and shampoo, and is also used in household cleaners and detergents (U.S. EPA 2019).

The first pesticide product containing methyl-dihydrojasmolate as an active ingredient was registered by the Agency in 2022. Currently, there are four registered products containing Methyl-dihydrojasmolate, one manufacturing-use product and three end-use products, ranging from 0.625%-94.0% active ingredient. Methyl-dihydrojasmolate is applied indoors as an insect repellent to repel the non-public health pest, ants. Methyl-dihydrojasmonate is naturally occurring in jasmine oil. It is also an approved flavoring in foods by the Joint FAO/WHO (Food and Agriculture Organization/ World Health Organization) Expert Committee on Food Additives (JECFA). In general, jasmonates occur ubiquitously across the plant kingdom and play a role in plant response to environmental stresses (U.S. EPA 2022a).

Table 1. Methyl jasmonate Use Information	
Ingredient Name	Methyl jasmonate
PC Code	028100
CAS Number	39924-52-2
Pesticide Classification	SAR or Insecticide
Use Site Locations	Agricultural (Outdoor)
Application Types	Seed Treatment
No. of Registrations	2 FIFRA Section 3 products[1]
Physical Forms	Liquid

Table 2. Prohydrojasmon Use Information	
Ingredient Name	Prohydrojasmon
PC Code	028000
CAS Number	158474-72-7
Pesticide Classification	Plant Growth Regulator, Repellent
Use Site Locations	Agricultural (Outdoor)
Application Types	Spray Drench
No. of Registrations	7 FIFRA Section 3 products[1]
Physical Forms	Liquid

[1] FIFRA labels can be obtained from the Pesticide Product Label System (ordspub.epa.gov/ords/pesticides/f?p=PPLS:1)

Table 3. *Cis*-jasmone Use Information	
Ingredient Name	*Cis*-jasmone
PC Code	130819
CAS Number	488-10-8
Pesticide Classification	Plant Growth Regulator, SAR, Nematicide
Use Site Locations	Agricultural (Outdoor)
Application Types	Seed treatment
No. of Registrations	2 FIFRA Section 3 products[1]
Physical Forms	Liquid

Table 4. Methyl-dihydrojasmolate Use Information	
Ingredient Name	Methyl-dihydrojasmolate
PC Code	031135
CAS Number	54562-27-5
Pesticide Classification	Repellent
Use Site Locations	Residential (Indoor)
Application Types	Spot treatment
No. of Registrations	4 FIFRA Section 3 products[1]
Physical Forms	Liquid

III. Scientific Assessments

A summary of the Agency's human health and ecological risk assessments for jasmonate and jasmolates are presented below. Refer to the Appendices for a listing of product analysis, human health assessment, and nontarget organism data that support the scientific assessments for this registration review. For further information on the human health and environmental risk assessments, including a summary of data and literature search findings, please see Appendices B and C.

A. Human Health Assessment

Summary of Hazard Characterization

The toxicological database is considered complete for characterizing hazard and assessing risk from the active ingredients in this case. Methyl jasmonate is classified as a toxicity category IV[2] for acute dermal toxicity, acute inhalation toxicity, acute inhalation toxicity, primary eye irritation, and primary dermal toxicity, and toxicity category III for acute oral toxicity. Prohydrojasmon, *cis*-jasmone, and methyl-dihydrojasmolate are classified as Toxicity Category III for acute oral toxicity, acute inhalation toxicity, primary eye irritation, and primary dermal irritation. According to available data, none of these chemicals are considered mutagenic or dermal sensitizers. The Agency does not anticipate the need for additional studies for this registration review. All data requirements, per 40 CFR § 158.2050, have been fulfilled for jasmonates and jasmolates (U.S. EPA, 2013a, 2013b, 2019, 2022b).

All human health data requirements have been fulfilled for jasmonates and jasmolates through a combination of acceptable studies and rationales. Hazard and exposure data, and other information on these active ingredients were evaluated against standards established by FIFRA and the Agency's regulations and scientific policies. The toxicology data and rationale provided are sufficient to demonstrate there are no foreseeable human health hazards likely to arise from these active

[2] See Section III of Chapter 7 of the Label Review Manual for a complete description of the Toxicity Categories.

ingredients when applied according to the approved product labels and in accordance with good agricultural practices. Based to their natural occurrence, negligible exposure, mitigation from personal protective equipment (PPE), low oral toxicity, low dermal and eye irritation, and lack of genotoxicity; the Agency does not anticipate the need for additional studies for the jasmonates and jasmolates registration review case. Please see Appendix B for additional information.

Summary of Dietary Exposure and Risk Characterization

Methyl Jasmonate

Human exposure to methyl jasmonate may occur via dietary exposure from treated seeds or drinking water. Although dietary and drinking water exposure to humans may occur, the Agency has determined that there is reasonable certainty of no harm to humans when exposed to residues of the active ingredient from pesticidal use when label instructions are followed. This conclusion is based on the following: 1) Methyl jasmonate is naturally occuring, a regular part of the human diet, and is a common flavoring agent; 2) the EP use pattern as a commercial seed treatment with a low application rate and is likely to result in lower levels of exposure than current estimated dietary exposure; and 3) available toxicology data and information indicate that the active ingredient has a low toxicity and is not likely to be a developmental toxicant, a mutagen, or toxic via repeat oral exposure. Therefore, potential risk from dietary exposure is not expected. Please see Appendix B for additional information.

Prohydrojasmon

Human exposure to prohydrojasmon may occur via dietary exposure to treated agricultural commodities or drinking water. Although dietary and drinking water exposure to humans may occur, the Agency has determined that there is reasonable certainty of no harm to humans when exposed to residues of the active ingredient from pesticidal use when label instructions are followed. This conclusion is based on the following: 1) exposure to the active ingredient from treated agricultural commodities or drinking water due to runoff is not expected above background levels of structurally similar and functionally identical jasmonic acid; 2) prohydrojasmon is approved for use as an indoor insect repellent, and therefore no dietary exposure is anticipated from this use pattern; and 3) prohydrojasmon degrades rapidly in the soil, thereby reducing the potential for uptake of the chemical residues by plants. Therefore, potential risk from dietary exposure is not expected. Please see Appendix B for additional information.

Cis-Jasmone

Human exposure to *cis*-jasmone may occur via dietary exposure to treated agricultural commodities or drinking water. Although dietary and drinking water exposure to humans may occur, the Agency has determined that there is reasonable certainty of no harm to humans when exposed to residues of the active ingredient from pesticidal use when label instructions are followed. This conclusion is based on the following: 1) the EP use patterns are commercial seed treatment and are not expected to result in residues in edible commodities grown from treated seed as no residues have been identified at or above the 0.005 ppm threshold that has been historically used by EPA for nonfood determinations for seed treatments; 2) products containing this active ingredient are registered for use in commercial seed treatment facilities only, and treated seeds are not to be used for food or feed or processed for oil; and 3) *cis*-jasmone is naturally occuring, a regular part of the human diet, and is commonly found in cosmetics and household products with no safety concerns identified in published assessments for

such uses. Therefore, potential risk from dietary exposure is not expected. Please see Appendix B for additional information.

Methyl-dihydrojasmolate

Methyl-dihydrojasmolate is currently only registered for indoor nonfood use as an insect repellent, and therefore, no dietary exposure is anticipated from this use pattern. Further, in the event that dietary exposure was to occur, methyl dihydrojasmonate is naturally occurring in jasmine oil and is an approved flavoring in foods. Therefore, a dietary exposure and risk characterization was not performed and no potential risk from dietary exposure is expected. Please see Appendix B for additional information.

Food Tolerances

Considering the available toxicity and exposure data discussed above, EPA concluded that there was a reasonable certainty that no harm would result to the U.S. population from aggregate exposure to residues of Methyl Jasmonate and prohydrojasmon when used according to label directions. Therefore, EPA established a tolerance exemption for residues of the active ingredients. The current tolerance exemptions are stated as follows:

> **§ 180.1320 Methyl jasmonate; exemption from the requirement of a tolerance.**
>
> An exemption from the requirement of a tolerance is established for residues of methyl jasmonate in or on all food commodities when methyl jasmonate is applied pre-harvest. [78 FR 22794, Apr. 17, 2013]
>
> **§ 180.1299 Prohydrojasmon; exemption from the requirement of a tolerance.**
>
> An exemption from the requirement of a tolerance is established for residues of the biochemical pesticide prohydrojasmon, propyl-3-oxo-2-pentylcyclo-pentylacetate, when used as a plant growth regulator in or on apple and grape pre-harvest, in accordance with label directions and good agricultural practices. [78 FR 75257, Dec. 11, 2013]

No registered pesticide products containing *cis*-jasmone or methyl-dihydrojasmolate are approved for food use. Therefore, no tolerance or tolerance exemption is needed for residues of *cis*-jasmone or methyl-dihydrojasmolate found in or on food.

Summary of Residential and Non-Occupational Exposure and Risk Characterization

Direct residential and non-occupational exposure from methyl jasmonate and *cis*-jasmone is not expected since there are no approved residential uses and are intended for commercial seed treatment only. Indirect residential and non-occupational exposure from spray drift is not expected based on labeled use patterns and application sites. Therefore, residential handlers (non-occupational) and post-application risks of concern are not expected.

Since EPs containing prohydrojasmon and methyl dihydrojasmolate are registered for residential indoor use, direct residential and non-occupational exposure to the active ingredients may occur through short and intermediate term dermal and inhalation routes of exposure. While residential and non-occupational exposure may occur, both active ingredients have an overall low toxicity. The Agency has determined that there is reasonable certainty of no harm to humans when exposed to residues of the active ingredients from pesticidal use when label instructions are followed. Therefore, risk from

residential and non-occupational exposure is not of concern. Please see Appendix B for additional information.

Summary of Occupational Exposure and Risk Characterization

Significant occupational exposure is not expected from commercial uses of methyl jasmonate, prohydrojasmon, and *cis*-jasmone when used in accordance with label instructions with appropriate PPE. Although dermal exposure may occur to applicators/handlers, all product labels require long sleeve shirt and long pants, shoes and socks, waterproof gloves, and protective eyewear that would mitigate the exposure. Further, inhalation exposure is not expected due to the contained nature of closed seed treatment mixture equipment. Other EPs containing prohydrojasmon, and methyl dihydrojasmolate are registered for residential use only. Therefore, risk is expected to be negligible based on low toxicity of the AI and use patterns of the EPs. As a result, risk from occupational exposure is not of concern for the AI that make up this registration review case.

Human Incidents

A search of the Office of Pesticide Programs' (OPP) Incident Data System conducted on August 12, 2024, revealed no reported incidents associated with methyl jasmonate, prohydrojasmon, *cis*-jasmone, and methyl-dihydrojasmolate. This database contains information dating back to the 1970s and is continuously updated as incidents are reported.

B. Summary of Environmental Risk Assessment

Methyl Jasmonate

All nontarget organism and environmental fate data necessary to meet the standard for jasmonates and jasmolates were satisfied through acceptable guideline data submissions or scientific rationales. Submitted data indicate that Methyl jasmonate is practically non-toxic to birds. Acceptable rationale demonstrated no reports of toxicity to other terrestrial organisms based on the active ingredients' natural occurrence, anticipated low exposure due to approved application methods and no reports of toxicity.

Prohydrojasmon

Submitted data indicate that prohydrojasmon is practically non-toxic to birds, and non-target plants, practically non-toxic to honeybees, and is moderately toxic to fish and aquatic invertebrates. However, GENEED model estimates indicate that the risk quotients for fish and aquatic invertebrates (0.0001 and 0.00005) are three and four orders of magnitude below the levels of concern (LOC) of 0.05-1 (U.S. EPA, 2013c).

Cis-Jasmone

Submitted data indicate that *cis*-jasmone is slightly toxic to birds, fish, and aquatic invertebrates, and is practically non-toxic to honeybees. Due to the active ingredient's slight toxicity to birds, EPA expects to model risk to birds from consumption of treated seeds in the registration review ecological risk assessment as part of this registration review case. Rationale indicates no nontarget plant toxicity based on low exposure due to low application rates, application methods, and *cis*-jasmone's natural occurrence in many plants.

Methyl-dihydrojasmolate

Based on submitted rationale and based on the fact that the active ingredient is approved for indoor use only, environmental and nontarget organism exposure to methyl-dihydrojasmolate is expected to be negligible when products containing the AI are used in accordance with approved labeling directions. Therefore, no further data or updated risk assessment is needed for this methyl-dihydrojasmolate at this time.

Since this registration review case includes methyl jasmonate, prohydrojasmon, and *cis*-jasmone, which are plant growth regulators, a full endangered species assessment will be performed as part of this registration review case in order to properly assess potential effects to listed threatened and endangered species and their designated critical habitat from the use of these active ingredients.

Ecological Incidents

A search of OPP's Incident Data System conducted on August 12, 2024, revealed no reported incidents associated with methyl jasmonate, prohydrojasmon, *cis*-jasmone, and methyl-dihydrojasmolate. This database contains information dating back to the 1970s and is continuously updated as incidents are reported.

Endangered Species Assessment

This section 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). Additional background specific to jasmonates and jasmolates appears at the conclusion of Appendix C.

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[3] 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.[4]

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

[3] https://www.epa.gov/endangered-species/interim-approaches-pesticide-endangered-species-act-assessments-based-nasreport

[4] https://www.epa.gov/endangered-species/revised-method-national-level-listed-species-biological-evaluations-conventional.

Quality (CEQ). The IWG outlines its recommendations and progress on implementing those recommendations in reports to Congress.[5]

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 malathion biological opinion[6] from FWS in February 2022 and a final biological opinion from NMFS on malathion, chlorpyrifos and diazinon in June 2022.[7] The Agency plans to implement both biological opinions according to the 18-month timeframes specified in the biological opinions.

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[8] 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*.[9] 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.

On November 16, 2022, EPA released the *ESA Workplan Update: Nontarget Species Mitigation for Registration Review and Other FIFRA Actions*.[10] As part of this update, EPA announced its plan to

[5] https://www.epa.gov/endangered-species/reports-congress-improving-consultation-process-under-endangered-species-act.
[6] https://www.epa.gov/endangered-species/biological-opinions-available-public-comment-and-links-final-opinions.
[7] https://www.epa.gov/endangered-species/biological-opinions-available-public-comment-and-links-final-opinions.
[8] https://www.epa.gov/newsreleases/epa-announces-endangered-species-act-protection-policy-new-pesticides.
[9] https://www.epa.gov/endangered-species.
[10] https://www.epa.gov/system/files/documents/2022-11/esa-workplan-update.pdf.

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 nontarget 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.

IV. Guidance for Commentors

Preliminary Work Plan

During the comment period, anyone may submit relevant data or information for the Agency's consideration. The public is invited to comment on the Agency's PWP. The areas below highlight topics of special interest to the Agency where comments, information and data, or reference to sources of additional information could be of particular use. The Agency will carefully consider all comments, as well as any additional information or data provided in a timely manner, prior to issuing a FWP for this case.

Additional Information

Stakeholders are also specifically asked to provide information and data that will assist the Agency in refining the risk assessments, including the ESA assessment. The Agency is interested in obtaining the following information regarding jasmonates and jasmolates:

i. Confirmation on the following label information:
   - *Sites of application*
   - *Formulations*
   - *Application methods and equipment*
   - *Maximum application rates*
   - *Frequency of application, application intervals, and maximum number of applications*
   - *Geographic limitations on use*
ii. Use or potential use distribution (e.g., acreage and geographical distribution of relevant use sites)
iii. Median and 90th percentile reported use rates from usage data – national, state, and county
iv. Application timing (date of first application and application intervals) – national, state, and county
v. Usage/use information for agricultural and nonagricultural uses
vi. Typical application interval (days)
vii. State or local use restrictions
viii. Monitoring data
ix. Foreign technical registrants not listed above who supply pesticide products containing jasmonates and jasmolates to the U.S. market
x. The Agency welcomes any information on the effects of jasmonates and jasmolates, including nontarget plant effects that would help refine the ESA assessment

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. To help address potential environmental

justice issues related to registration review decisions, the Agency seeks information on any 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 jasmonates and jasmolates compared to the general population or who may otherwise be disproportionately affected by the use of jasmonates and jasmolates as a pesticide. Please comment if you are aware of any such issues and can provide information to help the Agency to more fully consider and address potential environmental justice issues.

V. Next Steps and Timeline

A Federal Register Notice will announce the docket opening for the current cycle of registration review for jasmonates and jasmolates and a 60-day comment period for this *Preliminary Work Plan* to provide comments and additional information that will help the Agency's decision-making process for jasmonates and jasmolates. After the 60-day comment period closes, the Agency will review and respond to any comments received in a timely manner, then issue a Final Work Plan for jasmonates and jasmolates. The Agency's final decision on the jasmonates and jasmolates registration review case will occur following satisfaction of the Endocrine Disruptor Screening Program (EDSP) obligations under FFDCA § 408(p) and completion of an endangered species determination and any necessary consultation with the Services.

Table 5. Anticipated Registration Review Schedule for Jasmonates and Jasmolates

Anticipated Activity	**Estimated Month/ Year**
Opening the Docket	
Open Docket and 60-Day Public Comment Period for Preliminary Work Plan	September 2024
Close Public Comment Period	November 2024
Case Development	
Final Work Plan	March 2025
Registration Review Decision and Implementation	
Open 60-Day Public Comment Period for Proposed Registration Review Decision	March 2027
Close Public Comment Period	May 2027
Registration Review Decision	TBD

*The anticipated schedule will be revised as necessary (e.g., need arising under the Endocrine Disruptor Screening Program with respect to the active ingredients in this case).

Appendix A – Product Characterization

In evaluating product chemistry for registration review, the Agency is focused on the active ingredient (for practical purposes, the technical grade active ingredient or TGAI) and not the individual end- and manufacturing-use products. Provided in the tables below (tables 6-9) are the Biochemical Pesticides Product Chemistry Data Requirements (40 CFR 158.2030) and how they are met for each of the four active ingredients in this case. All are satisfied and support the registration review for methyl jasmonate, prohydrojasmon, *cis*-jasmone, and methyl-dihydrojasmolate (MDJ). All product chemistry tests were performed on the TGAIs.

Table 6. Summary of Product Analysis Data for Methyl Jasmonate (40 CFR § 158.2030)

Data Requirement	Guideline No.	Results / Findings	MRIDs
Product identity and composition	880.1100	Confidential Business Information Acceptable	48656602
Description of Starting Materials, Production and Formulation Process	880.1200	Confidential Business Information Acceptable	48656602
Discussion of Formation of Impurities	880.1400	Confidential Business Information Acceptable	48656602
Preliminary Analysis	830.1700	Confidential Business Information Acceptable	48656602
Certified Limits	830.1750	Confidential Business Information Acceptable	48656602
Enforcement Analytical Method	830.1800	Submitted data satisfy the data requirement	48656603
Color	830.6302	Pale yellow	48656604
Physical State	830.6303	Liquid	48656604
Odor	830.6304	Floral, true jasmine flower character	48656604
Stability to Normal and Elevated Temperatures, Metals, and Metal Ions	830.6313	TGAI should be fairly stable over long storage periods unless it is packaged in iron containers. The specific gravity of the samples stored at 54°C showed a very slight increase (1.0227 at 25°C). The refractive index remained constant over the 14-day test period.	48656604
pH	830.7000	5.35 at 25°C [1]	51772504
UV/Visible Light Absorption	830.7050	Molar absorption coefficients: max = 3.630 at 288.4 nm; min = 2.963 at 265.9 nm; max = 4.063 at 237.3 nm (0.3083 g/10 ml methanol)	48656604
Melting Point/Melting Range	830.7200	N/A; TGAI is a liquid	--
Boiling Point/Boiling Range	830.7220	313.62°C	48656604
Density/Relative Density/Bulk Density	830.7300	1.02 g/ml at 20°C	48656604
Particle Size, Fiber Length, and Diameter Distribution	830.7520	N/A; TGAI is a liquid	–

Partition Coefficient	830.7550-.7570	K_{ow} = 2.76	48656604
Water Solubility	830.7840	143.5 mg/L	48656604
Vapor Pressure	830.7950	0.000337 mm Hg	48656604

[1] This pH value is the pH of a surrogate chemical for methyl jasmonate, methyl-dihydrojasmolate (MDJ), due to its similar structure.

Table 7. Summary of Product Analysis Data for Prohydrojasmon (PDJ) (40 CFR § 158.2030)

Data Requirement	Guideline No.	Results / Findings	MRIDs
Product identity and composition	880.1100	Confidential Business Information Acceptable	47927801
Description of Starting Materials, Production and Formulation Process	880.1200	Confidential Business Information Acceptable	47927801
Discussion of Formation of Impurities	880.1400	Confidential Business Information Acceptable	47927801
Preliminary Analysis	830.1700	Confidential Business Information Acceptable	47927803
Certified Limits	830.1750	Confidential Business Information Acceptable	47927801
Enforcement Analytical Method	830.1800	Submitted data satisfy the data requirement	47927803
Color	830.6302	Light yellow and clear	47927804
Physical State	830.6303	Oily liquid	47927804
Odor	830.6304	No odor	47927804
Stability to Normal and Elevated Temperatures, Metals, and Metal Ions	830.6313	Stable at room temperature and at 54°C for 14 days. Stable in contact with iron, zinc, aluminum, and their acetates at room temperature and at 54°C for 14 days. Degrades at 342°C and above.	47927804
pH	830.7000	N/A; the product is not dispersible in water	47927804
UV/Visible Light Absorption	830.7050	The maximum was observed around 210 nm and around 293 nm. Exact values of the molar absorption coefficient were not obtained due to instability caused by the properties of the solution. There was no pH-dependent change in the coefficient occurring around 293 nm, with Ɛ between 28 and 30.	47927804
Melting Point/Melting Range	830.7200	N/A; TGAI is a liquid	47927804
Boiling Point/Boiling Range	830.7220	318°C	47927804
Density/Relative Density/Bulk Density	830.7300	0.974 g/cm^3 at 25°C	47927804
Particle Size, Fiber Length, and Diameter Distribution	830.7520	N/A; TGAI is a liquid	47927804
Partition Coefficient	830.7550-.7570	N/A; TGAI is partially or completely soluble in water	47927804

Water Solubility	830.7840	60.2 mg/L at 25°C	47927804
Vapor Pressure	830.7950	0.0167±0.00017 Pa at 25°C 0.324±0.0221 Pa at 50°C	47927804

Table 8. Summary of Product Analysis Data for *Cis*-Jasmone (40 CFR § 158.2030)			
Data Requirement	**Guideline No.**	**Results / Findings**	**MRIDs**
Product identity and composition	880.1100	Confidential Business Information Acceptable	50452701
Description of Starting Materials, Production and Formulation Process	880.1200	Confidential Business Information Acceptable	50457201
Discussion of Formation of Impurities	880.1400	Confidential Business Information Acceptable	50452701
Preliminary Analysis	830.1700	Confidential Business Information Acceptable	50452702
Certified Limits	830.1750	Confidential Business Information Acceptable	50452702
Enforcement Analytical Method	830.1800	Submitted data satisfy the data requirement	50452703
Color	830.6302	Pale yellow	50357902
Physical State	830.6303	Liquid at 25°C	50357902
Odor	830.6304	Strong floral	50357902
Stability to Normal and Elevated Temperatures, Metals, and Metal Ions	830.6313	The TGAI is stable for 14 days at room temperature and elevated temperature (54°C). The TGAI is compatible with aluminum foil, iron chips and aluminum acetate at room temperature and elevated temperature (54°C), but not compatible with iron (III) acetate at both temperatures.	50452704
pH	830.7000	6.07 (1% solution)	50357902
UV/Visible Light Absorption	830.7050	Neutral: A = 0.905; λ_{max} = 235.0 (nm) Acidic: A = 0.905; λ_{max} = 236.3 (nm) Basic: A = 0.924; λ_{max} = 235.5 (nm)	50357902
Melting Point/Melting Range	830.7200	N/A; TGAI is a liquid	--
Boiling Point/Boiling Range	830.7220	The boiling point of the TGAI was determined up to the point where decomposition was observed (decomposition occurred prior to the boiling point). Decomposition temperature was determined to be 201.7±0.6°C under ambient pressure of 101.325 kPa.	50357902
Density/Relative Density/Bulk Density	830.7300	0.9382 g/mL at 24°C	50357902
Particle Size, Fiber Length, and Diameter Distribution	830.7520	N/A; TGAI is a liquid	--
Partition Coefficient	830.7550-.7570	K_{ow} = 2.7	50357902
Water Solubility	830.7840	1.410 g/L at 20°C	50357902

Vapor Pressure	830.7950	0.0823 Pa at 20°C; 0.0931 Pa at 25°C	50357902

Table 9. Summary of Product Analysis Data for Methyl-dihydrojasmolate (40 CFR § 158.2030)			
Data Requirement	**Guideline No.**	**Results / Findings**	**MRIDs**
Product identity and composition	880.1100	Confidential Business Information Acceptable	51420027/ 51772503
Description of Starting Materials, Production and Formulation Process	880.1200	Confidential Business Information Acceptable	51420027/ 51772503
Discussion of Formation of Impurities	880.1400	Confidential Business Information Acceptable	51420027
Preliminary Analysis	830.1700	Confidential Business Information Acceptable	51420030
Certified Limits	830.1750	Confidential Business Information Acceptable	51420027/ 51772503
Enforcement Analytical Method	830.1800	Submitted data satisfy the data requirement	51420028
Color	830.6302	Colorless	51420029
Physical State	830.6303	Liquid	51420029
Odor	830.6304	Very weak, slightly folar, waxy odor	51420029
Stability to Normal and Elevated Temperatures, Metals, and Metal Ions	830.6313	Stable at room temperature and 54oC for 14 days; stable with iron chips, iron (III) acetate, aluminum foil, and aluminum acetate at both temperatures	51420029
pH	830.7000	5.35 @ 25°C	51772504
UV/Visible Light Absorption	830.7050	Neutral: A = 1.273; λ_{max} = 209.9 (nm) Acidic: A = 1.327; λ_{max} = 209.8 (nm) Basic: A = 1.261; λ_{max} = 213.7 (nm)	51420031
Melting Point/Melting Range	830.7200	N/A; TGAI is a liquid	--
Boiling Point/Boiling Range	830.7220	296.9 ± 0.1°C	51420032
Density/Relative Density/Bulk Density	830.7300	0.995 g/mL	51420029
Particle Size, Fiber Length, and Diameter Distribution	830.7520	N/A; TGAI is a liquid	--
Partition Coefficient	830.7550-.7570	K_{ow} = 3.39 ± 0.01	51420032
Water Solubility	830.7840	700 ± 0.01 mg/L	51420032
Vapor Pressure	830.7950	80.0 Pa at 10.0°C; 106.6 Pa at 21.1°C; 306.6 Pa at 50.0°C; 839.8 Pa at 80.0°C	51420033

Appendix B – Human Health Risk Assessment

Summary of Mammalian Toxicology Data

The toxicology data for these active ingredients are acceptable and the database is complete. Tables 10-13 summarize the current mammalian toxicology data requirements and results supporting registration review of methyl jasmonate, prohydrojasmon, *cis*-jasmone, and methyl-dihydrojasmolate. The Agency's existing risk assessments are sufficient to evaluate the uses of the active ingredients in the currently registered manufacturing and end-use products.

Table 10. Summary of Toxicology Data for Methyl Jasmonate (40 CFR § 158.2050)

Data Requirement	Guideline No.	Results / Findings	MRIDs
Acute Oral Toxicity - Rat	870.1100	LD_{50} = 3,129 mg/kg; Toxicity Category III ACCEPTABLE/GUIDELINE	48653901
Acute Dermal Toxicity	870.1200	LD_{50} > 5,050 mg/kg; Toxicity Category IV ACCEPTABLE/GUIDELINE	48653902
Acute Inhalation Toxicity	870.1300	LC_{50} > 2.23 mg/L; Toxicity Category IV ACCEPTABLE/GUIDELINE	48653903
Primary Eye Irritation – Rabbit	870.2400	Minimal eye irritation; Toxicity Category IV ACCEPTABLE/GUIDELINE	48653904
Primary Dermal Irritation	870.2500	Non-irritating; Toxicity Category IV ACCEPTABLE/GUIDELINE	48653905
Dermal Sensitization	870.2600	Not a contact dermal sensitizer ACCEPTABLE/GUIDELINE	48653906
90-Day Oral (One Species)	870.3100	No subchronic oral toxicity anticipated; data requirement satisfied with acceptable rationale which includes: (1) natural occurrence and long history of dietary exposure from fruits; (2) an acceptable dietary exposure identified at 540 µg/day (JECFA, 2005); and (3) potential pesticidal exposure expected to be well below current estimated dietary exposure.	48653908 JECFA, 2005 U.S. EPA, 2012
90-Day Dermal – Rat	870.3250	No subchronic dermal toxicity anticipated; data requirement satisfied with acceptable rationale which includes: (1) products are not intended for purposeful application to skin; (2) label uses will not result in prolonged dermal exposure; (3) long history of dermal exposure because the active ingredient naturally occurs in plants/fruits commonly handled by humans; (4) common flavoring agent; and (5) not known to metabolize differently following exposure by dermal route than oral route.	48653908
90-Day Inhalation – Rat	870.3465	No subchronic inhalation toxicity anticipated; data requirement satisfied with acceptable rationale which includes: (1) label uses will not result in repeated inhalation exposure; (2) long history of inhalation exposure because it naturally occurs and is a volatile component in plants/fruits; and (3) potential exposure is expected to be less than or equal to naturally occurring concentrations from crops/plants.	48653908
Prenatal Developmental	870.3700	No maternal or developmental toxicity anticipated; data requirement satisfied with acceptable rationale which includes:	48653908

		(1) long history of dietary exposure as the active ingredient naturally occurs in fruits; (2) common in diet as a flavoring agent; and (3) expected exposure from product use lower than current estimated dietary exposure.	
Bacterial Reverse Mutation Test	870.5100	Expected to be non-mutagenic; data requirement satisfied with acceptable rationale which includes: (1) long history of exposure because the active ingredient is naturally occurring in fruits; (2) common in diet as a flavoring agent; and (3) expected exposure lower than current estimated dietary exposure.	48653908
In vitro Mammalian Cell Assay	870.5300 870.5375	Expected to be non-genotoxic; data requirement satisfied with acceptable rationale which includes: (1) long history of exposure because the active ingredient is naturally occurring in fruits; (2) common in diet as a flavoring agent; and (3) expected exposure lower than current estimated dietary exposure.	48653908

Table 11. Summary of Toxicology Data for Prohydrojasmon (40 CFR § 158.2050)

Data Requirement	Guideline No.	Results / Findings	MRIDs
Acute Oral Toxicity - Rat	870.1100	LD_{50} = 5,000 mg/kg; Toxicity Category IV ACCEPTABLE/GUIDELINE	47927818, 47927825
Acute Dermal Toxicity	870.1200	LD_{50} > 2,000 mg/kg; Toxicity Category III ACCEPTABLE/GUIDELINE	47927818, 47927826
Acute Inhalation Toxicity	870.1300	LC_{50} > 5.0 mg/L; Toxicity Category IV ACCEPTABLE/GUIDELINE	47927818, 47927827
Primary Eye Irritation – Rabbit	870.2400	Minimal eye irritation; Toxicity Category IV ACCEPTABLE/GUIDELINE	47927818, 47927828
Primary Dermal Irritation	870.2500	Non-irritating; Toxicity Category IV ACCEPTABLE/GUIDELINE	47927818, 47927829
Dermal Sensitization	870.2600	Not a contact dermal sensitizer ACCEPTABLE/GUIDELINE	47927818, 47927830
90-Day Oral – Rat (Dietary)	870.3100	No Observed Adverse Effect Level (NOAEL) = 10,000 ppm (highest dose tested, 566-587 mg/kg/day) Doses: 0, 1,000, 3,000, 10,000 ppm ACCEPTABLE/GUIDELINE	47927831
90-Day Dermal – Rat	870.3250	No subchronic dermal toxicity anticipated; data requirement satisfied with acceptable rationale which includes: (1) that the EPs will not be purposefully applied to human skin; (2) PDJ is not known or expected to be metabolized differently by the dermal route than by the oral route; (3) there are no known metabolites of toxicological concern; (4) that it is a synthetic analog of a naturally-occurring plant hormone with no known adverse effects, and (5) low application rates.	48869006
90-Day Inhalation – Rat	870.3465	No subchronic inhalation toxicity; data requirement satisfied with acceptable rationale which includes: (1) low overall toxicity of PDJ; (2) that it is a synthetic analog of a naturally occurring plant	48869007

		hormone with no known adverse effects; and (3) low application rates.	
Prenatal Developmental – Rat (Gavage)	870.3700	Maternal NOAEL = 500 mg/kg/day (highest dose tested) Developmental NOAEL = 500 mg/kg/day (highest dose tested) Doses: 0, 30, 120, and 500 mg/kg ACCEPTABLE/GUIDELINE	47927832
Bacterial Reverse Mutation Test	870.5100	Non-mutagenic ACCEPTABLE/GUIDELINE	47927833
In vitro Mammalian Cell Assay	870.5375	Non-genotoxic in the *in vitro* mammalian chromosome aberration test ACCEPTABLE/GUIDELINE	47927834

Table 12. Summary of Toxicology Data for *Cis*-jasmone (40 CFR § 158.2050)

Data Requirement	Guideline No.	Results / Findings	MRIDs
Acute Oral Toxicity - Rat	870.1100	LD_{50} = 3,129 mg/kg; Toxicity Category III ACCEPTABLE/GUIDELINE	50357903
Acute Dermal Toxicity	870.1200	LD_{50} > 5,050 mg/kg; Toxicity Category IV ACCEPTABLE/GUIDELINE	50357904
Acute Inhalation Toxicity	870.1300	LC_{50} > 2.24 mg/L; Toxicity Category IV ACCEPTABLE/GUIDELINE	50357905
Primary Eye Irritation – Rabbit	870.2400	Minimal eye irritation; Toxicity Category IV ACCEPTABLE/GUIDELINE	50357906
Primary Dermal Irritation	870.2500	Slightly irritating; Toxicity Category IV ACCEPTABLE/GUIDELINE	50357907
Dermal Sensitization	870.2600	Not a contact dermal sensitizer ACCEPTABLE/GUIDELINE	50357908
90-Day Oral (One Species)	870.3100	Data requirement satisfied with acceptable rationale which includes negligible dietary exposure.	50245803
90-Day Dermal – Rat	870.3250	Data requirement satisfied with acceptable rationale which includes: (1) the acute LD_{50} dermal toxicity and skin irritation studies are classified as Toxicity Category IV; (2) based on the physical and chemical properties of *cis*-jasmone, there is a low likelihood of significant dermal absorption; (3) application rates are low (0.000002 lb AI/lb seed); (4) a hypothetical occupational handler risk assessment using toxicity data on a substance considered to have a higher systemic toxicity resulted in risk estimates that were not of concern; and (5) humans are already exposed to the substance in food, cosmetics and household products and no safety concerns have been identified in published assessments for these uses.	50357909
90-Day Inhalation – Rat	870.3465	Data requirement satisfied with acceptable rationale which includes: (1) the physical-chemical properties; (2) the chemical's low acute inhalation toxicity and minimal eye and dermal irritation; (3) application rates are very low (0.000002 lb AI/lb seed); (4) a hypothetical occupational handler risk assessment	50357909

		using toxicity data on a substance considered to have a higher systemic toxicity resulted in risk estimates that were not of concern; (5) handlers are required to wear a NIOSH approved particulate respirator or powered air purifying respirator due to the sensitization potential from repeated exposure to high concentrations of microbial proteins (currently registered EP contains a microbial active ingredient); and (6) humans are already exposed to *cis*-jasmone in food, cosmetics and household products and no safety concerns have been identified in published assessments for these uses.	
Prenatal Developmental	870.3700	Data requirement satisfied with acceptable rationale which includes: (1) the acute toxicity studies are classified as Toxicity Category IV; (2) based on the physical and chemical properties of *cis*-jasmone, there is a low likelihood of significant dermal absorption and thus low likelihood of systemic bioavailability; (3) application rates are low (0.000002 lb AI/lb seed); (4) a hypothetical occupational handler risk assessment using toxicity data on a substance considered to have a higher systemic toxicity resulted in risk estimates that were not of concern; (6) handlers are required to wear a NIOSH approved particulate respirator or powered air purifying respirator due to the sensitization potential from repeated exposure to high concentrations of microbial proteins (currently registered EP contains a microbial active ingredient); and (7) humans are already exposed to the substance in food, cosmetics and household products and no safety concerns have been identified in published assessments for these uses.	50357909; 50729102
Bacterial Reverse Mutation Test	870.5100	Non-mutagenic ACCEPTABLE/GUIDELINE	50357909; 50776701
In vitro Mammalian Cell Assay	870.5375	Non-genotoxic in Chinese Hamster Ovary (CHO) cell assay (in vitro chromosome aberration test) ACCEPTABLE/GUIDELINE	50357909

Table 13. Summary of Toxicology Data for Methyl-dihydrojasmolate[1] (40 CFR § 158.2050)

Data Requirement	Guideline No.	Results / Findings	MRIDs
Acute Oral Toxicity - Rat	870.1100	LD_{50} = 3,500 mg/kg; Toxicity Category III ACCEPTABLE/GUIDELINE	51420034
Acute Dermal Toxicity	870.1200	LD_{50} > 2,000 mg/kg; Toxicity Category III ACCEPTABLE/GUIDELINE	51420034
Acute Inhalation Toxicity	870.1300	Toxicity Category III Data requirement satisfied with acceptable rationale which includes: (1) absence of structural alerts for inhalation toxicity; and (2) presumed to be of low inhalation toxicity or non-toxic based on Category IV results from acute inhalation toxicity study from an analog (methyl dihydrojasmonate). The Agency has given	51420034

		the AI a Category III to be conservative since data on the actual AI are not available.	
Primary Eye Irritation – Rabbit	870.2400	Mild to moderate eye irritation; Toxicity Category III ACCEPTABLE/GUIDELINE	51420034
Primary Dermal Irritation	870.2500	Possible mild to moderate dermal irritation; Toxicity Category III ACCEPTABLE/GUIDELINE	51420034
Dermal Sensitization	870.2600	Not a contact dermal sensitizer ACCEPTABLE/GUIDELINE	51420034
90-Day Oral (One Species)	870.3100	Data requirement satisfied with acceptable rationale which includes: (1) non-food use that is not likely to result in repeated oral exposure to humans; and (2) lack of adverse effects in the 14-day oral dietary toxicity rat study on analog substance, methyl dihydrojasmonate; NOAEL = 400 mg/kg/day (highest dose tested); doses: 10, 50, 100, and 400 mg/kg/day	51420036
90-Day Dermal – Rat	870.3250	Data requirement satisfied with acceptable rationale which includes: (1) a weight of evidence (WOE) approach due to methyl-dihydrojasmolate being mildly irritating to the skin; (2) Toxicity Category III for acute dermal toxicity; (3) non-sensitizing to the skin; (4) naturally occurring; (5) analog (methyl jasmonate/jasmonic acid) being part of the human diet; and (6) no adverse effects were seen in 14-day oral toxicity study on analog substance, methyl dihydrojasmonate.	51420034
90-Day Inhalation – Rat	870.3465	Data requirement satisfied with acceptable rationale which includes: (1) a WOE approach due to methyl-dihydrojasmolate's analog (methyl dihydrojasmonate) having overall low toxicity (low acute inhalation and mild dermal toxicity); and (2) natural occurrence and long history of human exposure in food through plants in the human diet.	51420034
Prenatal Developmental	870.3700	Data requirement satisfied with acceptable rationale which includes: (1) supplemental developmental toxicity data; and (2) natural occurrence and long history of human exposure in food through plants in the human diet. Deficiencies identified in study submitted (several pieces of information were not reported including individual animal data, full necropsy findings, etc). Although the requested information[2] to upgrade the study is not critical to making risk conclusions at this time for the registered use, it would provide useful information for future reference and integrity of the Agency database. This information may be needed if use patterns change in the future; Maternal and Developmental NOAEL = 120 mg/kg/day (highest dose tested). SUPPLEMENTAL/GUIDELINE	51420038
Bacterial Reverse Mutation Test	870.5100	Non-mutagenic ACCEPTABLE/GUIDELINE	51420035
In vitro Mammalian Cell Assay	870.5300 870.5375	Data requirement satisfied with acceptable rationale which includes: (1) no evidence that the AI or any of its metabolites are	51420034

		structurally related to a known mutagen; and (2) minimal expected exposure.	

[1] All data are read-across data from the following analogs: methyl dihydrojasmonate, methyl jasmonate, and 2,6-dimethyl-4-heptanol as there are no data available on the compound MDJ itself and these analogs are closely related to MDJ in structure and function.
[2] US EPA, 2022b.

Hazard Characterization

The toxicological database is considered complete for characterizing hazard and assessing risk from the active ingredients in this case.

Methyl jasmonate can be classified as Toxicity Category III for acute oral toxicity and Toxicity Category IV for acute dermal toxicity, acute inhalation toxicity, primary eye irritation, and primary dermal irritation (U.S. EPA, 2013a). The Agency does not anticipate the need for additional studies for this registration review. All data requirements, per 40 CFR § 158.2050, have been fulfilled for methyl jasmonate.

Prohydrojasmon can be classified as Toxicity Category III for acute dermal toxicity, and Toxicity Category IV for acute oral toxicity, acute inhalation toxicity, primary eye irritation, and primary dermal irritation (U.S. EPA, 2013b). The Agency does not anticipate the need for additional studies for this registration review. All data requirements, per 40 CFR § 158.2050, have been fulfilled for prohydrojasmon.

Cis-jasmone can be classified as Toxicity Category III for acute oral toxicity and Toxicity Category IV for acute dermal toxicity, acute inhalation toxicity, primary eye irritation, and primary dermal irritation (U.S. EPA, 2019). The Agency does not anticipate the need for additional studies for this registration review. All data requirements, per 40 CFR § 158.2050, have been fulfilled for *cis*-jasmone.

Methyl-dihydrojasmolate can be classified as Toxicity Category III for acute oral, inhalation and dermal toxicity, primary eye irritation, and primary dermal irritation (U.S. EPA, 2022b). The Agency does not anticipate the need for additional studies for this registration review. All data requirements, per 40 CFR § 158.2050, have been fulfilled for methyl-dihydrojasmolate.

None of the chemicals are dermal sensitizers according to the available data (U.S. EPA, 2013a, 2013b, 2019, 2022b).

The 90-day oral toxicity requirement was addressed by rationales including natural occurrence and long history of dietary exposure from fruits for methyl jasmonate, no observed adverse effects in the 13-week oral toxicity study in rats for prohydrojasmon, negligible dietary exposure for *cis*-jasmone, and non-food use that is not likely to result in repeated oral exposure and lack of adverse effects in a 14-day oral dietary toxicity rat study for methyl-dihydrojasmolate. Adequate rationales to address the 90-day dermal and 90-day inhalation toxicity data requirements are on file and include one or more of the following considerations: natural occurrence, negligible exposure, mitigation from personal protective equipment (PPE) that should be protective, low oral toxicity, and low dermal and eye irritation. No maternal or developmental effects were noted up to the highest dose tested (500 mg/kg/day) in the prenatal developmental (non-guideline) study with prohydrojasmon. Adequate rationales are on file to address this requirement for the other chemicals, mainly related to natural occurrence and negligible exposure. All the chemicals were considered negative for genotoxicity in the Ames test and in the in

vitro mammalian cell assay. Currently, the Agency does not anticipate the need for additional studies for this registration review. All data requirements, per 40 CFR §158.2050, have been fulfilled for methyl jasmonate, prohydrojasmon, *cis*-jasmone, and methyl-dihydrojasmolate.

Dietary Exposure and Risk Characterization

Methyl Jasmonate

Methyl jasmonate is present in most fruits, is already a regular part of the human diet, and has a history of dietary exposure. A tolerance exemption exists for residues of methyl jasmonate in or on all food commodities when it is applied pre-harvest (40 CFR 180.1320). Additionally, methyl jasmonate is a Food and Agriculture Organization/World Health Organization (FAO/WHO) approved flavoring agent, and is commonly consumed in processed foods with peach, apricot, berry, plum, tutti –frutti, and tropical fruit flavors (JECFA, 2005). JECFA has also identified methyl jasmonate as having a "human exposure threshold" of 540 ug/day. This compound has a history of dietary exposure (U.S. EPA, 2012). The use pattern of the only end-use product for this active ingredient is a commercial seed treatment and is likely to result in exposure levels that are lower than the current estimated dietary exposure (U.S., EPA 2012). Dietary exposure of children and adults to methyl jasmonate calculated from food consumption information from the U.S. EPA Exposure Factors Handbook (U.S. EPA, 2009) was found to be less than dietary exposure from consumption of foods containing pesticide residues resulting from a maximum application. The handbook has been updated; however, the Agency does not expect any significant differences in the calculations. Although dietary and drinking water exposure to humans may occur, the Agency has determined that there is reasonable certainty of no harm to humans when exposed to residues of the active ingredient from pesticidal use when label instructions are followed. This conclusion is based on the following: 1) available toxicology data and information indicate that the active ingredient is of low toxicity and is not likely to be a developmental toxicant, a mutagen, or toxic via repeat oral exposure; 2) humans are already exposed to methyl jasmonate in the diet as it is naturally occurring in fruits; and 3) methyl jasmonate is moderately volatile, is applied at low application rates (3.7×10^{-3} lb AI/10,000 lb seed), (U.S. EPA, 2012), and is not directly applied to water. Therefore, potential risk from dietary exposure is not of concern.

Prohydrojasmon

Dietary exposure to residues of PDJ is expected to be insignificant. A tolerance exemption exists for residues of PDJ when used as a plant growth regulator in or on apple and grape pre-harvest (40 CFR 189.1299). One of the use patterns for PDJ is agricultural use; however, dietary exposure to residues of PDJ from treated fruit is not expected to exist above background levels of naturally occurring jasmonic acid, which is structurally similar and functionally identical to PDJ (U.S. EPA, 2013). The other use pattern is indoor ant repellent; therefore, no dietary exposure is anticipated from that use. Although dietary and drinking water exposure to humans may occur, the Agency has determined that there is reasonable certainty of no harm to humans when exposed to residues of the active ingredient from pesticidal use when label instructions are followed. This conclusion is based on the following: 1) available toxicology data and information indicate that the active ingredient is of low toxicity and is not likely to be a developmental toxicant, a mutagen, or toxic via repeat oral exposure; 2) humans are already exposed to jasmonic acid in the diet which is structurally similar and functionally identical to prohydrojasmon; and 3) prohydrojasmon degrades rapidly in the soil, thereby reducing the potential

for uptake of the chemical residues by plants (half-life 1.6-2.3 hours, U.S. EPA, 2013c). Therefore, potential risk from dietary exposure is not of concern.

Cis-Jasmone

Based on the use pattern (commercial seed treatment) and available residue data for *cis*-jasmone, it can be concluded that it is likely that there will be a lack of residues in the edible commodities (seed or grain) of cotton, soybean and corn grown from treated seed; therefore, residues from use as a pesticide are not expected in food. Additionally, treated seeds are not to be used for food, feed purposes, or processed for oil. In the case of *cis*-jasmone, based on the unlikelihood of dietary exposure, a quantitative dietary risk assessment was not performed. The Agency has determined that there is reasonable certainty of no harm to humans if exposed to residues of the active ingredient from pesticidal use when label instructions are followed. This non-food determination conclusion is based on the following: (1) in the submitted residue study (MRID 50245801), there were no detectable residues (limit of detection = 0.002 ppm) of *cis*-jasmone in the harvested corn, soybean or cotton seed/grain samples from whole plants that were grown from seeds treated with *cis*-jasmone; (2) no residues have been identified at or above the 0.005 ppm threshold that has been historically used by EPA for nonfood determinations for seed treatments (U.S. EPA, 2018a) (3) the substance is only proposed for use as a seed treatment in commercial seed treatment facilities, and treated seeds are not to be used for food, feed purposes or processed for oil; (4) *cis*-jasmone is expected to degrade rapidly in the environment based on the available physical and chemical properties data (U.S. EPA, 2019); and (5) humans are already exposed to *cis*-jasmone as it occurs naturally in foods, and is used as a food additive and in cosmetics and household products and no safety concerns have been identified in published assessments for these uses. In addition, drinking water exposure is not anticipated due to the use pattern as a commercial seed treatment and rapid degradation of *cis*-jasmone based on the available physical and chemical properties. Therefore, risk from dietary exposure is not of concern.

Methyl-dihydrojasmolate

Methyl-dihydrojasmolate is currently only registered for indoor nonfood use, therefore a dietary exposure and risk characterization was not performed.

Residential and Non-Occupational Exposure and Risk Characterization

Methyl jasmonate

Exposure to methyl jasmonate will be minimal in residential areas as the product containing this active ingredient is intended for use as a commercial seed treatment only. Significant spray drift from the use of the one registered EP is not anticipated as this is a commercial seed treatment used in commercial tank mix equipment. The Agency has determined that there is reasonable certainty of no harm to humans when exposed to residues of the active ingredient from pesticidal use when label instructions are followed. Therefore, risk from residential and non-occupational exposure is not of concern.

Prohydrojasmon

Short- and intermediate-term dermal and inhalation prohydrojasmon exposures are anticipated for residential handlers from the application of the residential ant repellent end-use products (EPA Reg. # 52991-38, 52991-40, 52991-41, and 52991-42). Residential post-application exposures can also occur for adults (dermal) and children (incidental oral and dermal) re-entering treated areas. Long-term

exposure to this AI is not expected for the proposed uses. PDJ has an overall low toxicity across its database, with no adverse effects noted up to the highest dose tested in the available subchronic toxicity studies, therefore it is presumed to have negligible risk to the general population.

Cis-Jasmone

Exposure to *cis*-jasmone will be minimal in residential areas as the product containing this active ingredient is intended for use as a commercial seed treatment only. The products are applied at very low application rates and solely as seed treatments in commercial seed treatment facilities. Any residues are expected to dissipate between application and planting. In addition, *cis*-jasmone is of low acute inhalation toxicity (Toxicity Category IV). The Agency has determined that there is reasonable certainty of no harm to humans when exposed to residues of the active ingredient from pesticidal use when label instructions are followed. Therefore, risk from residential and non-occupational exposure is not of concern.

Methyl dihydrojasmolate

Short and intermediate-term dermal and inhalation exposures to methyl-dihydrojasmolate can occur to residential handlers from the application of the registered end-use products. Long-term exposure to methyl-dihydrojasmolate is not expected for the proposed uses. Methyl-dihydrojasmolate has an overall low toxicity across its database, with no adverse effects noted up to the highest dose tested in the available subchronic studies. It has low acute inhalation toxicity (based on absence of structural alerts related to elevated acute toxicity and low acute toxicity via the dermal route) and minimal irritation to the eye or skin (Toxicity Category III). The Agency has determined that there is reasonable certainty of no harm to humans when exposed to residues of the active ingredient from pesticidal use when label instructions are followed. Therefore, risk from residential and non-occupational exposure is not of concern.

Occupational Exposure and Risk Characterization

Methyl jasmonate

Significant occupational exposure is not expected when methyl jasmonate is used according to label instructions with the appropriate baseline attire and PPE. Although some dermal exposure may occur to applicators/handlers, all product labels require long sleeve shirt and long pants, shoes and socks, and waterproof gloves thereby mitigating the exposure. Inhalation exposure is not expected due to the nature of the closed seed treatment mixture equipment. Nevertheless, in the case of minimal exposure, the risk is considered minimal as methyl jasmonate is a naturally occurring, ubiquitous substance in fruits, and no systemic toxicity has been identified in the toxicity database. Post-application inhalation and dermal exposure is expected to be minimal based on the nature of the closed seed treatment application. Therefore, risk from occupational exposure is not of concern.

Prohydrojasmon

Significant short- and intermediate-term dermal and inhalation occupational exposure is not expected when prohydrojasmon is used according to label instructions with the appropriate baseline attire and PPE for both the PGR and indoor repellent uses. Although some dermal exposure may occur to applicators/handlers for both uses, all product labels require long sleeve shirt and long pants, shoes and socks, and waterproof gloves thereby mitigating the exposure. Additionally, occupational handler

inhalation exposure and post-application inhalation exposure to prohydrojasmon may occur from the only proposed EP that may be used in commercial settings, Triple B Professional Repellent Concentrate. (The other EPs are for residential use only; the risk is expected to be negligible based on low toxicity of the active ingredient and long history of human exposure to its analog (jasmonic acid). Therefore, risk from occupational exposure is not of concern.

Cis-Jasmone

Occupational handler exposure and occupational post-application exposure to *cis*-jasmone are expected to be negligible based on very low application rates, physical/chemical properties of the AI and baseline attire and PPE requirements (long-sleeved shirt and long pants, waterproof or nitrile gloves, shoes plus socks, protective eyewear, and a NIOSH approved particulate respirator or powered air purifying respirator). As part of the WOE for waiving certain toxicity studies, a quantitative approach was used to support the negligible exposure finding and to show there are no risks of concern. A hypothetical occupational handler risk assessment using toxicity data on a substance considered to have a higher systemic toxicity resulted in risk estimates that were not of concern. Therefore, risk from occupational exposure is not of concern.

Methyl dihydrojasmolate

Occupational handler exposure and post-application exposure to methyl-dihydrojasmolate may occur from the only proposed EP that may be used in commercial settings, Triple B Professional Repellent Concentrate. The risk is expected to be negligible based on low toxicity of the AI, long history of human exposure to its analog, infrequent application (only as needed with increased ant activity), and moderate volatility. Therefore, risk from occupational exposure is not of concern.

Overall Human Health Risk Characterization and Conclusion

New human health risk assessments are not needed. Previous risk assessments concluded that adverse effects to humans are not expected to occur with labeled uses of methyl jasmonate, prohydrojasmon, *cis*-jasmone, and methyl-dihydrojasmolate (U.S. EPA, 2013a, 2013b, 2019, 2022b). All data requirements have been met and the database is complete, and no additional information has been found in the literature or incident database that would alter the Agency's risk conclusions. Therefore, previous risk conclusions are still applicable.

Hazard and exposure data, Agency risk assessments, and other information on these active ingredients were evaluated against standards established by FIFRA and the Agency's regulations and scientific policies.

The Agency has considered human exposure to all four active ingredients in light of the relevant safety factors in FQPA and FIFRA. A determination has been made that no unreasonable adverse effects to the U.S. population in general, and to infants and children in particular, will result from the use of these active ingredients as a pesticide when label instructions are followed.

Literature Search Findings

To support registration review, the Biopesticides and Pollution Prevention Division (BPPD) conducts searches of the literature and incident databases to determine if there are any reports of adverse effects that might change risk conclusions or change knowledge of the state of the science for methyl

jasmonate, prohydrojasmon, *cis*-jasmone, and methyl-dihydrojasmolate. Searches conducted for these active ingredients are described below.

Human Health Results:

A literature search was conducted using Google Scholar and PubMed for "methyl jasmonate," "prohydrojasmon," "propyl-dihydrojasmonate," "*cis*-jasmone", and "methyl-dihydrojasmolate," in combination with "toxicity", "endocrine," "estrogen," "androgen," and "hormone.".

For methyl jasmonate, ten relevant documents were found. The first article is an investigation on the potential use of methyl jasmonate as a therapeutic intervention against uterine fibroids (Ali, 2023). The second article demonstrates that methyl jasmonate administration may be a potential treatment for endometrial cancer (Bruchim, 2014). The third article indicates that methyl jasmonate may be a promising breast cancer treatment option (Jeoung, 2021). The fourth article shows that methyl jasmonate may be protective against testosterone propionate induced benign prostatic hyperplasia (BPH) via mechanisms that involve anti-inflammation, induction of apoptosis, and inhibition of phase I drug metabolizing enzyme (Adaramoye, 2017). The fifth article indicates that methyl jasmonate can increase the radiation sensitivity of AKR1C3-overexpressing KY170R cells by inhibiting the 11-ketoprostaglandin reductase activity of AKR1C3 and increasing cellular reactive oxygen species (ROS) levels (Li, 2023). The sixth article shows that methyl jasmonate has cytotoxic effects on paclitaxel resistant PC3 cells; this may contribute to the development of alternative new compounds for the prevention of chemosensitization of resistance to cancer drugs like paclitaxel (Seda, 2021). The seventh article shows that methyl jasmonate may represent an alternative for the transduction processes of important signals in the cellular renewal of the intestinal mucosa, therefore it could be a potential treatment of inflammatory bowel disease. The eighth article shows that methyl jasmonate is non-toxic to normal cells but causes damage to cancer cells via several mechanisms (Cesari, 2014). The ninth article shows that jasmonates have a synergistic effect with other anti-cancerous agents and may be a strong basis for future clinical cancer treatments (Elia, 2013). The tenth article shows that jasmonic acid in general, due to its similarity to prostaglandins, may be potentially used as a therapeutic agent not only in neo-plastic but also other diseases (Jarocka-Karpowicz, 2021). These studies do not raise any toxicity concerns.

For *cis*-jasmone, three relevant articles were found. The first article shows that *cis*-jasmone has pharmacological potential for the treatment of seizures, anxiety, inflammation, and acute orofacial nociception (Bezerra, 2023). The second article is a safety assessment of *cis*-jasmone performed by the Research Institute for Fragrance Materials (RIFM). It indicates that *cis*-jasmone is not genotoxic and has a margin of exposure > 100 for repeated dose toxicity and reproductive toxicity endpoints. Data show that there are no safety concerns for *cis*-jasmone for skin sensitization under the current level of usage. The article also shows that *cis*-jasmone does not pose any risks of concern to respiratory health. (Api, 2022) The third article shows that both methyl jasmonate and *cis*-jasmone could be useful in the management of advanced prostate cancer, due to their apoptotic abilities towards cancer cells (Yeruva, 2008). These studies do not raise any toxicity concerns.

For methyl-dihydrojasmolate and prohydrojasmon, no relevant articles were found.

Appendix C – Environmental Risk Assessment

Summary of Nontarget Organism Data

For methyl jasmonate, data cited from the open literature were submitted to satisfy data requirements for avian dietary, freshwater fish, freshwater invertebrates, nontarget terrestrial plant testing, and nontarget insect testing. The avian acute oral toxicity guideline was addressed by a guideline study.

For prohydrojasmon, guideline studies were submitted to satisfy data requirements for avian acute oral, avian dietary, freshwater fish, freshwater invertebrates, nontarget terrestrial plant testing, and nontarget insect testing.

For *cis*-jasmone, guideline studies were submitted to satisfy data requirements for avian acute oral, avian dietary, freshwater fish, freshwater invertebrates, and nontarget insect testing. The nontarget terrestrial plant testing requirements were addressed with scientific rationale.

For methyl-dihydrojasmolate, scientific rationale was submitted to satisfy data requirements for avian acute oral, avian dietary, freshwater fish, and freshwater invertebrate toxicity testing. Data was not required for nontarget plants nor terrestrial insects because the products registered are indoor use only. Plant toxicity data may be required if a new, outdoor use is requested.

The information provided is sufficient to satisfy the Tier I nontarget organism data requirements for ecological risk assessment for the four active ingredients in this case. Further testing of nontarget organisms at higher tiers is not required for the proposed label uses.

Table 14. Summary of Nontarget Organism Data for Methyl Jasmonate (40 CFR § 158.2060)

Data Requirement	Guideline No.	Results / Findings	MRIDs
Avian Acute Oral Toxicity (Northern Bobwhite)	850.2100	LD_{50} > 2,000 mg/kg Practically non-toxic ACCEPTABLE/GUIDELINE	48653907
Avian Dietary Toxicity	850.2200	Addressed by acceptable rationale: 1) birds are already exposed naturally to methyl jasmonate from flowers, fruits, and other plants; 2) the application rates of the EPs containing methyl jasmonate are below natural levels in the environment; and 3) literature search yielded no reports of avian toxicity from methyl jasmonate exposure	48653908
Fish Acute Toxicity, Freshwater	850.1075	Addressed by acceptable rationale: 1) fish are already exposed naturally to methyl jasmonate from aquatic plants; 2) the application rates of the EPs containing methyl jasmonate are below natural levels in the environment; 3) literature search yielded no reports of fish toxicity from methyl jasmonate exposure; and 4) modeling data (QSAR) is available for an analog of this active ingredient, methyl dihydrojasmonate (LC_{50} = 5.05 – 8.15 mg/L which indicates moderate toxicity (MRID 51420039))	48653908 51420039
Aquatic Invertebrate Acute Toxicity, Freshwater	850.1010	Addressed by acceptable rationale: 1) freshwater invertebrates are already exposed naturally to methyl jasmonate from aquatic plants; 2) the application rates of the EPs containing methyl jasmonate are below natural levels in the environment; 3)	48653908 51420039

Table 14. Summary of Nontarget Organism Data for Methyl Jasmonate (40 CFR § 158.2060)			
Data Requirement	**Guideline No.**	**Results / Findings**	**MRIDs**
		literature search yielded no reports of freshwater invertebrate toxicity from methyl jasmonate exposure; and 4) modeling data (QSAR) is available for an analog of this active ingredient, methyl dihydrojasmonate (LC_{50} = 15.27 – 47.76 mg/L which indicates slight toxicity (MRID 51420039))	
Terrestrial Plant Toxicity, Seedling Emergence	850.4100	Addressed by acceptable rationale that the seed treatment application rates of the EPs containing methyl jasmonate are very low (3.7×10^{-3} lb AI/10,000 lb seed), and will not result in exposure concentrations above the naturally occurring methyl jasmonate content in plants and therefore, use of methyl jasmonate is not expected to interfere with seedling emergence	48653908
Terrestrial Plant Toxicity, Vegetative Vigor	850.4150	Addressed by acceptable rationale that cites studies showing that low levels of methyl jasmonate improve the defense response in plants and the seed treatment application rates of the EPs containing methyl jasmonate are very low (3.7×10^{-3} lb AI/10,000 lb seed), and will not result in exposure concentrations above the naturally occurring methyl jasmonate content in plants and therefore, use of methyl jasmonate, is not expected to interfere with vegetative vigor	48653908
Nontarget Insect Testing (honeybees)	880.4350	Addressed by acceptable rationale: 1) honeybees are already exposed naturally to methyl jasmonate from flowers, fruits, and other plants; 2) the application rates of the EPs containing methyl jasmonate are below natural levels in the environment; and 3) literature search yielded no reports of honeybee toxicity from methyl jasmonate exposure	48653908

Table 15. Summary of Nontarget Organism Data for Prohydrojasmon (40 CFR § 158.2060)			
Data Requirement	**Guideline No.**	**Results / Findings**	**MRIDs**
Avian Acute Oral Toxicity (Northern Bobwhite)	850.2100	LD_{50} > 2,000 mg/kg Practically non-toxic ACCEPTABLE/GUIDELINE	47927835
Avian Dietary Toxicity (Japanese quail)	850.2200	LC_{50} > 5,000 ppm Practically non-toxic ACCEPTABLE/GUIDELINE	47927836
Fish Acute Toxicity, Freshwater *(Cyprinus carpio)*	850.1075	96 hr LC50 = 3.3 mg/L Moderately toxic ACCEPTABLE/GUIDELINE	47927837
Aquatic Invertebrate Acute Toxicity, Freshwater (daphnids)	850.1010	EC_{50} = 9.54 mg/L (immobilization) NOAEL = 1.29 mg/L Moderately toxic ACCEPTABLE/GUIDELINE	47927838
Terrestrial Plant Toxicity, Seedling Emergence[a]	850.4100	ER_{50} > 1,140 g AI/ha[1] (> 456 g AI/A)	48869004

		ACCEPTABLE/GUIDELINE	
Terrestrial Plant Toxicity, Vegetative Vigor[a]	850.4150	ER_{50} > 1,140 g AI/ha[1] (> 456 g AI/A) ACCEPTABLE/GUIDELINE	48869005
Honeybee Acute Toxicity	850.3020	LD_{50} > 98.94 µg AI/bee Practically non-toxic ACCEPTABLE/GUIDELINE	48869002

[a] Performed on the EP, BLUSH (Reg. No. 62097-29) containing 5.25% AI

[1] ER_{50} = the application rate at which a biological endpoint is affected by 50% compared to the control

Table 16. Summary of Nontarget Organism Data for *Cis*-jasmone (40 CFR § 158.2060)

Data Requirement	Guideline No.	Results / Findings	MRIDs
Avian Acute Oral Toxicity (Northern bobwhite)	850.2100	LD_{50} = 1432 mg/kg (95% C.I.: 1227 to 1696 mg/kg) NOAEL = 521 mg/kg Slightly toxic ACCEPTABLE/GUIDELINE	50357910
Avian Dietary Toxicity (Northern bobwhite)	850.2200	LC_{50} > 3463 ppm (902 mg/kg bw/day) NOAEC = 748 ppm (194 mg/kg bw/day) ACCEPTABLE/GUIDELINE	50357911
Fish Acute Toxicity, Freshwater *(Cyprinus carpio)*	850.1075	96-hour LC_{50} = 35.8 mg/L NOAEC = 6.7 mg/L Slightly toxic ACCEPTABLE/GUIDELINE	50357912
Aquatic Invertebrate Acute Toxicity, Freshwater (daphnids)	850.1010	48-hour EC_{50} = 70.8 mg/L (95% C.I.: 66.2 – 75.8 mg/L) NOAEC = 51.7 mg/L (based on mortality) Slightly toxic ACCEPTABLE/GUIDELINE	50357913
Terrestrial Plant Toxicity, Seedling Emergence	850.4100	Addressed by acceptable rationale: Exposure is expected to be negligible as the product is applied at very low application rates to seed in commercial seed treatment facilities and *cis*-jasmone is expected to degrade rapidly in the environment. Further, toxicity is also expected to be negligible as *cis*-jasmone occurs naturally in plants and promotes resistance to plant pathogens.	50557501
Terrestrial Plant Toxicity, Vegetative Vigor	850.4150	Addressed by acceptable rationale: Exposure is expected to be negligible as the product is applied at very low application rates to seed in commercial seed treatment facilities and *cis*-jasmone is expected to degrade rapidly in the environment. Further, toxicity is also expected to be negligible as *cis*-jasmone occurs naturally in plants and promotes resistance to plant pathogens.	50557501
Nontarget insect testing (honeybees)	880.4350 850.3020	48-hour contact LD_{50} > 100 µg AI/bee 48-hour oral LD_{50} > 47.5 µg AI/bee (actual uptake), > 100 µg AI/bee (nominal) Practically non-toxic ACCEPTABLE/GUIDELINE	50357914 50357915

Table 17. Summary of Nontarget Organism Data for Methyl-dihydrojasmolate (40 CFR § 158.2060)			
Data Requirement	**Guideline No.**	**Results / Findings**	**MRIDs**
Avian Acute Oral Toxicity	850.2100	Addressed by acceptable rationale: exposure to birds is not expected as the products are applied indoors only at a low application rate of 1 ounce product/10 ft^2; jasmonate and jasmolate compounds are naturally occurring in the environment and therefore birds are already acclimated to low levels of these compounds	51420011
Avian Dietary Toxicity	850.2200	Addressed by acceptable rationale: exposure to birds is not expected as the products are applied indoors only at a low application rate of 1 ounce product/10 ft^2; jasmonate and jasmolate compounds are naturally occurring in the environment and therefore birds are already acclimated to low levels of these compounds	51420011
Fish Acute Toxicity, Freshwater *(Cyprinus carpio)*	850.1075	Addressed by acceptable rationale: Exposure to fish is not expected as the products are applied indoors only; jasmonate and jasmolate compounds are naturally occurring in the environment and therefore fish are already acclimated to low levels of these compounds; modeling (QSAR) data exists for the analog (methyl-dihydrojasmonate, LC_{50} = 5.05 – 8.15 mg/L which indicates moderate toxicity)	51420039
Aquatic Invertebrate Acute Toxicity, Freshwater (daphnids)	850.1010	Addressed by acceptable rationale: Exposure to aquatic invertebrates is not expected as the products are applied indoors only; jasmonate and jasmolate compounds are naturally occurring in the environment and therefore aquatic invertebrates are already acclimated to low levels of these compounds; modeling (QSAR) data exists for the analog (methyl-dihydrojasmonate, LC_{50} = 15.27 – 47.76 mg/L which indicates slight toxicity)	51420039
Terrestrial Plant Toxicity, Seedling Emergence	850.4100	Not required per 40 CFR§ 158.2060: indoor use only	N/A
Terrestrial Plant Toxicity, Vegetative Vigor	850.4150	Not required per 40 CFR§ 158.2060: indoor use only	N/A
Nontarget insect testing	880.4350	Not required per 40 CFR§ 158.2060: indoor use only	N/A

Risk Characterization

When used in accordance with current labels, low risk is expected from the current biopesticide uses of methyl jasmonate, prohydrojasmon, *cis*-jasmone, and methyl-dihydrojasmolate. All nontarget organism and environmental fate data necessary to meet the standard for methyl jasmonate, prohydrojasmon, *cis*-jasmone, and methyl-dihydrojasmolate were satisfied through either the acceptance of scientific rationales or by data submissions.

Methyl jasmonate is practically non-toxic to birds as shown in a guideline avian acute oral toxicity study. All other Tier I nontarget organism data requirements were addressed with rationales based on

methyl jasmonate's natural occurrence in the environment, low exposure due to seed treatment uses only and low application rates compared to naturally occurring levels, and no reports of toxicity to terrestrial organisms in the public literature.

Prohydrojasmon is practically non-toxic to birds according to the guideline avian acute oral and dietary toxicity studies. Other guideline studies indicate that prohydrojasmon is moderately toxic to fish and aquatic invertebrates; however, the previous GENEEC model estimates indicate that the risk quotients for fish and aquatic invertebrates (0.0001 and 0.00005) are 3 and 4 orders of magnitude below the levels of concern (LOC) of 0.05-1 (U.S. EPA, 2013c). No effects were noted in the non-target plant studies. Prohydrojasmon is practically non-toxic to honeybees (U.S. EPA, 2013c).

Cis-jasmone is slightly toxic to birds, fish, and aquatic invertebrates according to the guideline studies submitted to the Agency. It is practically non-toxic to honeybees. The nontarget plants data requirements were addressed with rationale based on low exposure due to low application rates for seed treatments only and the natural occurrence of *cis*-jasmone in many plants (U.S. EPA, 2018b). Given the slight toxicity to birds, the EPA expects to model risk to birds from consumption of treated seeds in the registration review ecological risk assessment.

All Tier I nontarget organism data requirements for methyl-dihydrojasmolate were addressed with rationale based on available analog data (methyl-dihydrojasmonate) and the fact that this active ingredient is approved for indoor use only at this time, meaning that environmental exposure is expected to be negligible. No further data or updated risk assessment is needed at this time.

Endangered Species Act

The Agency 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 jasmonates and jasmolates's risks to listed species. However, EPA will complete its listed-species assessment and any necessary consultation with the Services before completing the jasmonates and jasmolates registration review. See the Endangered Species Assessment section above for more details. As such, only potential risks for nontarget species generally are described below.

Literature and Incident Search Findings

To support registration review, BPPD conducts searches of the literature and incident databases to determine if there are any reports of adverse effects that might change risk conclusions or change knowledge of the state of the science for methyl jasmonate, prohydrojasmon, *cis*-jasmone, and methyl-dihydrojasmolate. Searches conducted for these active ingredients are described below.

Ecological Results:

The literature searches for each of these active ingredients resulted in several articles which indicated beneficial effects to plants and promotion of plant defense mechanisms, however no other relevant information was gained from these searches that would alter BPPD's understanding of the current state of the science for any potential effects of these active ingredients on nontarget organisms.

Appendix D – Endocrine Disruptor Screening Program (EDSP)

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-related 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))[11].

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.[12]

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 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*

[11] For additional details of the EDSP, please visit https://www.epa.gov/endocrine-disruption.

[12] 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

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[13] and November 2022 ESA Workplan Update[14]). However, EPA notes that for 35 of the List 1 chemicals (33 active ingredients and 2 inert ingredients), Tier 1 WoE memoranda[15] 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 the chemical's potential to interact with 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 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,

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

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.

Although EPA has prioritized conventional active ingredients as presented in EPA's EDSP Strategies Notice, EPA is planning to develop similar strategies for biopesticide and antimicrobial pesticide (*i.e.*, nonconventional) active ingredients and will provide public updates on these strategies, when appropriate. At this time, EPA is making no findings associated with the implementation of EDSP screening of jasmonates and jasmolates. Such issues will be addressed in future updates by EPA on its strategies for implementing FFDCA section 408(p).

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