Methyl Anthranilate

Proposed Interim Registration Review Decision
Case Number 6056

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for Robert McNally, Director
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I. Introduction

This document is the Environmental Protection Agency's (EPA or the Agency) *Proposed Interim Registration Review Decision* for Methyl Anthranilate (Case 6056, PC Code 128725) and is being issued pursuant to 40 CFR sections 155.56 and 155.58. A registration review decision is the Agency's determination whether a pesticide meets, or does not meet, the standard for registration in the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). The Agency may issue, when it determines it to be appropriate, an interim registration review decision before completing a registration review. Among other things, the interim registration review decision may: 1) require new risk mitigation measures; 2) impose interim risk mitigation measures; 3) identify data or information required to complete the review; and 4) establish schedules for submitting the required data, conducting the new risk assessment and completing the registration review. For further information on Methyl Anthranilate, additional documents can be found in EPA's public docket (EPA-HQ-OPP-2011-0678) at www.regulations.gov.

FIFRA, as amended by the Food Quality Protection Act (FQPA) of 1996, mandated 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 risks 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 section 3(g). The Agency will review each registered pesticide every 15 years to determine whether it continues to meet the FIFRA standard for registration.

Given that the Final Work Plan (FWP) did not anticipate requiring any new or additional data nor was an updated risk assessment needed, the Agency is issuing this *Proposed Interim Registration Review Decision for Methyl Anthranilate,* pursuant to 40 CFR Sections 155.56 and 155.58.

This document is organized into five sections: the *Introduction*, which includes this summary and a summary of any public comments and the Agency's response; *Use and Usage*, which describes how and why methyl anthranilate is used and summarizes data on its use; *Scientific Assessments*, which summarizes the Agency's risk assessments, any revisions, and risk conclusions; *Proposed Interim Registration Review Decision*, which describes the regulatory rationale for the Agency's proposed interim registration review decision; and, last, the *Next Steps* and *Timeline* for completion of this registration review case.

A. Summary of Methyl Anthranilate Registration Review

Pursuant to 40 CFR section 155.50, the Agency formally initiated registration review for methyl anthranilate (Case 6056). The following list highlights significant events that have occurred during the registration review of methyl anthranilate. Documentation of these events for methyl anthranilate can be found in the Agency's public docket, EPA-HQ-OPP-2011-0678 available at www.regulations.gov.

- September 30, 2011 – Publication of *Methyl Anthranilate Preliminary Work Plan* (PWP) for a 60-day public comment period. The comment period closed November 29, 2011. The Agency received one comment correcting a typographical error concerning the date the first product was registered. The Agency appreciates this comment and incorporated the revision into the *Methyl Anthranilate Final Work Plan*.

- February 1, 2018 – Publication of the *Methyl Anthranilate Final Work Plan* (FWP) - The FWP confirmed that the most recent exposure and risk assessments still support the registration of pesticide products containing methyl anthranilate. It was determined that no additional data were needed for the methyl anthranilate registration review because sufficient information was available to conduct a qualitative risk assessment, supporting a proposed interim registration review decision, pursuant to 40 CFR section 155.53(b).

- September 2018– The Agency is now publishing the *Methyl Anthranilate Proposed Interim Registration Review Decision* for a 60-day public comment period.

II. Use and Usage

The first pesticide product containing methyl anthranilate was registered as a pesticide by the Agency in 1994 for use as a bird repellent. Products containing methyl anthranilate are used on agricultural sites and on other sites where nuisance birds create hazard, such as at airports and on turf. Methyl anthranilate works through a non-toxic mode of action by causing a pain response in the trigeminal nerve of birds. Birds are then conditioned not to return to the place of their discomfort. It is formulated as a liquid and is applied by foliar spray or fogger or aerially. It also is applied as a seed treatment. Water in small non-fish bearing fountains, lakes and ponds may also be treated.

Table 1. Methyl Anthranilate Use and Usage Information

Summary of Use	Biochemical registered for use as a bird repellent
Use Sites	For commercial, agricultural and home use sites including: agricultural crops, orchards, nurseries, ornamental turf and plants and golf courses. Non-fish bearing bodies of water (tailing ponds, lakes, ornamental fountains, commercial or industrial water impoundments) and dams, fish hatchery buildings, industrial or agricultural buildings/structures (outdoor), airports, parks, playgrounds, public buildings, bird roosting areas, bird nesting sites, land fill areas, boat docks, parks, garages, and warehouses
Summary of Usage	N/A
Formulation Types	Technical chemical, soluble concentrate, ready to use solution, microencapsulated; pressurized liquid
Application Method	Spray (ground and aerial); hand sprayers; conventional spray equipment, hydroseeders and other liquid; thermal and mechanical foggers as well as specialized fogging and aerosol equipment; mixed into paints, stains, varnishes and pigments; mixed into vaporizing gels, adhesives, fillers and resins
Technical Registrants	Roth Chemical Company, LTD.; Avian Enterprises Limited LLC
No. of Registrations	12 FIFRA Section 3 products[1]
Restricted Use	No

[1] FIFRA Section 3 product labels can be obtained from the Pesticide Product Label System (PPLS) website (https://iaspub.epa.gov/apex/pesticides/f?p=PPLS:1).

III. Scientific Assessments

A summary of the Agency's human health, environmental and ecological risk assessments for methyl anthranilate is presented below. Based on available data and information, the Agency does not foresee the need for new data or new human health risk assessments for this active ingredient. Hazard and exposure information as well as Agency risk assessments on methyl anthranilate were evaluated against current safety standards established by statute, the Agency's scientific policies and regulations, and it was determined that there is no need to conduct additional risk assessments. For the detailed risk assessments, see the methyl anthranilate public docket (EPA-HQ-OPP-2011-0678) at www.regulations.gov.

A. Human Health Assessment

Hazard Characterization

Methyl anthranilate is a naturally occurring ester found in plants such as corn, grapes, cherries, cocoa and black tea. It is present in those commonly consumed foods at higher concentrations than in any pesticidal exposure scenarios. Data indicate that when methyl anthranilate is consumed, it is metabolized easily in the intestines and liver, obviating any systemic dietary exposure. This substance is used as a flavoring in candy and sodas and is considered GRAS by FDA for consumption as a flavoring agent (21 CFR 182.60), and is also used in perfumes. (U.S. EPA, 2011a).

All acute toxicity data requirements were fulfilled for pesticidal uses of methyl anthranilate per 40 CFR 158.2050. All data show that methyl anthranilate is virtually non-toxic to mammals through all routes of exposure. In the acute oral, dermal, inhalation toxicity and eye irritation studies, methyl anthranilate was toxicity category III. In the acute dermal irritation study, the chemical was toxicity category IV. Methyl anthranilate did not cause dermal sensitization in laboratory tests either. No acute toxic endpoints have been established for methyl anthranilate; and it degrades rapidly into non-toxic components such as anthranilic acid (U.S. EPA, 2011a). No additional studies are anticipated to be needed for registration review.

Dietary Exposure Assessment

Given low use rates, pre-harvest intervals and rapid degradation for products containing methyl anthranilate, no significant residues are expected at harvest. Further, since pesticidal use of methyl anthranilate has shown no mammalian toxicity and it is rapidly metabolized in human intestines and liver, no dietary risks are anticipated. Likewise, residues of methyl anthranilate are very unlikely to be found in drinking water, because in addition to the low use rates and the rapid photodegradation, methyl anthranilate is also prone to microbial degradation (U.S. EPA, 2011a).

Due to the low toxicity, metabolism, rapid degradation and long history of dietary exposure to this naturally occurring biochemical, chronic and subchronic data were waived. No other toxic endpoints were identified; therefore, no reference dose and no observable effect level were established. Because of a lack of significant acute toxicity and minimal exposure due to low application rates and rapid degradation. The Agency's conclusions, as reported in its PWP, are still current: potential pesticidal residues of methyl anthranilate in food and drinking water are anticipated to be minimal, thus, no significant risk of dietary toxicity relative to pesticidal exposure to methyl anthranilate is expected.

Therefore, the continued use of methyl anthranilate as a pesticide does not present any concern to the Agency (U.S. EPA, 2011a).

Food Tolerances

In light of available toxicity and exposure data, the 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 anthranilate. Therefore, the EPA established a tolerance exemption for residues of this active ingredient. The current tolerance exemption for this active ingredient is stated as follows:

> **§ 180.1143 Methyl anthranilate; exemption from the requirement of a tolerance.** Residues of methyl anthranilate, a biochemical pesticide, are exempt from the requirement of a tolerance in or on all food commodities, when used in accordance with good agricultural practices. [67 FR 51088, Aug. 7, 2002]

Residential and Occupational Exposure

Residential exposure is expected to be minimal via the dermal and inhalation routes due to the largely commercial nature of the use patterns and the low application rates for methyl anthranilate EPs with residential uses. Additionally, exposure is anticipated to be limited based on biodegradation.

Occupational exposure is expected to individuals who handle this pesticide through mixing and loading and to those who apply the pesticide. The exposure is expected to be insignificant due to low application rates of these products, rapid biodegradation of the active ingredient and label PPE requirements (U.S. EPA, 2011a).

Human Incidents

A search of the Office of Pesticide Programs' (OPP) Incident Data System (IDS) (version 2.1.1) conducted on August 16, 2018, revealed no additional reported incidents associated with methyl anthranilate beyond the three reported in the PWP that appear to be associated with applicator error (U.S. EPA, 2011a). This database contains information dating back to the 1970s and is continuously updated as incidents are reported.

B. Ecological Risk Assessment

Methyl anthranilate is a naturally occurring substance in plants such as corn, sunflowers, grapes and cherries as well as cocoa and black tea (U.S. EPA, 1994). Honey made from citrus floral sources has been reported to contain from 3.60 to 5.04 mg/kg of methyl anthranilate (Ferreres et al., 1994; White & Bryant, 1996). Methyl anthranilate is extremely volatile and degrades rapidly into non-toxic components such as anthranilic acid. Numerous studies are available evaluating residues on crops and aquatic environments following application of methyl anthranilate at maximum label use rates for the respective use sites. In both terrestrial and aquatic exposure scenarios, the potential residues were well below the naturally occurring levels found in cherries (35 ppm) and grapes (33 ppm), and far below any level of concern for non-targets. The non-target insect contact toxicity LD_{50} for honey bee was >25 ug/bee, which is categorized as practically non-toxic. No toxic effects were observed at the highest rate used in laboratory testing (U.S. EPA, 2011b).

As mentioned above, honey made from citrus floral sources has been reported to contain methyl anthranilate indicating regular dietary and contact exposure to this naturally-occurring chemical by pollinators. Based on these data, the Agency has no concerns to non-target to bees and other insects. Even in the event of exposure, toxicity data on nontarget organisms confirm that methyl anthranilate is virtually non-toxic to non-target plants, insects (including pollinators), mammals, and birds and slightly to moderately toxic to fish. It is slightly toxic to aquatic invertebrates, but at levels far below any expected exposure scenario. In sum, use of methyl anthranilate as a bird repellent will not result in significant residues and any residues are considered to be virtually non-toxic. (U.S. EPA, 2011b).

Endangered Species Assessment

Methyl anthranilate undergoes rapid biodegradation in the environment and the Agency's Levels of Concern (LOCs) are not exceeded for listed species (U.S. EPA, 2011b). There are no concerns for any non-target organism when methyl anthranilate is applied in accordance with EPA-approved product labeling (U.S. EPA, 2011b). Based on this information, the Agency has come to a "No Effect" determination under the Endangered Species Act (ESA) for all threatened and endangered species and their designated critical habitat. As a result, the Agency has concluded that consultation with the Fish and Wildlife Service and the National Marine Fisheries Service under ESA section 7 (a)(2) is not required. The Agency anticipates conducting no further analysis of potential risks to endangered or threatened species, unless data or information are obtained during the registration review process that would indicate such an assessment would be needed to inform the Agency's decision.

Ecological Incidents

A search of OPP's Environmental Incident Information System (EIIS) conducted on August 17, 2018, revealed no reported ecological incidents associated with methyl anthranilate. This database contains information dating back to the 1970s and is continuously updated as incidents are reported.

C. Endocrine Disruptor Screening Program

As required by the Administrator under the Federal Food, Drug, and Cosmetic Act (FFDCA) section 408(p), the Agency has developed the Endocrine Disruptor Screening Program (EDSP) and has begun to implement the screening program that is to be used to test all pesticides in order to determine whether certain substances (including pesticide active and other ingredients) may have an effect in humans or wildlife similar to an effect produced by a "naturally occurring estrogen, or other such endocrine effects as the Administrator may designate."

EPA has developed the EDSP to determine whether certain substances (including pesticide active and other ingredients) may have an effect in humans or wildlife similar to an effect produced by a "naturally occurring estrogen, or other such endocrine effects as the Administrator may designate." The EDSP employs a two-tiered approach to making the statutorily required determinations. 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 (E, A, or T) hormonal systems. Chemicals that go through Tier 1 screening and are found to have the potential to interact with E, A, or T hormonal systems will proceed to the next stage of the EDSP where EPA will determine which, if any, of the Tier 2 tests are necessary based on the available data. Tier 2 testing is designed to identify any adverse endocrine-related effects

caused by the substance, and establish a dose-response relationship between the dose and the E, A, or T effect.

Under FFDCA section 408(p), the Agency must screen all pesticide chemicals. Between October 2009 and February 2012, EPA issued test orders/data call-ins for the first group of 67 chemicals, which contains 58 pesticide active ingredients and 9 inert ingredients. The Agency has reviewed all of the assay data received for the List 1 chemicals and the conclusions of those reviews are available in the chemical-specific public dockets. A second list of chemicals identified for EDSP screening was published on June 14, 2013[2] and includes some pesticides scheduled for registration review and chemicals found in water. Neither of these lists should be construed as a list of known or likely endocrine disruptors. Methyl anthranilate is not on either list. For further information on the status of the EDSP, the policies and procedures, the lists of chemicals, future lists, the test guidelines and the Tier 1 screening battery, please visit our website.[3]

Additionally, FFDCA section 408(p)(4) authorizes the Administrator, by order, to exempt from the requirements of the Estrogenic Substances Screening Program a biologic substance or other substance if a determination is made that the substance is not anticipated to produce any effect in humans similar to an effect produced by a naturally occurring estrogenic substance.

In this proposed interim decision, the Agency is making no human health or environmental safety findings associated with the EDSP screening of methyl anthranilate. Before completing this registration review, the Agency will make an EDSP FFDCA section 408(p) determination.

D. Benefits Assessment

By definition, biochemical pesticides are naturally-occurring substances (or substances structurally-similar and functionally identical to naturally-occurring substances) with a history of exposure to humans and the environment demonstrating minimal toxicity. Benefits of biochemical pesticides, such as methyl anthranilate, as compared to conventional pesticides typically include lower toxicity profiles for humans and nontarget organisms, and faster degradation in the environment.

IV. Proposed Interim Registration Review Decision

In accordance with 40 CFR §155.56 and 155.58, the Agency is issuing this *Proposed Interim Registration Review Decision*. Except for the EDSP component of this case, the Agency has made the following Proposed Interim Decision: (1) no additional data are required at this time; and (2) no changes to the affected registrations and their labels are needed at this time. In this proposed interim decision, the Agency is making no human health or environmental safety findings associated with the EDSP screening of methyl anthranilate. The Agency's final registration review decision for methyl anthranilate will be made following completion of an EDSP FFDCA §408(p) determination.

[2] See www.regulations.gov/#!documentDetail;D=EPA-HQ-OPPT-2009-0477-0074 for the final second list of chemicals.
[3] www.epa.gov/endo/

V. Next Steps and Timeline

In accordance with 40 CFR § 155.56 and 155.58, the Agency is issuing this *Proposed Interim Registration Review Decision* for Methyl Anthranilate (Case 6056), and posting it in the methyl anthranilate registration review docket (EPA-HQ-OPP-2011-0678). A Federal Register Notice will announce a 60-day comment period for this *Proposed Interim Registration Review Decision*. The Agency's final decision on the methyl anthranilate registration review case will occur following an EDSP FFDCA §408(p) determination.

Activities	Estimated Month/Year*
Opening the Docket/Case Development	
Open Docket and 60-Day Public Comment Period for Methyl Anthranilate	September 2011
Close Public Comment Period	November, 2011
Issue Final Work Plan	February 2018
Proposed Interim and Final Registration Review Decision	
Open 60-Day Public Comment Period for Proposed Interim Registration Review Decision	September 2018
Close Public Comment Period	November 2018
Interim Registration Review Decision	March 2019
Final Decision	TBD

* This schedule is subject to revision should unforeseen issues arise during the registration review process. In the event an issue arises, such as the failure to acquire an EDSP exemption, an amended Final Work Plan will be issued at that time that will set forth a new timeline and, if applicable, any new data requirements will be included in the amended document and a Data Call-In Notice will be issued.

References

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U.S. EPA, 1994. SAB review of the product chemistry, toxicology, summary information, and toxicology and residue chemistry waivers submitted for the registration of technical methyl anthranilate and an end-use product, "Bird Shield Repellent." Product chemistry (Case# 008125; Chemical # 128725; Submission # S455617; DP barcode D197915). Memorandum from S. K. Reilly to R. Forrest, dated 11/17/1994. https://www3.epa.gov/pesticides/chem_search/cleared_reviews/csr_PC-128725_17-Nov-94_017.pdf

U.S. EPA, 2011a. Methyl Anthranilate Preliminary Work Plan and Summary Document, September 20, 2011. https://www.regulations.gov/document?D=EPA-HQ-OPP-2011-0678-0007

U.S. EPA, 2011b. Non-target Organism and Endangered Species Screening Risk Assessment for the Methyl Anthranilate (Benzoic Acid, 2-Amino, Methyl Ester) Registration Review Preliminary Work Plan from Russell Jones to Chris Pfeifer. Dated August 24, 2011. https://www.regulations.gov/document?D=EPA-HQ-OPP-2011-0678-0002

White, J. W. and V. M. Bryant. 1996. Assessing Citrus Honey Quality: Pollen and Methyl Anthranilate Content. Journal of Agricultural and Food Chemistry, 1996, 44 (11), pp 3423–3425.