UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

MEMORANDUM

SUBJECT: Registration Review Scoping Document for Fatty Acid Monoesters Case No. 6016. (PC Codes: 082074, 011288), (CAS Nos. 27194-74-7, 68332-79-6)

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I. Executive Summary

The Risk Assessment Branch (RAB) has completed this scoping document for the product chemistry, human health risk, and ecological risk of fatty acid monoesters (FAMs) for registration review. This document specifically addresses the fatty acid monoesters propylene glycol monolaurate and propylene glycol monocaprylate as they are the only FAM active ingredients that are currently in registered pesticide products. This document describes the data on fatty acid monoesters that are available within the databases of the U.S. Environmental Protection Agency (EPA), as well as any additional data found in the public literature that are relevant to human health or ecological risk assessment and adverse incidents that have been reported to the EPA. This scoping document also describes the current state of knowledge regarding human health and ecological risks and describes data and/or new risk analyses that may be needed, if any.

The fatty acid monoesters were first registered as a pesticide in 2003 as manufacturing-use products (MPs). The Agency did not complete a Reregistration Eligibility Decision (RED) for fatty acid monoesters because the first product was registered after 1984.

Glycerol fatty acid monoesters occur naturally in vegetable oils and the propylene glycol fatty acid monoesters are approved for use as direct food additives by the Food and Drug Administration (FDA) under 21 CFR 172.856. Propylene glycol alone and monoglycerides (glycerol fatty acid esters) are considered by FDA to be Generally-Recognized-As-Safe (GRAS) direct food additives when used according to the conditions specified under 21 CFR 184.1666 and 184.1505, respectively

Since the previous registration review decision, no additional assessments have been performed. Based on the review of the data available and these previous risk assessments, the RAB makes the following conclusions for FAMs regarding completeness of the database, human health risk, and ecological risk:

- All product chemistry data requirements have been met and the data provided are acceptable. These data support the registration review of FAMs.
- All mammalian toxicology data requirements have been met and the data provided are acceptable for FAMs. Toxicity studies are available for manufacturing use products or products consisting principally of propylene glycol monolaurate or propylene glycol monocaprylate. Mammalian acute toxicity data requirements have been fulfilled for both propylene glycol monolaurate and propylene glycol monocaprylate and subchronic data requirements or waivers are available for propylene glycol monocaprylate and have been bridged to propylene glycol monolaurate due to their substantial chemical, structural and functional similarity. These data support the registration review of FAMs. Human health risks have been assessed and no risks of concern are anticipated as a result of the current labeled uses of FAMs.
- All nontarget organism data requirements have been met and the data provided are acceptable for propylene glycol monolaurate. Nontarget organism studies are available for manufacturing use products or products consisting principally of propylene glycol monolaurate. Nontarget organism data for propylene glycol monocaprylate have been bridged from propylene glycol monolaurate due to their substantial chemical, structural and functional similarity. These data support the registration review of FAMs. Nontarget organism risks have been assessed and no risks of concern are anticipated as a result of the current labeled uses of FAMs. Additionally, a "no effect" determination is made for direct and indirect effects to federally listed threatened and endangered species and their designated critical habitat for such species.

II. Registration Review Case Overview

Propylene glycol monolaurate (dodecanoic acid, monoester with 1,2- propanediol) and propylene glycol monocaprylate (octanoic acid, monoester with 1,2-propanediol) belong to the family of chemicals commonly referred to as fatty acid monoesters (FAMs). Propylene glycol fatty acid monoesters are synthetically manufactured but are structurally similar and functionally identical to glycerol fatty acid monoesters that occur naturally in all living organisms. All FAMs have been found to display similar toxicity and are metabolized by the same metabolic pathways (US EPA, 2017-0353-002). Studies with propylene glycol show that it is readily absorbed from the gastrointestinal tract and rapidly converted in the liver to glycogen or carbon dioxide (CO_2). Studies with glycerol show that it is metabolized into expired CO_2, blood glucose, liver fat, glycogen and phosphatides within 15 minutes (Federal Register, 2004; US EPA, 2017-0353-002). Biopesticide products containing fatty acid monoesters as active ingredients are registered as fungicides, bacteriocides, and miticides for use on food crops (pre-harvest to protect against mites and post-harvest to prevent microbial damage during storage) and ornamentals. Furthermore, polyglycerol esters of fatty acids are approved by the Food and Drug Administration (FDA) for use in/on food and feed in accordance with the conditions described in the regulation (21 C.F.R. 172.854). Fatty Acid Monoesters with Glycerol or Propanediol are exempt from the requirements of tolerances under 40 CFR §180.1250.

Table 1 Active ingredient identification for Fatty Acid Monoesters (Case No. 6016)

Chemical Name	Results	
Common Name	Propylene glycol monolaurate	Propylene glycol monocaprylate
Chemical Name	Propylene glycol monolaurate	Octanoic acid, ester with 1,2-propanediol
IUPAC Name	2-hydroxypropyl dodecanoate	2-hydroxypropyl octanoate
Molecular formula	$C_{15}H_{30}O_3$	$C_{11}H_{22}O_3$
Molecular Weight	258.40g·mol^{-1}	202.29 g·mol^{-1}
CAS Number	27194-74-7	68332-79-6
PC Code	011288	082074
First registered in US	09/30/2003	09/30/2003
Use Sites: **Agricultural Use Sites:** **Non-agricultural Use Sites:**	Ag sites: Food/non-food crops Non-ag sites: Ornamentals	Post-harvest fruits and vegetable Antimicrobial use patterns
Target Pests:	Miticide: mites Post-harvest bacteria/fungi: erwinia, fusarium, soil-borne fungal diseases	Fungi or bacteria that cause decay of post-harvest fruits and vegetables
End-Use Formulation Types	Liquid concentrate, soluble concentrate	No registered EPs
Application Methods	Dunking crop for post-harvest bacteria/fungal control Foliar spray	No registered EPs
Mechanism(s) of action	Membrane disruptor	Membrane disruptor
First registered in US	09/30/2003	09/30/2003
BPPD Registered Products	See Table 2 for details	

Table 2. Biopesticide Products Containing Fatty Acid Monoesters

Chemical Name	Registration #	Product Name	Company Name	Percent Active Ingredients (%)	Date of Registration
Propylene glycol monolaurate	10350-67 (MP)	VWX-42 Technology Propylene Glycol Monolaurate	3M	75.85	09/30/2003
	11581-3 (EP)	Acaritouch	Oat Agrio Co., LTD	70.81	10/12/2004
Propylene glycol monocaprylate	10350-527 (MP)	Propylene Glycol Monocaprylate	3M	97.18	11/14/2013

There is currently one product registered with BPPD for outdoor (agricultural) use for which nontarget organism data requirements have been addressed (Acaritouch®; EPA Reg. No. 11581-3). While all the other BPPD registered products are MPs, their instructions allow for the formulation of EPs for both indoor and outdoor uses. If registrants submit outdoor use EPs, these data requirements would need to be addressed. However, all FAMs are considered structurally similar and functionally identical to one another. Therefore, information submitted for one FAM is used to support all FAMs, and the conclusions for Acaritouch® could be applied to all FAMs (U.S. EPA, 2019).

Tolerance(s) or Tolerance Exemption: The active ingredients in this registration review case are associated with the following tolerance exemption:

40 CFR §180.1250 C8, C10, and C12 fatty acid monoesters of glycerol and propylene glycol; exemption from the requirement of a tolerance.

The C8, C10, and C12 straight-chain fatty acid monoesters of glycerol (glycerol monocaprylate, glycerol monocaprate, and glycerol monolaurate) and propylene glycol (propylene glycol monocaprylate, propylene glycol monocaprate, and propylene glycol monolaurate) are exempt from the requirement of a tolerance in or on all food commodities when used in accordance with approved label rates and good agricultural practice. [69 FR 34944, June 23, 2004]

Previous Registration Eligibility Decision (RED), Biopesticide Registration Action Document (BRAD) or Previous Reg. Review Docket: The following registration, reregistration, and registration review documents are associated with the active ingredients in this registration review case.

The fatty acid monoesters were first registered as a pesticide in 2003 as manufacturing-use products (MPs). The Agency did not complete a Reregistration Eligibility Decision (RED) for fatty acid monoesters because the first product was registered after 1984.

On June 23, 2004, EPA published a FRN to establish an exemption from the requirement of a tolerance for the fatty acid monoesters, and to eliminate the requirement of a tolerance for the fatty acid monoesters of glycol and propylene glycol (Federal Register, 2004).

On September 21, 2005, EPA published a FRN to modify the previous tolerance exemption dated June 23, 2004, in order to amend the existing tolerance exemption to allow post-harvest uses of fatty acid monoesters of glycol and propylene glycol (EPA-OPP-2004-0344; FRL-7719-7).

The C8, C10, and C12 straight – chain fatty acid monoesters of glycerol (glycerol monocaprylate, glycerol monocaprate, and glycerol monolaurate) and propylene glycol (propylene glycol monocaprylate, propylene glycol monocaprate, and propylene glycol monolaurate) are exempt from the requirement of a tolerance in or on all food commodities when used in accordance with approved label rates and good agricultural practice (Federal Register, 2004).

A previous registration review docket was established on December 26, 2017 in docket number EPA-HQ-OPP-2017-0353 with the publication of the Fatty Acid Monoesters Preliminary Work Plan (PWP) (U.S. EPA, 2017). Additional assessments have been performed for proplyene glycol monolaurate and propylene glycol monocaprylate including, updated waivers for non-target terrestrial plant data (U.S. EPA, 2018) and an updated risk assessment for non-target organisms and environmental fate (U.S. EPA, 2019). In February 2020, the Agency issued the Fatty Acid Monoesters Combined Final Work Plan (FWP) and Proposed Interim Registration Review Decision (U.S. EPA, 2019 - FWP). The combined FWP and PID confirmed the most recent risk assessments still supported the registration of all pesticide products containing fatty acid monoesters and no additional data were anticipated. With no public comments received on the combined FWP and PID, the Agency issued the Fatty Acid Monoesters Interim Registration Review Decision (U.S. EPA, 2020) in June 2020. The FAMs discussed here were initially registered under FIFRA as manufacturing-use products (MPs) on September 30, 2003, by 3M Corporation (April 14, 2004; FRL-7352-4).

New uses since last Registration Review Decision: There are no new uses since the previous Interim Registration Review Decision in 2020.

III. Summary of Existing Product Analysis Data

The available product chemistry data for the Fatty Acid Monoesters are acceptable to support the current registration review. The current product chemistry data requirements (Group A and Group B) and results supporting registration are summarized in Tables 3 and 4 based on product data requirements in 40 CFR 158.2030.

Table 3. Product Chemistry Data for Fatty Acid Monoesters (Group A)

Data Requirement	Guideline Number	MRID PC Code: 011288	MRID PC Code: 082074
Product Identity and Composition	880.1100	45405401; 45852401; 49443901	45405401; 48838301
Description of Starting Materials, Production, and Formulation Process	880.1200	45405401; 45852401; 49443901	45405401; 48838301
Discussion of Formation of Impurities	880.1400	45405401; 45852401; 49443901	45405401; 48838301
Preliminary Analysis	830.1700	45405501; 45852401; 49443901	45405501; 48838302; 48838306

Data Requirement	Guideline Number	MRID PC Code: 011288	MRID PC Code: 082074
Certified Limits	830.1750	45405501; 45852401	45405501; 48838301
Enforcement Analytical Method	830.1800	45405504; 45852401; 49443903	45405504; 48838307

Physical and Chemical Properties

Acceptable physical and chemical properties for the fatty acid monoesters in support of registration review are summarized in Table 4. The are no data gaps based on product data requirements in 40 CFR 158.2030. There are no reported impurities of toxicological concern.

Table 4. Data of Physical and Chemical Properties for Fatty Acid Monoesters (Group B)

Guideline No./Data Requirement	Result/ MRID PC Code: 011288	Result/ MRID PC Code: 082074
830.6302-Color	Pale yellow (MRID 45852401) (MRID 49443902)	Clear (MRID 45405502) (MRID 48838303)
830.6303-Physical State/	Liquid (MRID 45852401) (MRID 49443902)	Oily liquid (MRID 45405502) (MRID 48838301)
830.6304-Odor	Cooking oil odor (MRID 45852401) (MRID 49443902)	Cooking oil odor (MRID 45405502) (MRID 48838301)
830.6313-Stability to Normal and Elevated Temperatures, Metals and Metal Ions	Stable to metals, decomposition starts at 200°C (MRID 45852401)	Stable at 54°C for up to 14 days; not anticipated to come into contact with metals or metal ions during storage. (MRID 45405503) (MRID 48838301)
830.6317-Storage Stability	Not required for a TGAI	Not required for a TGAI
830.6319-Miscibility	Not required for a TGAI	Not required for a TGAI
830.6320-Corrosion Characteristics	Not required for a TGAI	Not required for a TGAI
830.7000-pH	5.9 (1% solution TGAI) (MRID 45852401)	5.0 ± 0.3 at 23°C (MRID 48838303)
830.7050-UV/Visible Light Absorption	A_{max} 210 nm [Ɛ 64.78] (MRID 45852401) (MRID 45852402)	Data for PC Code 011288 can be used to support the data requirement for this PC Code

Guideline No./Data Requirement	Result/ MRID PC Code: 011288	Result/ MRID PC Code: 082074
830.7100-Viscosity	Not required for a TGAI	11.3 cP at 24.9° C (MRID 48838303)
830.7200-Melting Point	8.3°C (MRID 45852401) (MRID 45852402)	Not required: not a solid
830.7220-Boiling Point	246.6°C (MRID 45852401) (MRID 45852402) 138-141°C at 0.6 torr (MRID 49443902)	280°C (MRID 45405502) 267.6°C (MRID 48838303)
830.7300-Density/ Relative Density/Bulk Density (Specific Gravity)/	0.92 g/ml at 25°C (MRID 45852401) 0.905-0.915 g/ml (MRID 49443902)	0.9318 g/cm^3 at 27°C (MRID 45405502) 0.9374 g/ml at 23°C (MRID 48838303)
830.7520-Particle Size, Fiber Length, and Diameter Distribution/	Not required: not a water insoluble and fibrous substance	Not required: not a water insoluble and fibrous substance
830.7550 830.7560 830.7570 Partition Coefficient (n-Octanol Water)	log P = 4.83*	log P = 3.35*
830.7840-Water Solubility/	4 mg/l; Practically insoluble (MRID 45852401) (MRID 45852402) (MRID 49443902)	82 mg/l at 23°C (MRID 48838303)
830.7950-Vapor Pressure/	0.162 Pa or 1.2 x 10-3 mg Hg at 25°C (MRID 45852401) (MRID 45852402)	4.1 x 10-3 mm Hg at 20°C; 7.0 x 10-2 mm Hg at 55°C (MRID 48838303)

*Value obtained using EPA's Chemistry Dashboard: https://comptox.epa.gov/dashboard//

IV. Summary of Existing Mammalian Toxicology Data

Fatty Acid Monoesters (Propylene Glycol Monolaurate and Propylene Glycol Monocaprylate)

The database of submitted toxicity studies and published literature is sufficient to assess the uses of propylene glycol monolaurate and propylene glycol monocaprylate. Summaries of acute and subchronic toxicity data and subchronic toxicity data waiver rationales are provided in Tables 5 and 6 and in the following text. The available toxicity databases for these active ingredients consist of acute toxicity,

acute irritation, dermal sensitization and subchronic oral toxicity studies. Although not all toxicity studies are available for propylene glycol monolaurate, data have been bridged from propylene glycol monocaprylate based on the substantial chemical, structural and functional similarity of these substances. Data waivers for the subchronic dermal and inhalation toxicity, developmental toxicity and genotoxicity data requirements were originally granted by the Agency in 2003 (US EPA, 2003a; Federal Register, 2004; US EPA 2003b). The subchronic toxicity data waivers were based on the following: 1) humans have long been exposed to the fatty acid monoesters in the diet. Glycerol fatty acid monoesters occur naturally in vegetable oils and the propylene glycol fatty acid monoesters are approved for use as direct food additives by the Food and Drug Administration (FDA) under 21 CFR 172.856. Propylene glycol alone and monoglycerides (glycerol fatty acid esters) are considered by FDA to be Generally-Recognized-As-Safe (GRAS) direct food additives when used according to the conditions specified under 21 CFR 184.1666 and 184.1505, respectively; 2) humans are exposed dermally to the substances as they are used in a variety of personal care products, such as make-up, shampoos and conditioners, lotions, and cleansers (MRID 49016301; MRID 49443902); 3) no adverse effects have been reported from exposure to these substances; 4) the substances are rapidly metabolized in vertebrate systems to polyols and free fatty acids. Upon ingestion, the substances become indistinguishable from those substances already present in living systems; 5) appropriate personal protective equipment (PPE) requirements on the label will mitigate exposure to applicators/handlers; and 6) the available toxicity data indicate no adverse effects.

With regard to the available toxicity information, acute toxicity studies indicate that fatty acid monoesters are of low oral, dermal and inhalation toxicity (Toxicity Category IV). Eye irritation studies revealed slight to mild irritation in rabbits (Toxicity Category III-IV) and dermal irritation studies revealed mild irritation in rabbits (Toxicity Category IV). The available data suggest that propylene glycol monocaprylate is a potential skin sensitizer (these data have been bridged to the other propylene glycol monoesters) and that propylene glycerol monolaurate is not a skin sensitizer (these data have been bridged to the other glycerol monoesters). A guideline 90-day oral toxicity study in the rat conducted using propylene glycol monocaprylate showed no adverse effects up to and including the limit dose of 650 mg/kg/day.

While no developmental and genotoxicity data have been submitted to the Agency for the active ingredients, there are assessments and information available on the constituents of the substances. The reproductive and developmental effects of propylene glycol were evaluated by the National Toxicology Program in 2004 and it was determined that “there is negligible concern for adverse developmental or reproductive toxicity from propylene glycol exposures in humans”. From a metabolic perspective, fatty acid monoesters and their natural metabolites/degradates are not known to be reproductive or developmental toxicants. There is no evidence of special sensitivity in infants or children. There is no evidence available indicating that these substances are of mutagenic or genotoxic concern (US EPA, 2015).

Glycerol fatty acid monoesters are natural components of dietary fats and natural breakdown products from the metabolism of fat (triacylglycerol) in all living systems. The propylene glycol monoesters are metabolized in such systems by the same pathways. Glycerol and propylene glycol monoesters are almost identical metabolically, as demonstrated by a substantial list of published studies. The particular fatty acid moiety is inconsequential, because vertebrate systems are capable of metabolizing each of the acids in the range of C8 to C18 (the active ingredients are the C8, C10, and C12 straight-chain fatty acid monoesters of glycerol and propylene glycol) with equal facility. The glycerol monoesters are indistinguishable from the natural acylglycerols and fatty acids found in the intestines after the ingestion of fats. Studies with propylene glycol show that it is readily absorbed from

the gastrointestinal tract and rapidly converted in the liver to glycogen or CO_2, blood glucose, liver fat, glycogen and phosphatides within 15 minutes (Federal Register 2004; MRID 49016301; MRID 49443902). For the reasons discussed above, the Agency has concluded that the available toxicology data can be used to represent all of the fatty acid monoesters, where applicable.

There is a long history of consumption and use in personal care products of the fatty acid monoesters and the Agency is unaware of any instances of toxic effects from exposure to these substances.

No additional useful information was found in a search of the National Library of Medicine's Toxicology Data Network[1] and the RapidTox[2] database. Comprehensive reviews from the Food and Drug Administration (FDA), the Cosmetic Ingredient Review Expert Panel (CIR) and the Joint Food and Agricultural Organization of the United Nations (FAO)/World Health Organization (WHO) Expert Committee on Food Additives (JECFA) are available, and no risks have been identified.[4,5,6]

Because no adverse effects have been observed in the available studies, a quantitative risk assessment was not conducted for the fatty acid monoesters. The Agency considers its previous assessment to be sufficient and has determined that a qualitative risk assessment is appropriate for the pesticidal uses. The dietary, residential, and occupational exposure qualitative risk assessment is discussed below.

Dietary, Residential and Occupational Exposure and Risk Assessment

The Agency does not anticipate any dietary (food and drinking water) risks because of the following: 1) a lack of toxicity: no adverse effects have been identified in the available toxicity studies, particularly the 90-day oral toxicity study; 2) humans have long been exposed to the fatty acid monoesters in the diet. Glycerol fatty acid monoesters occur naturally in vegetable oils and both types of fatty acid monoesters (glycerol and propylene glycol) are approved for use as direct food additives by the Food and Drug Administration (FDA) under 21 CFR 172.856; 3) the substances are rapidly metabolized in vertebrate systems to polyols and free fatty acids. Upon ingestion, the substances become indistinguishable from those substances already present in living systems. Glycerol and propylene glycol monoesters are almost identical metabolically; and 3) no adverse effects have been reported from dietary exposures to these substances.

There is potential for residential and/or occupational dermal and inhalation exposure to the fatty acid monoesters. Due to the lack of toxicity, a quantitative occupational risk assessment for exposure was not conducted. Therefore, the Agency conducted a qualitative assessment. EPA has concluded that occupational and residential risks to these active ingredients are negligible and not of concern. In addition, agricultural use of the pesticide is subject to the Worker Protection Standards (WPS); personal protective equipment (PPE) is required on labels: a long-sleeved shirt, long pants, shoes, socks and waterproof gloves; and a 4-hour Restricted Entry Interval (REI) is also required.

Table 5. Summary of the current toxicology data requirements (40 CFR § 158.2140) supporting registration of Propylene Glycol Monolaurate (PC Code 011288) in this case.

Data Requirement	OCSPP Guideline No.	MRID No(s).	Do Existing Data Support Registration Review? (Results / Findings)
Acute Oral Toxicity (rat)	870.1100	45852403	Acceptable – Category IV LD_{50} > 40,000 mg/kg

[1] PubChem. August 2021. https://pubchem.ncbi.nlm.nih.gov/
[1] TOXNET. August 2021. TOXLINE in PubMed
[2] RapidTox. August 2021. https://comptox.epa.gov/dashboard.

Data Requirement	OCSPP Guideline No.	MRID No(s).	Do Existing Data Support Registration Review? (Results / Findings)
Acute Dermal Toxicity (rat)	870.1200	45428503	Acceptable Data bridged from PC Code 082074 based on chemical similarity
Acute Inhalation Toxicity (rat)	870.1300	45405506	Acceptable Data bridged from PC Code 082074 based on chemical similarity
Primary Eye Irritation (rabbit)	870.2400	45852404	Acceptable Mildly irritating
Primary Dermal Irritation (rabbit)	870.2500	45852405	Acceptable Mildly irritating
Skin Sensitization	870.2600	45448201	Acceptable Data bridged from PC Code 082074 based on chemical similarity
90-Day Oral Toxicity	870.3100	45428505	Acceptable Data bridged from PC Code 082074 based on chemical similarity
90-Day Dermal Toxicity	870.3250	48838304 48838305 49016301 49016303 49526401	Waived
90-Day Inhalation Toxicity	870.3465	48838304 48838305 49016301 49016303 49526401	Waived
Prenatal Developmental Toxicity	870.3700	48838304 48838305 49016301 49016303	Waived
Bacterial Reverse Mutation Test	870.5100	48838304 48838305 49016301 49016303 49526401	Waived
In vitro Mammalian Cell Assay	870.5300 870.5375	48838304 48838305 49016301 49016303 49526401	Waived

Table 6. Summary of the current toxicology data requirements (40 CFR § 158.2140) supporting registration of Propylene Glycol Monocaprylate (PC Code 082074) in this case.

Data Requirement	OCSPP Guideline No.	MRID No(s).	Do Existing Data Support Registration Review? (Results / Findings)
Acute Oral Toxicity (rat)	870.1100	45428501	Acceptable – Category IV LD_{50} > 5,000 mg/kg
Acute Dermal Toxicity (rat)	870.1200	45428503	Acceptable – Category IV LD_{50} > 5,000 mg/kg
Acute Inhalation Toxicity (rat)	870.1300	45405506	Acceptable – Category IV LC_{50} > 4.92 mg/L
Primary Eye Irritation (rabbit)	870.2400	45405509	Acceptable Slightly irritating
Primary Dermal Irritation (rabbit)	870.2500	45405511	Acceptable Mildly irritating
Skin Sensitization	870.2600	45448201	Acceptable Potential sensitizer
90-Day Oral Toxicity	870.3100	45428505 45441101	Acceptable NOAEL ≥ 650 mg/kg/day[1]
90-Day Dermal Toxicity	870.3250	48838304 48838305 49016301 49016303 49526401	Waived
90-Day Inhalation Toxicity	870.3465	48838304 48838305 49016301 49016303 49526401	Waived
Prenatal Developmental Toxicity	870.3700	48838304 48838305 49016301 49016303	Waived
Bacterial Reverse Mutation Test	870.5100	48838304 48838305 49016301 49016303 49526401	Waived
In vitro Mammalian Cell Assay	870.5300 870.5375	48838304 48838305 49016301 49016303 49526401	Waived

[1] In a 90-day (MRID 45428505) and 28-day oral toxicity study for propylene glycol monocaprylate, the highest dose tested (HDT) was 1,000 mg/kg/day of a 65% active ingredient solution. There were no adverse effects noted so the highest reportable NOAEL is ≥ 650 mg/kg/day.

V. Summary of Existing Non-Target Organism and Environmental Fate Data

Fatty Acid Monoesters Propylene Glycol Monolaurate and Propylene Glycol Monocaprylate

There is currently one product registered with BPPD for outdoor (agricultural) use for which nontarget organism data requirements have been addressed (Acaritouch®; EPA Reg. No. 11581-3). While all the other BPPD registered products are MPs, their instructions allow for the formulation of EPs for both indoor and outdoor uses. If registrants submit outdoor use EPs, these data requirements would need to be addressed. However, all FAMs are considered structurally similar and functionally identical to one another. Therefore, information submitted for one FAM is used to support all FAMs, and the conclusions for Acaritouch® could be applied to all FAMs (U.S. EPA, 2019).

Acaritouch® contains 70.81% propylene glycol monolaurate (PC Code: 011288) as its active ingredient. Acute toxicity data for freshwater fish, aquatic invertebrates, nontarget insects and algae are available and were conducted using this chemical as the test substance. In lieu of guideline studies for the avian toxicity and terrestrial plant toxicity studies, requests for waivers with supporting rationales were submitted to satisfy the data requirements (US EPA, 2003b). An August, 2021 search of EPA's ECOTOXicology[3] did not reveal any nontarget organism toxicity data for propylene glycol monolaurate (PGML). The toxicity data and waiver rationales are summarized in Table 7 and in the following text.

The available toxicity data indicate that PGML is moderately toxic to fish and algae, highly toxic to aquatic invertebrates, and practically nontoxic to nontarget insects (bees and predatory mites).

Data waiver rationales were submitted for the avian acute oral and dietary toxicity data requirements and are acceptable. The information provided was based on the ability of birds to metabolize propylene glycol fatty acid monoesters into innocuous substances via the same metabolic pathways present in mammals, as previously discussed in this document. Additionally, propylene glycol has extremely low toxicity to birds, and is even recommended for use as a vehicle for test substance suspension in the OCSPP guideline study for avian oral toxicity (OCSPP 850.2100). Based on the information above, toxicity to avian species from exposure to PGML is not anticipated.

Data waiver rationales were submitted for the terrestrial plant toxicity seedling emergence and vegetative vigor data requirements and are acceptable. In lieu of guideline studies, the registrant submitted a compendium of 18 product performance studies conducted between the years 2000 through 2006 on the following crops: pome fruits (3); cucurbits (1); grapes (3); stone fruit (1); nut crops (3); berries (2); fruiting vegetables (1); hops (2); and cereals (1). All studies were conducted using Acaritouch® according to EPA-approved label use directions. Phytotoxicity was not observed or mentioned in any of the studies. Although none of the studies provided information to specifically address seedling emergence and seedling vigor, the weight-of-evidence from other technical sources indicate that there is little concern for adverse effects on seedlings and seedling vigor following application of Acaritouch®. First, a search of OPP's Ecological Incident Information System (EIIS) version 2.1.1 conducted on August 23, 2021, revealed no ecological incidents associated with the fatty acid monoesters; this database contains information dating back to the 1970s and was most recently updated 08/23/2021 (EPA, 2019). Second, a USDA evaluation of Propylene Glycol Monolaurate (USDA, 2012) did not express any concerns for phytotoxicity and cited a report by Heaton (2003) to the

[3] ECOTOX. August 2021. https://cfpub.epa.gov/ecotox/.

California Department of Pesticide Regulation that Propylene Glycol Monolaurate was "Negative" for phytotoxicity.

Environmental Fate Profile

Some environmental fate information is available for PGML; this information was reviewed in the Antimicrobials Division (US EPA, 2015). Propylene glycol monolaurate is not expected to hydrolyze or degrade by photolysis, but it is expected to partition to sediment. Based on results from a Level III Fugacity Model, 69.2% of PGML is expected to partition into soil. The environmental fate estimation program developed by EPA and Syracuse Research Corp. (Estimation Programs Interface Suite [EPI Suite]) predicted half-lives of PGML to be 30 days in soil/sediment and 15 days in water. These data will be used to inform the risk assessment.

Threatened/Endangered Species

The Agency has prepared a risk assessment that supports a complete endangered species determination for the fatty acid monoesters case. Based upon the results of toxicity tests, rapid degradation in the environment, and the low potential for exposure, adverse effects to terrestrial and aquatic organisms are expected to be negligible (U.S. EPA, 2019). Therefore, EPA has reached a "No Effect" determination, either direct or indirect, on threatened or endangered terrestrial and aquatic animal species, or on any designated critical habitat, as listed by the U.S. Fish and Wildlife Service and the National Marine Fisheries Service. As a result, the Agency has concluded that consultation with the U.S. Fish and Wildlife Service and the National Marine Fisheries Service under the Endangered Species Act (ESA) section 7 (a)(2) is not required (U.S. EPA, 2019).

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.

Table 7. Summary of the current non-target organism data requirements (40 CFR § 158.2150) supporting registration of Propylene Glycol Monolaurate (PC Code 011288) in this case.

Data Requirement	OCSPP Guideline No.	MRID No(s).	Do Existing Data Support Registration Review? (Results / Findings)
Avian Acute Oral Toxicity	850.2100	No MRID[2]	Acceptable Waived based on lack of toxicity and known metabolism into innocuous substances.
Avian Dietary Toxicity	850.2200	No MRID[2]	Acceptable Waived based on lack of toxicity and known metabolism into innocuous substances.
Fish Acute Toxicity, Freshwater	850.1075	45852412	Acceptable 96-hour LC_{50} = 4.8 mg/l NOEC = 3.80 mg/l Moderately toxic
Aquatic Invertebrate Acute Toxicity, Freshwater	850.1010	45852413	Acceptable 48-hour EC_{50} = 0.52 mg/l NOEC = 0.18 mg/l Highly toxic
Terrestrial Plant Toxicity, Seedling Emergence	850.4100	50555801	Waived based on lack of observed toxicity in 18 field efficacy trials at the maximum label rate and known metabolism into innocuous substances.

Data Requirement	OCSPP Guideline No.	MRID No(s).	Do Existing Data Support Registration Review? (Results / Findings)
Terrestrial Plant Toxicity, Vegetative Vigor	850.4150	50555801	Waived based on lack of observed toxicity in 18 field efficacy trials at the maximum label rate and known metabolism into innocuous substances.
Nontarget Insect Testing	880.4350	45852415[3] 45852416[3]	Acceptable Honey bee (*Apis mellifera*): 48-hour LD_{50} > 66 to <132 µg a.i./bee Predatory mite (*Phytoseiulus persimilis*): No apparent effects on mites at application rates of up to 10.5 mg a.i./6-8 mites. Eggs exposed to same application rate had survival rates of up to 96.4%. Practically nontoxic
Algal Toxicity	850.4500[1]	45852417	Growth rate inhibition: 72-hour EC_{50} = 1.99 mg/l 72-hour NOEC = 0.44 mg/l 24 to 48-hour EC_{50} = 4.72 mg/l 24 to 72-hour EC_{50} = 5.11 mg/l 24 to 48-hour NOEC = 2.13 mg/l 24 to 72-hour NOEC = 2.13 mg/l Moderately toxic

[1] The algal growth inhibition study is not a BPPD or AD data requirement.
[2] Waivers were provided in a document entitled "Volume 70231-E-17 Request for Waivers of Specific Data Requirements. The waivers were discussed in the memorandum from Jones, Russell S. to Frazer, Carol. Science Review in Support of the Registration of Acaritouch (EPA File Symbol No. 70231-E). September 29, 2003.
[3]The honeybee and predatory mite acute contact toxicity studies were conducted using the EP (Acaritouch); the amount of the active ingredient in each dose was calculated and estimated by the reviewers.

VI. Literature Search Findings and Adverse Incidents

To support scoping efforts for 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 fatty acid monoesters (propylene glycol monolaurate and propylene glycol monocaprylate). Searches conducted are described below.

A search of OPP's Incident Data System (IDS) from 1992 through August 23, 2021, revealed no human health incidents associated with pesticide products containing the fatty acid monoesters as the active ingredient. A search of OPP's Ecological Incident Information System (EIIS) version 2.1.1 conducted on August 23, 2021, revealed no ecological incidents associated with the fatty acid monoesters; this database contains information dating back to the 1970s and was most recently updated 08/23/2021. Four literature databases were searched, including PubChem, Researchgate, PubMed, and Google Scholar.

Search terms and results included:

	# Results / # Relevant Results in Each Database			
Search Terms	PubChem	Researchgate	PubMed	Google Scholar
"Fatty acid Monesters" AND toxicity	13 / 0	1 / 0	2 / 0	462 / 0

“Fatty acid Monesters” AND “subchronic toxicity”	0 / 0	0 / 0	0 / 0	8 / 0
“Fatty acid Monesters” AND developmental toxicity	0 / 0	0 / 0	0 / 0	9 / 0
“Fatty acid Monesters” AND mutagenicity	0 / 0	0 / 0	0 / 0	25 / 0
“Fatty acid Monesters” AND genotoxicity	0 / 0	0 / 0	0 / 0	28 / 0
“Fatty acid Monesters” AND oral toxicity	0 / 0	0 / 0	0 / 0	23 / 0
“Fatty acid Monesters” AND dermal toxicity	0 / 0	0 / 0	0 / 0	8 / 0
“Fatty acid Monesters” AND inhalation toxicity	0 / 0	0 / 0	0 / 0	3 / 0

No evidence of human health risks, concerns, or adverse effects/incidents from exposure to fatty acid monoesters were found in the literature search.

No evidence of ecological risks, concerns, or adverse effects/incidents from exposure to fatty acid monoesters were found in the literature search.

No additional information was gained from these searches that would alter the BPPD’s understanding of the current state of the science for any potential effects of fatty acid monoesters

VII. Conclusions

The BPPD reviewed data requirements for registration review pursuant to Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) section 3(g). It was determined that the data/information on file adequately satisfies current biochemical data requirements for product chemistry, mammalian toxicology, and nontarget organisms (refer to 40 CFR Subpart U § 158.2000) and that the database for Fatty Acid Monoesters (propylene glycol monolaurate and propylene glycol monocaprylate) are complete. No data gaps currently exist for these active ingredients, and literature and incident searches did not reveal any information raising new concerns such that additional data would be needed.

Adequate mammalian toxicology data/information were submitted to support registration of Fatty Acid Monoesters (propylene glycol monolaurate and propylene glycol monocaprylate). Acceptable acute toxicity guideline studies and subchronic toxicity waivers were submitted for all Tier I toxicity data requirements. New analyses to determine human health risks are not needed to support the registration review for Fatty Acid Monoesters (propylene glycol monolaurate and propylene glycol monocaprylate). Based on minimal hazard as indicated in guideline studies and/or minimal exposure, there are no dietary, residential, or occupational risks of concerns for humans. As noted above, Fatty Acid Monoesters (propylene glycol monolaurate and propylene glycol monocaprylate) are of low oral, dermal and inhalation toxicity (Toxicity Category IV). Eye irritation studies revealed slight to mild irritation in rabbits (Toxicity Category III-IV) and dermal irritation studies revealed mild irritation in rabbits (Toxicity Category IV).

Ecological effects data requirements for Fatty Acid Monoesters (propylene glycol monolaurate and propylene glycol monocaprylate) were fulfilled by acceptable guideline studies and additional data/information from the scientific literature sufficient to support data waivers for the remaining Tier I requirements. Fatty Acid Monoesters (propylene glycol monolaurate and propylene glycol

monocaprylate) are naturally occurring, rapidly metabolized, and are not expected to persist in the environment. Use of the one registered product in accordance with EPA-approved labeling would present minimal exposure to fish and aquatic invertebrates, and exposure to nontarget plants is expected to be minimal and limited to spray drift. Fatty Acid Monoesters (propylene glycol monolaurate and propylene glycol monocaprylate) are practically non-toxic to birds and nontarget insects, including pollinators. The Agency does not anticipate the need to conduct another ecological risk assessment. The single registered end-use product is used on agricultural crop plants as a miticide. The EPA is making a "No Effect" determination for Fatty Acid Monoesters (propylene glycol monolaurate and propylene glycol monocaprylate) for federally listed threatened species and their designated critical habitats.

Fatty Acid Monoesters (propylene glycol monolaurate and propylene glycol monocaprylate) were exempted from the requirements of tolerances on food under 40 CFR 180.1250 and are considered by the FDA to be a Generally-Recognized-As-Safe (GRAS) direct food additives when used according to conditions specified under 21 CFR 184.1666 and 184.1505, respectively.

When used in accordance with current labels, no risks of concern are expected to occur from the current biopesticide uses of fatty acid monoesters as labeled.

VIII. References

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