BIOPESTICIDES REGISTRATION ACTION DOCUMENT

Trimethylamine
PC Code 221801

U.S. Environmental Protection Agency
Office of Pesticide Programs
Biopesticides and Pollution Prevention Division

(Last updated May 26, 2009)

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I. EXECUTIVE SUMMARY:

Trimethylamine, a new active ingredient, is a naturally-occurring product of decomposition of plants and animals. It is the substance mainly responsible for the fishy odor associated with fouling fish, bacterial vaginal infections, and bad breath. Trimethylamine is ubiquitous in the environment at low concentrations and has fly-attracting properties because the odor suggests a food source or medium suitable for depositing fly eggs. Trimethylamine is a small nitrogen-containing molecule, is miscible in water, is a plant nutrient, and will not accumulate in the environment. It is also found in food products and is generally regarded as safe (GRAS) at a level of 0.10 ppm in soups.

With regard to toxicity, the Material Safety Data Sheet (MSDS) notes that the acute oral LD_{50} of trimethylamine is 500 mg/kg. Inhaled, trimethylamine is a sensory irritant at 61 ppm. It is also corrosive to the eyes and skin. The proposed product, Bull Run Fly Attractant, contains only 2.8% trimethylamine or under 2 grams for the largest proposed net weight for the EP. In the proposed product, trimethylamine and the other active ingredients will be enclosed in a water-soluble vapor-barrier packet that will be placed inside a fly trap. Due to the use pattern, no exposure to the active ingredient is expected.

Guideline toxicity and nontarget organism studies were not submitted in support of the registrant's application. In lieu of studies, the registrant requested data waivers from the requirements for all guideline studies and submitted a compendium of information in support of the data waivers. The registrant also provided adequate justification for waiving data requirements based on the proposed use pattern, which would result in no exposure to the active ingredient. Therefore, the Agency believes that this product containing trimethylamine can be used without causing unreasonable adverse effects to humans or the environment.

Based on data and acceptable waivers submitted by the registrant, there is no reason to believe that any non-target organisms, including honeybees and other beneficial insects, would be attracted to or adversely affected by the use of trimethylamine in a fly trap. Data submitted by the registrant indicated that only insects classified as "filth flies" were attracted to the fly trap.

Due to the negligible risk concerns resulting from lack of exposure, trimethylamine meets the criteria as specified in §3(c)(5) of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), as amended, and is thus eligible for unconditional registration. It was determined that the data/information submitted adequately satisfy current guideline requirements per 40 CFR Subpart U §158.2000.

II. ACTIVE INGREDIENT OVERVIEW

Common Name: Trimethylamine

Chemical Names: Methanamine, N,N-dimethyl-

Trade & Other Names: Dimethylmethanamine, N-Trimethylamine

CAS Registry Number: 75-50-3

OPP Chemical Code: 221801

Type of Pesticide: Biochemical pesticide, attractant

Application rates and methods vary depending on the product. For specific information regarding the product*(s)* refer to Appendix B.

III. REGULATORY BACKGROUND

On April 4, 2008, the Agency received an application from Bull Run Scientific, VBT to register trimethylamine as an active ingredient in an end-use product (EP) containing 2.8% trimethylamine. A notice of receipt of the application for registration for trimethylamine as a new active ingredient was published in the Federal Register on March 11, 2009, with a 30 day comment period. No comments were received as a result of this publication.

A. Classification

On April 15, 2008, the Biochemical Classification Committee determined that trimethylamine can be classified as a biochemical pesticide due to its non-toxic mode of action, natural occurrence in the environment, and history of exposure to humans and the environment demonstrating minimal toxicity.

B. Food Clearances/Tolerances

Currently, this active ingredient is not registered for use on food or feed commodities. A tolerance or exemption from the requirement of a tolerance is not relevant.

IV. RISK ASSESSMENT

A. Active Ingredient Characterization

The new active ingredient, trimethylamine, will be formulated as an EP for use as an attractant for filth flies. The technical grade active ingredient (TGAI) is a colorless gas at room temperature and is highly flammable. It has a fishy odor at low concentrations and a strong ammonia-like odor at higher concentrations.

The mode of action of trimethylamine is to produce fishy odors that attract filth flies seeking a food source or medium in which to deposit their eggs. As part of a water-soluble attractant insert in a disposable or re-useable trap, it draws filth flies into the apparatus where they are trapped.

The product chemistry data submitted by the registrant, including manufacturing process, discussion of formation of impurities, analysis of samples, and certified ingredients limits satisfied the requirement for product identity. Refer to Table 1 in Appendix A for a summary of product chemistry data requirements. Refer to Table 2 in Appendix A for the summary of physical and chemical characteristics for trimethylamine.

All product chemistry data requirements for registration of trimethylamine have been **satisfied.**

B. Human Health Assessment

1. Toxicology

For acute toxicity data requirements, toxicity categories are assigned based on the hazard(s) identified from studies and/or information on file with the Agency. The active ingredient is classified into Toxicity Category I, II, III or IV where Toxicity Category I indicates the highest toxicity and Toxicity Category IV indicates the lowest toxicity. For more information, refer to 40 CFR § 156.62.

Adequate mammalian toxicology data/information are available to support registration of trimethylamine. All toxicology data requirements for trimethylamine have been **satisfied.**

a. Acute Toxicity

Acute toxicity testing is required to 1) determine systemic toxicity from acute exposure via the dermal, inhalation and oral routes, 2) determine irritant effects from exposure to the eyes and 3) determine the potential for skin sensitization (allergic contact dermatitis). All required toxicology data for trimethylamine are waived. No additional toxicological data are needed. The decision to waive these data is based on: 1) the product is naturally occurring, 2) possesses a non-toxic mode of action, 3) will not accumulate in the environment because it is a plant nutrient, and 4) due to the design of the trap, there is no anticipated exposure to the attractant pouch ingredients. For more information regarding the acute toxicity data requirements, refer to Table 3 in Appendix A.

b. Subchronic Toxicity

Subchronic data is required to determine a no-observed-effect-level (NOEL) and toxic effects (if any) associated with repeated or continuous exposure to a test substance for a period of 90 days. The request submitted by the registrant to waive subchronic mammalian toxicity data was determined to be acceptable. For more information regarding the subchronic data requirements, refer to Table 3 in Appendix A.

c. Developmental Toxicity and Mutagenicity

The Agency waived data requirements for developmental toxicity and mutagenicity of trimethylamine based on 1) its natural occurrence in the environment, 2) little to no potential for exposure to humans based on the EP attractant packet and fly trap designs and 3) the fact that it is a plant nutrient that will not accumulate in the environment. For more information regarding these data requirements, refer to Table 3 in Appendix A.

e. Effects on the Endocrine System

EPA is required under the Federal Food, Drug, and Cosmetics Act (FFDCA), as amended by the Food Quality Protection Act (FQPA), to develop a screening program to determine whether certain substances (including all pesticide active and other ingredients) "may have an effect in humans that is similar to an effect produced by a naturally-occurring estrogen, or other such endocrine effects as the Administrator may designate." Following the recommendations of its Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC), EPA determined that there was scientific basis for including, as part of the program, the androgen and thyroid hormone systems, in addition to the estrogen hormone system. EPA also adopted EDSTAC's recommendation that the program include evaluations of potential effects in wildlife. For pesticide chemicals, the Agency will use FIFRA and, to the extent that effects in wildlife may help determine whether a substance may have an effect in humans, FFDCA authority to require the wildlife evaluations. As the science develops and resources allow, screening of additional hormone systems may be added to the Endocrine Disruptor Screening Program (EDSP).

The Agency is not requiring information on the endocrine effects of trimethylamine at this time. The Agency has considered, among other relevant factors, available information concerning whether the active ingredient may have an effect on humans similar to an effect produced by naturally-occurring estrogen or other endocrine effects. There is no known metabolite that acts as an endocrine disrupter produced by this active ingredient. Based on the low potential exposure level associated with the proposed use, the Agency expects no incremental adverse effects to the endocrine or immune systems.

2. Dose Response Assessment

No toxicological endpoints were identified; therefore, a dose response assessment was not required.

3. Drinking Water Exposure and Risk Characterization

Based on use patterns, no significant exposure is expected from use of trimethylamine in the environment when used according to label instructions.

4. Occupational, Residential, School and Day Care Exposure and Risk Characterization

a. Occupational Exposure and Risk Characterization

Occupational exposures are not a concern based on the use pattern, low potential for exposure due to trap design, and because trimethylamine is naturally occurring in the environment and possesses a non-toxic mode of action. The application method of trimethylamine inside a water-soluble pouch that is placed within a trap poses no significant concern for dermal, eye, and inhalation exposures. Based on little or no potential for exposure and the small percentage of trimethylamine in the attractant pouch, worker exposure data on trimethylamine are not required. Based on the nature, use pattern, non-toxic mode of action, and relative safety of trimethylamine in this product, including the battery of information from the open scientific literature, the toxicity category has been characterized as IV and the product label will bear the signal word "Caution." No reentry interval is required in conjunction with the use of the EP.

b. Residential, School and Day Care Exposure and Risk Characterization

The end use product containing trimethylamine is intended for use in a residential or agricultural setting. Again, because trimethylamine is naturally occurring, possesses a non-toxic mode of action, and the trap design will result in low potential for exposure, the Agency is not concerned about the potential exposure to children.

5. Risk Characterization

The Agency considered human exposure to trimethylamine in light of the relevant safety factors in 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 trimethylamine when label instructions are followed.

C. ENVIRONMENTAL ASSESSMENT

1. Ecological Hazards

Based on the natural occurrence of trimethylamine as a product of the decomposition of plants and animals, that it is a plant nutrient, and the fact that trimethylamine is not expected to cause adverse effects on non-target organisms, adequate rationales for waiving non-target toxicology data were submitted to support registration of trimethylamine. All non-target toxicology data requirements for trimethylamine have been **satisfied.**

For more information regarding the non-target toxicity data requirements, refer to Table 4 in Appendix A.

2. Environmental Fate and Ground Water Data

The need for environmental fate and groundwater data was not triggered because results of the acute toxicity studies did not trigger any additional Tier I studies.

3. Ecological Exposure and Risk Characterization

4. Endangered Species Assessment

Adverse effects on threatened and endangered species are not expected based on available information about the use pattern of the product, product performance data, and habitat of Diptera species currently listed as threatened or endangered.

D. PRODUCT PERFORMANCE DATA (EFFICACY)

Submission of product performance data (OPPTS 810.3000) is listed as a requirement for all pesticide products. Customarily, the Agency requires efficacy data to be submitted for review only in connection with the registration of products directly pertaining to the mitigation of disease bearing human health organisms and certain designated quarantine pests, i.e., ticks, mosquitoes, fleas, Mediterranean fruit flies, gypsy moths, Japanese beetles, etc. For a list of organisms considered by the Agency as "public health pests", please refer to Pesticide Registration Notice 2002-1 (http://www.epa.gov/PR_Notices/pr2002-1.pdf).

Based on the data submitted by the registrant, the Agency determined that product performance data were acceptable.

V. Risk Management Decision

A. Determination of Eligibility for Registration

Section 3(c)(5) of FIFRA provides for the registration of new active ingredients if it is determined that (A) its composition is such as to warrant the proposed claims for it; (B) its labeling and other materials required to be submitted comply with the requirements of FIFRA; (C) it will perform its intended function without unreasonable adverse effects on the environment; and (D) when used in accordance with widespread and commonly recognized practice it will not generally cause unreasonable adverse effects on the environment.

The four criteria of the Eligibility Determination for Pesticidal Active Ingredients are satisfied by the science assessments supporting products containing trimethylamine. Such products are not expected to cause unreasonable adverse effects, and are likely to provide protection as claimed when used according to label instructions. Therefore, trimethylamine is eligible for registration for the labeled uses.

B. Regulatory Decision

The data submitted fulfill the requirements of registration for use as an ingredient in a water-soluble fly attractant packet inside an insect trap. Refer to Appendix B for product-specific information.

1. Conditional/Unconditional Registration

All data requirements are fulfilled and EPA has determined that unconditional registration of trimethylamine is appropriate.

C. Environmental Justice

EPA seeks to achieve environmental justice - the fair treatment and meaningful involvement of all people, regardless of race, color, national origin, or income - in the development, implementation, and enforcement of environmental laws, regulations, and policies. At this time EPA does not believe that use of pesticide products containing trimethylamine will cause harm or a disproportionate impact on at-risk communities.

For additional information regarding environmental justice issues, please visit EPA's website at: http://www.epa.gov/compliance/environmentaljustice/index.html.

VI. ACTIONS REQUIRED BY REGISTRANTS

The Agency evaluated all of the data submitted in connection with the initial registration of trimethylamine and determined that these data are sufficient to satisfy current registration data requirements. No additional data are required to be submitted to the Agency at this time. For new uses and/or changes to existing uses, additional data may be required.

Not withstanding the information stated in the previous paragraph, it should be clearly understood that certain, specific, data are required to be reported to the Agency as a requirement for maintaining the Federal registration for a pesticide product. A brief summary of these types of data are listed below.

A. Reporting of Adverse Effects

Reports of all incidents of adverse effects to the environment must be submitted to the Agency under the provisions stated in FIFRA, Section 6(a)(2).

B. Reporting of Hypersensitivity Incidents

Additionally, all incidents of hypersensitivity (including both suspected and confirmed incidents) must be reported to the Agency under the provisions of 40 CFR Part 158.2050(d).

VII. Appendix A. Data Requirements (40 CFR Part 158-Subpart U)

*NOTE: MRID numbers listed in the following tables are representative of supporting data for the original registration of the product containing this active ingredient. Subsequent to this registration, there may be additional MRIDs that support registration of other products containing this active ingredient.

TABLE 1. Product Chemistry Data Requirements for Trimethylamine (40 CFR § 158.2030)

OPPTS Guideline No.	Study	Results	MRID
830.1550 to 830.1670	Product identity; Manufacturing process; Discussion of formation of unintentional ingredients	Submitted data satisfy the requirements for product identity, manufacturing process, and discussion of formation of impurities.	473969-28
830.1700	Analysis of samples	Submitted data satisfy the requirements for analysis of samples.	473969-28
830.1750	Certification of limits	Limits listed in the CSF are adequate / acceptable.	473969-28
830.1800	Analytical method	Acceptable.	473969-28

TABLE 2. Physical and Chemical Properties of Trimethylamine (40 CFR § 158.2030)

OPPTS Guideline No.	Property	Description of Result	MRID
830.6302	Color	colorless	473969-29
830.6303	Physical State	gas at room temperature	473969-29
830.6304	Odor	fishy odor at low concentrations, ammonia-like odor at higher concentrations	473969-29
830.6313	Stability to Normal and Elevated Temperatures, Metals and Metal Ions	Stable when stored in a cool, dry, well-ventilated area in tightly-sealed containers. Should be stored separately from mercury, strong oxidizing materials, strong acids, and metals.	473969-29
830.6315	Flammability	Highly flammable	473969-29
830.6317	Storage Stability	As part of Bull Run Fly Attractant, stable for over 12 months.	473969-29
830.6319	Miscibility	Miscible in water	473969-32
830.6320	Corrosion Characteristics	Not required for EP	N/A
830.7000	pH	11.3	473969-30
830.7050	UV/Visible Light Absorption	Not required for EP	N/A
830.7100	Viscosity	Not applicable	N/A
830.7200	Melting Point/Range	Not required for EP	N/A
830.7220	Boiling Point/Range	Not required for EP	N/A
830.7300	Density	0.67 g/mL at 0°C	473969-29
830.7520	Particle Size, Fiber Length and Diameter Distribution	Not required for EP	N/A
830.7550 830.7560 830.7570	Partition Coefficient (n-Octanol/Water)	Not required for EP	N/A
830.7840	Water Solubility	Miscible	473969-29
830.7950	Vapor Pressure	1.69×10^3 mm Hg at 25°C	473969-29

Table 3. Human Toxicology Data Requirements for Trimethylamine (40 CFR § 158.2050)			
Study/OPPTS Guideline No.	**Results**	**Toxicity Category/Description**	**MRID**
Acute oral toxicity (rat) (870.1100)	Waiver requested*	Acceptable	473969-33
Acute dermal toxicity (rat) (870.1200)	Waiver requested*	Acceptable	473969-33
Acute inhalation toxicity (rat) (870.1300)	Waiver requested*	Acceptable	473969-33
Primary eye irritation (rabbit) (870.2400)	Waiver requested*	Acceptable	473969-33
Primary dermal irritation (rabbit) (870.2500)	Waiver requested*	Acceptable	473969-33
Dermal sensitization (guinea pig) (870.2600)	Waiver requested*	Acceptable	473969-33
Hypersensitivity incidents (885.3400)	Waiver requested*	Acceptable	473969-33
90-Day oral toxicity (870.3100)	Waived due to lack of exposure	N/A	
90-Day dermal toxicity (870.3250)	Waived due to lack of exposure	N/A	
90-Day inhalation toxicity (870.3465)	Waived due to lack of exposure	N/A	
Mutagenicity (870.5100, 5300 and 5375)	Waived due to lack of exposure	N/A	
Developmental toxicity (870.3700)	Waived due to lack of exposure	N/A	

* Due to the fact that no significant human exposure is expected, the Agency did not require human health data on the Technical Grade Active Ingredient (TGAI). This is due to the fact that the active ingredient is enclosed in a water-soluble vapor barrier packet which is placed inside the fly trap, resulting in no exposure to the product handler. The Agency did, however, require data for the EP.

TABLE 4. Non-Target Organism Toxicity Requirements for Trimethylamine (40 CFR § 158.2060)			
Study/OPPTS Guideline No. /MRID No.	**Results**	**Toxicity Category/Description**	**MRID**
Avian acute oral toxicity *Colinus virginianus* (850.2100)	Waived only for the proposed use pattern of the EP contained within a water-soluble vapor barrier packet inside the fly trap	Acceptable	473969-32
Avian dietary toxicity *Colinus virginianus* (850.2200)	Waived only for the proposed use pattern of the EP contained within a water-soluble vapor barrier packet inside the fly trap	Acceptable	473969-32
Avian dietary toxicity *Anas platyrhynchos* (850.2200)	Waived only for the proposed use pattern of the EP contained within a water-soluble vapor barrier packet inside the fly trap	Acceptable	473969-32
Aquatic invertebrate acute toxicity (*Daphnia magna*) (850.1010)	Waived only for the proposed use pattern of the EP contained within a water-soluble vapor barrier packet inside the fly trap	Acceptable	473969-32
Freshwater fish LC_{50} (*Oncorhynchus mykiss*) (850.1075)	Waived only for the proposed use pattern of the EP contained within a water-soluble vapor barrier packet inside the fly trap	Acceptable	473969-32
Non-target plant studies (850.4000-4800, as applicable)	Waived only for the proposed use pattern of the EP contained within a water-soluble vapor barrier packet inside the fly trap	Acceptable	473969-32
Non-target insect testing (880.4350)	The study, Product performance data indicated no evidence that the product attracts non-target insects.	Acceptable	473696-03

VIII. Appendix B.

For product specific information, please refer to http://www.epa.gov/pesticides/pestlabels/

IX. Appendix C.

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