BIOPESTICIDES REGISTRATION ACTION DOCUMENT

Oriental Mustard Seed (OMS)
PC Code 014921

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

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BIOPESTICIDES REGISTRATION ACTION DOCUMENT TEAM

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I. EXECUTIVE SUMMARY:

Oriental Mustard Seed (OMS) (which has been de-oiled) is a new active ingredient. This active ingredient has been grinded such that it contains the natural components of the mustard seed (Oriental Mustard Bran and Oriental Mustard Meal); the enzyme myrosinase and glucosolinate sinigrin less the oil of mustard. The OMS technical product is therefore a pellet. Myrosinase and glucosolinate do not exhibit any pesticidal activity. However, when these components (as part of OMS) are in the presence of water, a catalytic reaction occurs whereby allyl isothiocyanate (AITC) is created. AITC is a federally registered active ingredient and thus is the residue of concern since, as described above, when water is added to the OMS pellet in the field, AITC is released. The toxicity profile of AITC has been well characterized by the Agency (Refer to Reregistration Eligibility Decision Flower and Vegetable Oils). For these reasons and since AITC, as derived from OMS is the residue of concern, this document will focus largely on the risks (if any) as presented by AITC.

Adequate mammalian toxicology data on the technical grade active ingredient (TGAI) are available to support registration of products containing OMS that do not contain oil of mustard. Acceptable acute guideline studies and waivers were submitted, and data for mutagenicity, developmental toxicity, and subchronic study requirements were submitted to Biopesticides and Pollution Prevention Division (BPPD) on the technical material. Adequate information from the scientific literature were submitted to address the nontarget data requirements. All of the literature supported the fact that there would be no toxicity or adverse effects to nontarget organisms with the exception of certain insects and honey bees. Data demonstrated that the AITC, the residue of concern is highly toxic to honey bees and mildly toxic to other nontarget insects. The Agency has concluded that the honey bee toxicity issue can be appropriately addressed thru label mitigation.

The Agency considered human exposure to OMS in light of the relevant safety factors in FQPA and FIFRA. A determination has been made that there are no unreasonable adverse effects to the U.S. population in general, and to infants and children. No significant exposure via drinking water is expected when OMS is used according to the product label directions. The product is not to be applied directly to water or to areas where surface water is present. Aquatic exposure should not occur when the product is applied according to label directions.

Based on the information discussed above, the Agency has determined that registered use of OMS as an active ingredient will have **No Adverse Effects (NAE)** on threatened and/or endangered species. Exposure to endangered or threatened species is not expected since the currently listed endangered or threatened species pursuant to the Endangered Species Act of 1973, 16 U.S.C. 1531, et seq., are not found in locations where the product is intended for use.

The Biopesticides and Pollution Prevention Division (BPPD) considered data submitted for granting registration under Section 3(c)(5) of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) and determined that the data/information submitted in support of OMS technical grade active ingredient (TGAI) adequately satisfy current guideline requirements (refer to 40 CFR Subpart U § 158.2000).

II. ACTIVE INGREDIENT OVERVIEW

Common Name: Oriental Mustard Seed

Chemical Names: Oriental Mustard Seed; Allyl isothiocyanate

Trade & Other Names: CA-1 for Turf and Ornamentals

CAS Registry Number: 57-06-7

OPP Chemical Code: 014921

Type of Pesticide: Biochemical pesticide (Nematicide/Fungicide).

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

III. REGULATORY BACKGROUND

On March 13, 2003, the Agency received an application filed by Nematrol, Inc., 15 Prince Andrew Court, St. Catharines, Ontario L2N 3Y2, Canada (submitted by Technology Sciences Group, Inc., 1150 18th Street, N.W., Suite 1000, Washington, DC 20036 . On September 14, 2006 Nematrol, Inc. retained Walter G. Talarek, PC as their agent. Nematrol wishes to the product CA-1 containing the new biochemical active ingredient Oriental Mustard Seed at 98%. A notice of receipt of this application was published in the Federal Register August 11, 2004 (690 FR 154).

A. Classification

On March 18, 2002, the Biochemical Classification Committee determined that the active ingredient Oriental Mustard Seed is naturally occurring, is widespread in the diet, and is therefore a biochemical pesticide.

B. Food Clearances/Tolerances

Currently, this active ingredient is not registered for use on food or feed commodities because applications are for turf and ornamentals. Therefore a tolerance or exemption from the requirement of a tolerance is not relevant.

IV. RISK ASSESSMENT

A. Active Ingredient Characterization

Oriental Mustard Seed (OMS) is the active ingredient; however, AITC is the residue of concern in products to control nematodes and fungi. The end use product is a granular (pellet) formulation.

The descriptions of the product formulation and production process as well as the formation of impurities were examined by BPPD and found to be acceptable in meeting current guideline standards.

All product chemistry data requirements for registration of Oriental Mustard Seed (TGAI) have been **satisfied.**

TABLE 1. Physical and Chemical Properties for TGAI and EP of OMS for Turf and Ornamentals[a]

Guideline Reference No./Property	TGAI	EP
830.6302 Color	Yellow brown at room temperature	Yellow brown at room temperature
830.6303 Physical State	Not required for TGAI	Solid at 20°C
830.6304 Odor	Slightly pungent mustard	Slightly pungent mustard
830.6313 Stability	Stable at room temperature; not expected to be unstable at elevated temperature or in metals or metal ions.	Not required for EP
830.6314 Oxidation/Reduction: Chemical Incompatibility	Not required for TGAI	Product does not contain oxidizing or reducing agents.
830.6315 Flammability	Not required for TGAI	Product does not contain combustible liquids.
830.6316 Explodability	Not required for TGAI	Product is not potentially explosive and has no explosive characteristics.
830.6317 Storage Stability	Not required for TGAI	Product is stable for one year when stored in the original container per label directions.
830.6319 Miscibility	Not required for TGAI	Product is not an emulsifiable liquid and is not to be diluted with petroleum solvents.
830.6320 Corrosion Characteristics	Not required for TGAI	Product is corrosive for one year when stored in the original container per label directions.
830.6321 Dielectric Breakdown Voltage	Not required for TGAI	Not required for EP; product is not a liquid and is not intended for use around electrical equipment.

B. Human Health Assessment

1. Toxicology

AITC

Since AITC is created when the technical material is wetted, AITC is the residue of concern. AITC has already been assessed by the Agency (See Vegetable Oil RED, December 1993) and the Agency has concluded that adequate mammalian toxicology data are available to support AITC. The oral LD_{in} in rats is 339 mg/kg. There are no incident reports on file with EPA for AITC. Human exposure to AITC is expected to be minimal from products in this registration.

The active ingredient is not likely to result in adverse human health effects, based upon available reports and information.

OMS

The Agency has concluded that adequate mammalian toxicology are available to support registration of products containing the new active ingredient OMS. Acceptable acute guideline studies were submitted, and waivers requested for the mutagenicity, developmental toxicity, and subchronic study requirements were granted by BPPD based on submissions from the scientific literature.

With regard to the Human Health Toxicity profile for OMS, all toxicity data requirements have been satisfied.

a. Acute Toxicity

OMS is classified into toxicity category IV for acute oral toxicity, acute dermal toxicity, and primary dermal irritation. OMS is classified into toxicity category III for primary eye irritation and is considered to be a skin sensitizer. The acute inhalation toxicity requirement was waived due to the inability to generate a dust of respirable size. No additional toxicity data are required to support the nonfood use of this of this active ingredient.

b. Subchronic Toxicity

Literature was cited to satisfy the 90-day oral toxicity data reqirement. There were three studies classified as acceptable. In the first study, a six-week study in rats (Lewerenz et al., 1988) the lowest observed adverse effect level (LOAEL) was determined to be 20 mg/kg-day based on decreased food consumption, urine specific gravity, and increased dilation and desquamation of kidney distal tubules. The no observed adverse effect level (NOAEL) was 10 mg/kg-day. In the second (13-week in rats) and third studies (13-week in mice) (MRIDs 46252501, 46120401 and 46675001), the LOAEL was not determined and the NOAEL was determined to be 25 mg/kg-day. The 90-day dermal toxicity data requirement was waived based on the low dermal toxicity and irritation effects observed in the acute studies and lack of repeated dermal exposure based on the proposed uses. The 90-day inhalation toxicity data requirement was waived for the same reason the acute inhalation toxicity study was waived.

c. Developmental Toxicity and Mutagenicity

Of the data and information submitted to support the developmental toxicity data requirement, four NTP studies (using rats, mice, hamsters and rabbits) were cited and considered acceptable. Oil of mustard (93-97% AITC purity) was used as the test substance for these studies. Data from the rabbit and hamster studies suggested that fetal effects (such as increases in the incidence of extra sternebrae and incomplete ossification of the sternebrae) occurred at test doses (LOAEL = 2.8 and 23.8 mg/kg-day, respectively; NOAEL = 0.60 and 5.12 mg/kg-day, respectively) that were less than that inducing maternal effects (LOAEL > 12.3 and > 23.8 mg/kg-day, respectively). Similar-dose testing with rats resulted in no maternal or developmental toxicity and similar-dose testing with mice resulted in fetal toxicity at maternally toxic doses. Many studies were cited and submitted to satisfy the mutagenicity data requirements. Of the fourteen individual tests in the studies classified as acceptable that were conducted using AITC, eight were considered to be negative for mutagenic effects, three were positive, one was weakly

positive, and two were considered equivocal. All of the bacterial tests and all except one of the *in vivo* tests were classified as negative or equivocal for mutagenicity while all of the *in vitro* tests were classified as positive or weakly positive.

The Agency considered human exposure to OMS when AITC is the residue of concern in light of the relevant safety factors in FIFRA. It is not expected that use of the product where AITC is the residue of concern would result in significant human exposure when the product is used as directed. The available data and information support the conclusion that the proposed use of OMS to formulate a product in which AITC will be released poses no foreseeable risks to human health or the environment. There is a reasonable certainty of no harm to the general US population from exposure to this active ingredient when products are used according to label instructions.

d. Chronic exposure and oncogenicity assessment

Two studies using AITC as the test substance were cited to address chronic toxicity and carcinogenicity, one in mice and one in rats. In rats, the LOAEL was determined to be 12 mg/kg-day based on chronic myocardial inflammation in male rats and dose-dependent hyperplastic changes in the bile-duct in female rats. The NOAEL was not determined because the LOAEL was the lowest dose tested. Neoplastic changes were observed in both sexes. In the mouse study, the LOAEL was determined to be 12 mg/kg-day based on dose-dependent increases in cytoplasmic vacuolization of the liver in males. The NOAEL was not determined because the LOAEL was the lowest dose tested. Carcinogenic effects were also observed in both sexes, but all of these pathologies were marginally above the average and below the range of historical control incidents. However, there is a reasonable certainty of no harm to the general US population from chronic exposure to the active ingredient when the product is used according to label instructions"

e. Effects on the Endocrine System

The US Environmental Protection Agency (Agency) is required under the Federal Food, Drug, and Cosmetics Act (FFDCA), as amended by Food Quality Protection Act, 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). Based on the weight of the evidence of available data, no endocrine system-related effects have been identified for OMS and none is expected since it does not share any structural similarity to any known endocrine disruptor.

2. Dose Response Assessment

A dose response assessment was not conducted because, although toxicological endpoints were identified, based on the proposed uses of the product and precautionary and personal protective equipment (PPE) language on the label, human exposure is not expected.

3. Drinking Water Exposure and Risk Characterization

No significant drinking water exposure is expected from OMS, where residues of AITC are concerned, in the aquatic environment when the product containing the active ingredient is used according to label directions. Based on the data available to the Agency, the proposed uses of the product containing OMS and AITC (no direct addition to water) and that AITC (the residue of concern) degrades rapidly in the environment, AITC residues are not expected in drinking water.

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

a. Occupational Exposure and Risk Characterization

Occupational exposure is not expected due to mitigation through precautionary language and the requirement of personal protective equipment (PPE) on the label. Applicators subject to the Worker Protection Standard are to wear long-sleeved shirts, long pants, shoes, socks and gloves. Additionally, the product is not inhalable; therefore inhalation exposure is not likely to occur. The potential for dermal, eye, and inhalation exposure to AITC for handlers and applicators is mitigated as long as the product is used according to label directions. The Agency will require labels to include the appropriate signal word and precautionary statements, including the requirement for personal protective equipment, to mitigate any risk of exposure.

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

No indoor residential, school, or day care uses are currently approved for the product containing AITC.

5. Risk Characterization

The Agency considered human exposure to AITC in light of the relevant safety factors in FQPA and FIFRA since AITC is the residue of concern. 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 OMS were AITC residues are of concern when label instructions are followed.

C. ENVIRONMENTAL ASSESSMENT

1. Ecological Hazards

Ecological effects data requirements for OMS were fulfilled by data and/or waivers submitted for acute avian toxicity, nontarget plant toxicity, nontarget insect toxicity, freshwater invertebrate acute toxicity, and freshwater acute toxicity.

Acute studies on northern Bobwhite quail (MRID 46120401) and the mallard duck (MRID 46120401) showed that AITC was practically non-toxic to avian species; LC_{50} = 82,000 mg/L for both species. These studies are acceptable.

Nontarget plant toxicity data was bridged from product performance data presented in MRIDs 46120405, 47049301, and 47049302. The registrant also provided the following label language under "Environmental Hazards:" - "This product may be phytotoxic to plants if it is applied at more than the prescribed application rate." and under "For use on Ornamentals, before transplanting or seeding" - "Excess amount of application (more than the above recommended rate) may cause phytotoxicity (yellowing of the turf, reduced germination and/or damage to the root of transplanted young seedlings)".

The registrant requested to be waived from testing the guidelines for the certain nontarget insect testing and honey bee study on the basis of strongly prohibitive label language: "This product is toxic to insects and highly toxic to bees exposed to direct treatment on blooming crops or weeds. Do not apply this product or allow it to drift to blooming crops or weeds while bees are actively visiting the treatment area". As with phytotoxicity studies, when considered together, studies, rate labeling, and the precautionary labeling presented sufficient information to fulfill the nontarget insect toxicity data requirement and for BPPD to grant this waiver request.

Two studies were submitted to fulfill the freshwater acute toxicity data requirement (Holcombe et al., 1995; Geiger et al., 1990; MRID 46263501, 46263502). The studies were run on rainbow trout and bluegill sunfish and showed LC_{50} = 11.9-17.3 mg/L which indicates only slight toxicity.

All nontarget toxicology data requirements for OMS have been **satisfied.**

2. Environmental Fate and Ground Water Data

The need for environmental fate and groundwater data was not triggered because AITC, the residue of concern, was practically non-toxic in the avian acute oral study, and the remaining Tier I studies that were waived.

3. Ecological Exposure and Risk Characterization

Based on the studies and rationale for the data waiver discussed above, exposure and risk from the proposed use of OMS are expected to be minimal for nontarget organisms (with the exception of honey bees). Although the active ingredient is toxic to honey bees exposure should not occur when the product is applied according to label directions.

4. Endangered Species Assessment

The use of this product as a nematicide for turf and ornamentals should result in low exposure and "no effect" to terrestrial or aquatic endangered species.

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).

No efficacy data were required to be submitted with this pesticide application because the active ingredient will not be used to control any disease bearing human health organisms and certain designated quarantine pests as discussed above.

V. Risk Management Decision

A. Determination of Eligibility for Registration

Section 3(c)(5) of FIFRA provides for the registration of a new active ingredient 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 OMS. 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, OMS is eligible for registration for the labeled uses.

B. Regulatory Decision

The data submitted fulfill the requirements of registration for use of OMS to control nematodes and fungi. Refer to Appendix B for product-specific information.

Conditional/Unconditional Registration

All data requirements are fulfilled and EPA has determined that unconditional registration of OMS 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. To help address potential environmental justice issues, 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 OMS, where AITC is the residue of concern, compared to the general population. Please comment if you are aware of any sub-populations that may have atypical, unusually high exposure compared to the general population.

VI. ACTIONS REQUIRED BY REGISTRANTS

The Agency evaluated all of the data submitted in connection with the initial registration of OMS 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.

Notwithstanding 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 2. Human Toxicology Data Requirements for AITC (40 CFR § 158.2050)

Study Type, Species, OPPTS Guideline	Regulatory Decision	LD_{50}/LC_{50}/LOAEL/NOAEL Results	Toxicity Category	MRID Review Date
Acute Oral Toxicity, rat, OPPTS 870.1100	Acceptable	**>5000 mg CA-1/kg** for M, F, and combined	IV	45883603 01/11/06

Acute Dermal Toxicity, rat, OPPTS 870.1200	Acceptable	**> 5000 mg CA-1/kg** for M, F, and combined	IV	45883604 01/11/06
Acute Inhalation Toxicity, rat, OPPTS 870.1300	Acceptable, Waiver	Inhalable aerosol of **CA-1** unable to be generated	IV	45883605 01/11/06
Acute Eye Irritation, rabbit, OPPTS 870.2400	Acceptable	**CA-1**-induced reversible **corneal opacity and mild irritation clearing by 72 hours**	III	45883606 01/11/06
Acute Dermal Irritation, rabbit, OPPTS 870.2500	Acceptable	**CA-1**-induced slight **edema and erythema clearing by 48 hours**	IV	45883607 01/11/06
Skin Sensitization, guinea pig, OPPTS 870.2600	Acceptable	**CA-1**-induced **sensitization**	Sensitizer	45883602 01/11/06

Table 3. Nontarget Organism, Fate and Expression Data Requirements for AITC (40 CFR § 158.2060)

Study/OPPTS Guideline No.	Results	MRID #(s)
Avian acute oral toxicity (850.2100)	LC_{50} = 82,000 mg/L >2038 mg/kg (practically nontoxic)	46120401
Nontarget plant toxicity (850.4150)	phytotoxic	46120405, 47049301, 47049302
Nontarget insect toxicity (850.4350)	Highly toxic to honey bees (waived)	
Freshwater fish (850.1010)	48 hr. EC_{50} > 32 mg/L (slightly toxic)	47271803
Freshwater acute toxicity (850.4100)	LC_{50} = 11.9-17.3 mg/L (slight toxicity)	46263501, 46263502

VIII. Appendix B.

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

IX. Appendix C.

REFERENCES

Allyl isothiocyanate. (1985). International Agency for Research on Cancer (IARC) Summaries and Evaluations. Vol:36 p. 55. http://www.inchem.org/documents/iarc/vol36/allylisothiocyanate.html

Allyl isothiocyanate. (1999). International Agency for Research on Cancer (IARC) Summaries and Evaluations. Vol:73 p. 37. http://www.inchem.org/documents/iarc/vol73/73-01.html

Carcinogenesis Bioassay of Allyl Isothiocyanate. (1982). National Toxicology Program Technical Report Series No. 234. http://ntp.niehs.nih.gov/ntp/htdocs/LT_rpts/tr234.pdf

Lewerenz, H.-J., Plass, R., Bleyl, D.W.R., and R. Macholz. (1988). Short-term toxicity study of allyl isothiocyanate in rats. Die Nahrung. 32(8). 723-728.

Memorandum: USEPA Carlson to D. Greenway dated April 30, 2008

Reregistration Eligibility Decision (RED) Flower and Vegetable Oils 738-R-93-031, December, 1993