BIOPESTICIDES REGISTRATION ACTION DOCUMENT

FARNESOL AND NEROLIDOL

March 10, 2009

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

(last updated March 10, 2009)

This document is for informational purposes only and is representative of the Agency's justification in registering products containing this active ingredient. This is not a legal document. (Need OGC language)

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I. EXECUTIVE SUMMARY:

Farnesol and Nerolidol are naturally-occurring, sesquiterpene mite attractants that were originally isolated from essential oils found in plants such as rose, citronella, and lemon grass. More recently, these compounds were isolated from female mites, where the compounds act as sex pheromones to attract male mites for mating. Farnesol and Nerolidol are now synthesized in the laboratory and natural sources are no longer needed. Due to the distinctly different plant and insect sources from which naturally-occurring Farnesol and Nerolidol may be isolated, these semiochemicals are more properly defined as parapheromones. Farnesol and Nerolidol have been grouped into one case due their practically identical chemical structure, differing only in the position of one of three double bonds on the aliphatic carbon chain and in the position of a hydroxyl group.

Registered products containing Farnesol and Nerolidol are applied to plants in a foliar spray mixture that is used in combination with a conventional chemical miticide to control eotetranychid, tetranychid, and panonychid mites on agricultural crops and ornamental plants. There are no residential uses. One registered product also contains two other chemically-related active ingredients, citronellol and geraniol. The parapheromones cause the male mites to become more active as they try to locate the presumed nearby female. This extra activity causes the males to have longer contact exposure with the conventional chemical miticide.

The Biopesticides and Pollution Prevention Division (BPPD) reviewed data requirements for granting registration under Section 3(c)(5) of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA). It was determined that the data/information submitted adequately satisfy current guideline requirements (refer to 40 CFR Subpart U § 158.2000). Adequate mammalian toxicology data/information were submitted to support registration of Farnesol and Nerolidol. Acceptable acute toxicity guideline studies were submitted, and data waivers were granted by the Agency to fulfill the remaining Tier I toxicity data requirements based on the lack of toxicity of the active ingredients and their natural occurrence in plants and mites. The Agency does not anticipate that another human health assessment will be needed for Farnesol and Nerolidol.

Ecological effects data requirements for Farnesol and Nerolidol 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. Use of the products in accordance with EPA-approved labeling would not present direct exposure to fish and aquatic invertebrates. Farnesol and Nerolidol are practically non-toxic to birds, insects and plants. The Agency does not anticipate the need to conduct another ecological risk assessment, including an endangered species assessment, for Farnesol and Nerolidol. Registered Farnesol and Nerolidol products are used on agricultural crop plants as mite parapheromones. Since Farnesol and Nerolidol only affect (attract) mites, EPA has determined that there is limited exposure or risk to non-target organisms, habitats or water. Therefore, EPA is making a No Effects (NE) determination for Farnesol and Nerolidol in regard to the Endangered Species Act (ESA).

Farnesol and Nerolidol were exempted from the requirements of tolerances on food in 1987 under 40 CFR 180.1086, and a Tolerance Reassessment was completed on 08/28/2003. Farnesol and Nerolidol are generally recognized as safe (GRAS) by FDA under 21 CFR 182.60.

II. ACTIVE INGREDIENT OVERVIEW

Common Names: Farnesol and Nerolidol

Chemical Names: 3, 7, 11-Trimethyl-2,6,10-dodecatriene-1-ol and
3, 7, 11-Trimethyl-1,6,10-dodecatriene-1-ol

Trade & Other Names: Stirrup M® and Biomite™

CAS Registry Numbers: 4602-84-0 and 7212-44-4

OPP Chemical Codes: 128910 and 128911

Type of Pesticide: Biochemical pesticide: parapheromone

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

III. REGULATORY BACKGROUND

Fermone Chemicals, Inc. submitted an application for the registration of the end use product (EP), Stirrup M® EPA Registration Number 53871-2 containing the active ingredients Farnesol and Nerolidol on September 3, 1985. A notice of receipt of an application for registration Stirrup M® containing the active ingredients Farnesol and Nerolidol, was published in the Federal Register on September 17, 1986 (51 FR 32955). An unconditional registration for the product Stirrup M® containing the active ingredients Farnesol and Nerolidol was issued on April 21, 1987**.** The product registration is currently held by Troy BioSciences (formerly Fermone Chemicals, Inc.).

A notice of receipt of an application from Fermone Chemicals, Inc. for a tolerance exemption for Stirrup M® containing the active ingredients Farnesol and Nerolidol, was published in the Federal Register on October 29, 1986 (51 FR 39577) with a 30-day comment period. No comments were received following this publication. A permanent exemption from the requirements of tolerances for Farnesol and Nerolidol was issued on August 5, 1987.

A notice of receipt of an application from Natural Plant Protection S. A. for registration of Biomite™ containing the active ingredients Farnesol, Nerolidol, Citronellol, and Geraniol, was published in the Federal Register on August 28, 2002 (67 FR 55234) with a 30-day comment period. No comments were received following this publication. An unconditional registration for the product Biomite™ containing the active ingredients Farnesol, Nerolidol, Citronellol, and Geraniol was issued on April 27, 2004 (69 FR 78016)**.**

There are no Technical Grade Active Ingredient (TGAI) products registered for the active ingredients, Farnesol and Nerolidol.

A. Classification

Farnesol and Nerolidol were classified as biochemical pesticide active ingredients in 1986 (Memorandum from W. Nelson to F. Betz, dated 09/17/1986).

B. Food Clearances/Tolerances

Farnesol and Nerolidol were exempted from the requirements of tolerances on food in 1987 under 40 CFR 180.1086, and a Tolerance Reassessment was completed for Farnesol and Nerolidol on 08/28/2003. Farnesol and Nerolidol are generally recognized as safe (GRAS) by FDA under 21 CFR 182.60. There are no CODEX maximum residue levels (MRLs) established for Farnesol and Nerolidol.

IV. RISK ASSESSMENT

A. Active Ingredient Characterization

Farnesol and Nerolidol are naturally-occurring, sesquiterpene mite attractants that were originally isolated from essential oils found in plants such as rose, citronella, and lemon grass. By 1960, chemists learned how to manufacture these compounds and natural plant sources were no longer needed. More recently, these compounds were isolated from female mites, where the compounds act as sex pheromones to attract male mites for mating. Farnesol and Nerolidol are practically identical in chemical structure, differing only in the position of one of three double bonds on the aliphatic carbon chain and the position of a hydroxyl group (see Figures 1 and 2 below). They are identical in their mode of action as mite parapheromones.

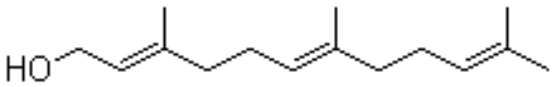

Fig. 1. Farnesol
3, 7, 11-Trimethyl-2,6,10-dodecatriene-1-ol

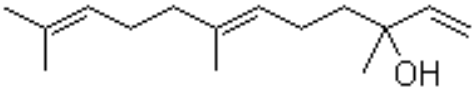

Fig. 2. Nerolidol
3, 7, 11-Trimethyl-1,6,10-dodecatriene-1-ol

The descriptions of the product formulation and production process for both registered products, as well as the formation of impurities, were examined by the Agency and found to be acceptable in meeting current guideline standards. Preliminary analyses were conducted on both Stirrup M® and Biomite™ to determine the Farnesol and Nerolidol content in five batches of each product, and the results were determined to be acceptable by the Agency. The analytical methods used to determine the content of the active ingredients is also acceptable. Physical and chemical properties were submitted for the active ingredients and are adequate. 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 Farnesol and Nerolidol.

All product chemistry data requirements for registration of Farnesol and Nerolidol 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.

Adequate mammalian toxicology data/information are available to support registration of Farnesol and Nerolidol. All toxicology data requirements for Farnesol and Nerolidol 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).

The registrant for Stirrup®-M submitted data for technical Farnesol and Nerolidol. Technical Farnesol and Nerolidol are classified in Toxicity Category IV for acute oral toxicity, Toxicity Category III for acute dermal toxicity, primary eye irritation and primary dermal irritation, and Toxicity Category II for acute inhalation toxicity. No dermal sensitization studies were available for the TGAIs.

Both registrants submitted toxicity data in support of the registration of their respective EPs [Stirrup®-M (Accession No. 261309);and Biomite^{TM} (MRIDs 452620-03 to -07)]. Toxicity categories varied slightly between the two EPs, although these differences were likely due to the differences in the inert (other) ingredients between the two products. Neither EP was a dermal sensitizer.

For more information regarding the acute toxicity data requirements, refer to Tables 3a, 3b and 3c in Appendix A.

b. Subchronic Toxicity

Subchronic data is usually 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. No subchronic studies were conducted for Farnesol and Nerolidol, but none were required.

The 90-day oral feeding study was waived by the Agency. In 1987, Farnesol and Nerolidol were exempted from the requirement of tolerances in or on all raw food commodities under 40 CFR 180.1086; the tolerance exemption was reassessed in 2003 and deemed acceptable. Both biochemical active ingredients also are classified as food additives permitted for direct addition to food for human consumption by the US Food and Drug Administration (FDA) under 21 CFR 172.515 (updated 2003) and are widely used in foods as flavoring substances and adjuvants. In a report on flavoring agents in foods, FAO/WHO (2003) stated that there were no dietary concerns

for Farnesol and Nerolidol. Due to the extremely low application rates and volatility of the active ingredients, little or no residues are expected in or on food or feed commodities treated with products containing Farnesol and Nerolidol.

The 90-day dermal toxicity data requirement was also waived by the Agency. Dermal metabolism of the product is not expected to differ from its oral metabolism. In the acute guideline studies, the product was demonstrated to have low acute dermal toxicity (LD_{50} >2020 mg/kg), was not a dermal irritant, and was not a dermal sensitizer. Prolonged or repeated human dermal exposure is highly unlikely. Due to the extremely low application rates and volatility of the active ingredients, little or no residues are expected in or on plants treated with products containing Farnesol and Nerolidol.

Based on the lack of toxicity (Toxicity Category IV) demonstrated in the acute inhalation toxicity study and the anticipated lack of repeated inhalation exposure under the conditions of product use at a concentration that is likely to be toxic, the requirement for a 90-day inhalation study was waived by the Agency.

c. Developmental Toxicity, Mutagenicity, and Immunotoxicity

No developmental toxicity studies were conducted for Farnesol and Nerolidol, but none are required. Farnesol and Nerolidol are mite parapheromones and are not expected to have any activity in mammals. Literature cited by the registrant for Biomite™ indicated that Farnesol increased the egg laying capacity of female two-spotted spider mites with topical applications at 200 ppm, suggesting gonadotropic effects on two-spotted spider mite, but no toxicity was reported. In laboratory studies, Farnesol has also been shown to inhibit DNA synthesis and induce cell morphology changes in the ovary cells of mosquitoes (*Culex molestus*). No data were available for mammals. However, neither biochemical active ingredient is known to be a mutagen in mammals and they are not chemically related to any known mutagens. Furthermore, the extremely low application rates, volatility of the active ingredients, and lack of expected residues preclude any significant exposure to female humans. Therefore, based on a lack of developmental toxicity, mutagenicity, and immunotoxicity data on mammals, minimal potential for exposure, and prior approvals for uses in or on food by EPA (under 40 CFR 180.1086 in 1987, and reassessed in 2003), FDA (under 21 CFR 172.515; updated 2003), and by FAO/WHO (2003), these substances are not considered to be developmental toxicants.

d. Tier II & Tier III Toxicity/Special Testing

Based on data and information used in fulfillment of Tier I Toxicity data requirements, no Tier II or Tier III/Special Testing data requirements were required.

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 Farnesol and Nerolidol at this time and has no knowledge of Farnesol and Nerolidol being endocrine disruptors. Farnesol and Nerolidol are mite parapheromones that act by a non-toxic mode of action as attractants of mites and have no apparent activity in other animal taxa. Consequently, endocrine-related concerns did not adversely impact the Agency's safety finding for Farnesol and Nerolidol.

2. Dose Response Assessment

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

3. Food Quality Protection Act (FQPA) Considerations

a. Dietary Exposure and Risk Characterization

The Agency did not conduct a new dietary exposure risk assessment for Farnesol and Nerolidol. Due to the extremely low application rates and volatility of the active ingredients, little or no residues are expected in or on food or feed commodities treated with products containing Farnesol and Nerolidol. The EPA (1987 and 2003), FDA (2003), and FAO/WHO (2003) have previously evaluated these substances and have determined that there are no dietary concerns.

b. Drinking Water Exposure and Risk Characterization

The Agency determined that there would be no direct exposure to water from the mite parapheromone products as they are applied at extremely low rates to terrestrial plants and there are no direct application to aquatic sites. In a Hazard Assessment conducted by EPA in support of the registration of Stirrup M® to determine the potential for indirect exposure (i.e. runoff) to aquatic sites (see discussion under Environmental Fate below), the Estimated Environmental Concentration (EEC) of Farnesol + Nerolidol in aquatic ecosystems, following a seasonal applications of either Stirrup M® or Biomite™ was calculated to be 1.29 parts per billion (ppb) and 3.16 ppb, respectively. These levels are well below the highest doses used for acute oral toxicity testing (see Tables 3a, 3b, and 3c in Appendix A) that were categorized as practically non-toxic. Farnesol and Nerolidol are mite parapheromones, and as such, are volatile compounds that would rapidly diffuse into the atmosphere. Therefore, movement of the substances from terrestrial sites of application to surface water or via spray drift, or groundwater via runoff or movement through soil is highly unlikely.

c. Acute and Chronic Dietary Risks for Sensitive Subpopulations Particularly Infants and Children

FFDCA section 408 provides that the Agency shall apply an additional tenfold margin of exposure (safety) for infants and children in the case of threshold effects to account for pre- and post-natal toxicity and the completeness of the database unless the Agency determines that a different margin of exposure (safety) will be safe for infants and children. Margins of exposure (safety) are often referred to as uncertainty (safety) factors. In this instance, based on all the available information, the Agency has concluded that there is reasonable certainty that no harm to infants and children or adults will result from the use of Farnesol and Nerolidol when label instructions are followed.

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

No occupational, residential and day care exposure assessment was conducted for products containing Farnesol and Nerolidol, but none are required. Based on the use patterns of products containing Farnesol and Nerolidol as active ingredients, anticipated exposure is not likely to result in unreasonable risk to humans or the environment. Appropriate personal protective equipment (PPE) instructions on the current product label will mitigate occupational exposure to workers/handlers and applicators. All intended uses are agricultural. There will be no residential, school, or day care exposure.

5. Aggregate Exposure from Multiple Routes Including Dermal, Oral, and Inhalation

There is reasonable certainty that no harm to the US population will result from aggregate exposure to residues of Farnesol and Nerolidol. This includes all exposures for which there is reliable information. The Agency arrived at this conclusion based on the lack of toxicity of Farnesol and Nerolidol and the already widespread exposure to Farnesol and Nerolidol without any reported adverse effects on human health. The risks from aggregate exposure via oral, dermal and inhalation exposure are a compilation of three low-risk exposure scenarios and are negligible.

6. Cumulative Effects

Based on the information available to the Agency, there is no indication that toxic effects associated with exposure to Farnesol and Nerolidol are cumulative. Because of Farnesol and Nerolidol lack of toxicity, cumulative effects with other substances that share a common mechanism of toxicity are not expected.

7. Risk Characterization

The Agency considered human exposure to Farnesol and Nerolidol in light of the relevant safety factors in FQPA and FIFRA. A determination has been made that no unreasonable adverse effects to the U.S. population in general, and to infants and children in particular, will result from the use of Farnesol and Nerolidol when used in accordance with EPA-approved labeling.

C. ENVIRONMENTAL ASSESSMENT

1. Ecological Hazards

Adequate non-target toxicology data/information are available to support registration of Farnesol and Nerolidol. All non-target toxicology data requirements for Farnesol and Nerolidol have been **satisfied.**

The registrant for Stirrup M® submitted non-target organism studies for birds, freshwater fish, and freshwater aquatic invertebrates (Accession No. 264426). These studies were bridged to support the registration of Biomite™. Stirrup M® is practically non-toxic to birds on a acute oral and dietary toxicity basis and there are no known adverse effects for non-target plants and non-target insects. The product was moderately toxic to freshwater fish and freshwater aquatic invertebrates. Farnesol and Nerolidol are ubiquitous in plants as essential oils and are not likely to be toxic to plants. Farnesol and Nerolidol, have a non-toxic mode of action, and are parapheromones that are only attractive to eotetranychid, tetranychid and panonychid mites, all of which are plant pests.

a. Non-Target Avian Toxicity and Exposure

In the original Hazard Assessment conducted by EPA/OPP/EFED (see Memorandum from R. Pilsucki to M. Slimak, dated 12/2/1986), using the nomogram developed by Hoeger and Kenaga (1972), it was estimated that the total potential residue of Farnesol + Nerolidol following 6 applications of Stirrup M® (based on label use directions) would be 310 ppb on fruit, assuming that there was no dissipation following application.

The same approach was used to determine the potential residues that may occur following applications of Biomite™. Using the same equations as above for Stirrup M®, the total potential residue following 6 applications of Biomite™ was estimated to be 700 ppb (see Memorandum from R. S. Jones to S. Morrill, dated 01/31/2008).

The estimated residue values for both products are well below the lowest avian acute toxicity value of >2000 mg/kg and the lowest avian dietary toxicity value of > 5000 ppm; and are well below any Levels of Concern (LOCs) for birds. Therefore, it is highly unlikely that there will be any adverse effects on birds resulting from the use of Stirrup M® or Biomite™.

b. Non-Target Aquatic Organism Toxicity and Exposure

In a Hazard Assessment conducted by EPA in support of the registration of Stirrup M® to determine the potential for indirect exposure (i.e. runoff) to aquatic sites (see discussion under Environmental Fate below), the Estimated Environmental Concentration (EEC) of Farnesol + Nerolidol in aquatic ecosystems, following a seasonal applications of either Stirrup M® or Biomite™ was calculated to be 1.29 parts per billion (ppb) and 3.16 ppb, respectively. Both aquatic EEC values are well below the lowest aquatic organism toxicity value of 1.8 parts per million (ppm). Therefore, it is highly unlikely that there will be any adverse effects on fish or aquatic invertebrates resulting from the use of Stirrup M® or Biomite™.

c. Non-Target Plant, Insect, and Terrestrial Wildlife

No non-target plant studies were submitted, but none are required. Farnesol and Nerolidol are widespread in plants and are found as naturally-occurring components in the essential oils of rose, citronella, and lemon grass, and as a volatile from apricot fruit. Furthermore, application rates are extremely low and the high volatility of Farnesol and Nerolidol would not result in persistent residues. There are no concerns for non-target plants.

Non-target insect studies or waiver requests were not submitted, but were not required. Farnesol and Nerolidol have a non-toxic mode of action and are parapheromones that are only attractive to eotetranychid, tetranychid and panonychid mites, all of which are plant pests. Application rates for Farnesol and Nerolidol are extremely low and the high volatility of Farnesol and Nerolidol would not result in persistent residues. There are no concerns for non-target insects.

There are no known effects on terrestrial wildlife when the products are used in accordance with approved labeling. Farnesol and Nerolidol are mite parapheromones that act by a non-toxic mode of action and are only attractive to eotetranychid, tetranychid and panonychid mites.

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

2. Environmental Fate and Ground Water Data

In the original Hazard Assessment conducted by EPA/OPP/EFED (see Memorandum from R. Pilsucki to M. Slimak, dated 12/2/1986), it was calculated that when Stirrup M® was applied in accordance with approved labeling, the maximum rate of active ingredient would be approximately 0.007 lb/A/application. The label specified only that the product could be applied as needed, but it was assumed that the product would only be applied when it was necessary to apply miticides. Based on an average generation time of three weeks for mites, and assuming that the product would be applied once a generation over a 4-month growing season, it was estimated that the product would be applied approximately six times per growing season. The seasonal application rate was then estimated to be 0.042 lb total active ingredient (Farnesol + Nerolidol) per acre.

Application rates of Biomite™ were calculated similarly. Although Biomite™ contains less than half the total Farnesol + Nerolidol content of Stirrup M®, it is applied at substantially higher rates (up to 8 qts formulated product on food crops and up to 12 qts formulated product

on ornamentals). The maximum rate is equivalent to approximately 0.017 lbs active ingredient/A/application. Based on these application rates, and assuming a maximum of 6 applications per growing season, the seasonal application rate was estimated to be 0.103 lbs/A of Farnesol + Nerolidol.

Using the information above, the Estimated Environmental Concentration (EEC) of Farnesol + Nerolidol in aquatic ecosystems, following a seasonal application of Stirrup M®, was calculated to be 1.29 ppb. Using these same equations in a more recent risk assessment (see Memorandum from R. S. Jones to S. Morrill, dated 01/31/2008), the EEC of Farnesol + Nerolidol, following application of Biomite™ was estimated to be 3.16 ppb.

3. Ecological Exposure and Risk Characterization

Based on the review of the above stated non-target organisms and environmental fate studies, and the Endangered Species Assessment (see below), EPA has determined that anticipated risk is not likely to result in unreasonable risk to non-target organisms or the environment when products containing Farnesol and Nerolidol are used in accordance with EPA-approved label use directions.

The potential for exposure to non-target wildlife is minimal. Based on the data obtained from non-target organism laboratory studies and information presented in the Environmental Fate and Groundwater Data section above, it is highly unlikely that non-target organisms, particularly aquatic organisms, would be exposed to potentially toxic levels of Farnesol and Nerolidol via runoff and/or movement through the soil. Farnesol and Nerolidol are extremely volatile and undergo rapid biodegradation in soil and water. Therefore, no unreasonable adverse effects to the environment are expected from the use of Farnesol and Nerolidol when used in accordance with EPA-approved labeling.

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

4. Endangered Species Assessment

Farnesol and Nerolidol are naturally-occurring compounds isolated from the essential oils of a wide variety of plants and also are produced by tetranychid mites as sex pheromones. The active ingredients are applied at extremely low concentrations (approximately 0.017 lbs/A/growing season) and are intended for use as attractants for mite pests of crops. The active ingredients have no known toxicity, but are applied with USEPA-registered miticides to control tetranychid mite pests of crops. Farnesol and Nerolidol are practically non-toxic to birds (on an acute and dietary basis), practically non-toxic to mammals, and moderately toxic to fish and aquatic invertebrates. When applied in accordance with approved labeling, estimated environmental concentrations (EECs) will be well below any known toxic endpoints for fish and aquatic invertebrates by approximately 1000 fold. No adverse effects to non-target plants or insects are anticipated. No ecological effects incidents have been reported since the first of two products were registered in 1986. The active ingredients are naturally-occurring and are found in many plants. The presence of Farnesol and Nerolidol in plants results in regular exposure to

insects on a contact and dietary basis. When the registered products are applied in accordance with approved labeling, the active ingredients are applied at extremely low concentrations

(approximately 0.017 lbs/A/growing season) and may potentially result in only minimal residues on treated plants.

Based on this screening level assessment, EPA has determined that there will be **No Effects (NE)** of Farnesol and Nerolidol on threatened or endangered terrestrial or aquatic species as listed by the U.S. Fish and Wildlife Service (USFWS) when products containing this active ingredient are used in accordance with EPA-approved labeling.

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).

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 Farnesol and Nerolidol. Such products are not expected to cause unreasonable adverse effects, and are likely to provide protection as claimed when used in accordance with EPA-approved labeling. Therefore, Farnesol and Nerolidol is eligible for registration for the labeled uses.

B. Regulatory Decision

The data submitted fulfill the requirements of registration for use in the control eotetranychid, tetraychid, and panonychid mites on agricultural crops and ornamental plants when used in combination with a conventional chemical miticide. Refer to Appendix B for product-specific information.

VI. ACTIONS REQUIRED BY REGISTRANTS

The Agency evaluated all of the data submitted in connection with the initial registration of Farnesol and Nerolidol 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 and other supporting documents listed or footnoted in the following tables are representative of supporting data for the original registration of the products containing Farnesol and Nerolidol as their active ingredients. Subsequent to this registration, there may be additional MRIDs and references that support registration of other products containing these active ingredients.

TABLE 1. Product Chemistry Data Requirements for Farnesol and Nerolidol (40 CFR § 158.2030)

OPPTS Guideline No.	Study	Results
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.
830.1700	Analysis of samples	Submitted data satisfy the requirements for analysis of samples.
830.1750	Certification of limits	Limits listed in the CSF are adequate / acceptable.
830.1800	Analytical method	Acceptable.

TABLE 2. Physical and Chemical Properties of *Active Ingredient* (40 CFR § 158.2030)			
OPPTS Guideline No.	**Property**	**Description of Result [1]**	
		Farnesol	**Nerolidol**
830.6302	Color	Colorless [2] to Pale yellow	Straw yellow
830.6303	Physical State	Liquid	Liquid
830.6304	Odor	Light woody floral to citrus-lime [2]	Rose and apple
830.6313	Stability to Normal and Elevated Temperatures, Metals and Metal Ions	Stable, incompatible with strong oxidizing agents [4]	No data available, but likely is identical to Farnesol due to strong chemical similarity
830.6315	Flammability	96 °C [4]	-
830.6317	Storage Stability	Stable for 1 year	Stable for 1 year
830.6319	Miscibility	Not intended for dilution with petroleum solvents	Not intended for dilution with petroleum solvents
830.6320	Corrosion Characteristics	Not available	Not available
830.7000	pH	Not applicable; substance is an oil	Not applicable; substance is an oil
830.7050	UV/Visible Light Absorption	192-196 nm [2]	
830.7100	Viscosity	Not available	Not available
830.7200	Melting Point/Range	Not applicable; substance is a liquid	Not applicable; substance is a liquid
830.7220	Boiling Point/Range	263 °C	276 °C
830.7300	Density	0.887	0.875
830.7520	Particle Size, Fiber Length and Diameter Distribution	Not applicable; substance is a liquid	Not applicable; substance is a liquid
830.7550 830.7560 830.7570	Partition Coefficient (n-Octanol/Water)	$\log K_{ow} = 5.77$ [3]	-
830.7840	Water Solubility	Insoluble	Insoluble
830.7950	Vapor Pressure	3.94×10^{-5} mm Hg [3]	-

[1] Data from Appendix IV to Memorandum from S. Malak to B. Mandava, dated 12/29/1986, except where otherwise indicated.
[2] MRID 45262010, pp. 12, 13, 23
[3] HSDB (2008 update)
[4] Oxford (2003 update)

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Table 3a. Human Toxicology Data Requirements for Undiluted Farnesol and Nerolidol (40 CFR § 158.2050) [1]			
Guideline .	Results	Toxicity Categories	Accession No.
Acute oral toxicity (rat) (870.1100)	Farnesol & Nerolidol: LD_{50} >5050 mg/kg	IV	264527
Acute dermal toxicity (rat) (870.1200)	Farnesol & Nerolidol: LD_{50} >2010 mg/kg	III	
Acute inhalation toxicity (rat) (870.1300)	Farnesol LD_{50} = 0.917 mg/L	II	
	Nerolidol LD_{50} = 1.448 mg/L		
Primary eye irritation (rabbit) (870.2400)	Farnesol & Nerolidol: Minimally irritating	III	
Primary dermal irritation (rabbit) (870.2500)	Farnesol: Practically non-irritating	IV	
	Nerolidol: Slight irritant	III	
Dermal sensitization (guinea pig) (870.2600)	No data for TGAIs; Stirrup™ (0.972% Farnesol & 0.788% Nerolidol) not a sensitizer	-	
Hypersensitivity incidents (870.3400)	None reported	-	-
90-Day oral toxicity (870.3100)	Waived; no subchronic oral exposure expected	-	-
90-Day dermal toxicity (870.3250)	Waived; no subchronic dermal exposure expected	-	-
90-Day inhalation toxicity (870.3465)	Waived; no subchronic inhalation exposure expected	-	-
Mutagenicity (870.5100, 5300, and 5375)	Waived; no mammalian activity expected	-	-
Developmental toxicity (870.3700)	Waiver; no mammalian activity expected	-	-

[1] DERs contained in Memorandum from W. Woodrow to A. Kocialski, dated 05/28/1987.

Table 3b. Human Toxicology Data Requirements for Stirrup™ (0.972% Farnesol and 0.788% Nerolidol) (40 CFR § 158.2050) [1, 2]			
Guideline .	Results	Toxicity Categories	Accession No.
Acute oral toxicity (rat) (870.1100)	LD_{50} = 5050 mg/kg (males and females)	IV	261309
Acute dermal toxicity (rat) (870.1200)	LD_{50} >2020 mg/kg (males and females)	III	
Acute inhalation toxicity (rat) (870.1300)	LC_{50} > 3.37 mg/L (males and females)	IV	
Primary eye irritation (rabbit) (870.2400)	Slight ocular irritation at 1 hr post-instillation that cleared within 24 hr.	IV	
Primary dermal irritation (rabbit) (870.2500)	Slight irritation at 1 hr post dosing that cleared within 24 hr	IV	
Dermal sensitization (guinea pig) (870.2600)	Not a sensitizer	-	264527 [3]

. [1] The DERs reviewed under Accession No. 262309 indicate that the Farnesol content of the test substance was 0.923%, whereas the product label and CSF state that the Farnesol content is 0.972%.

[2] DERs contained in Memorandum from W. Woodrow to A. Kocialski, dated 07/09/1986 (except for Dermal Sensitization).

[3] DER contained in Memorandum from W. Woodrow to A. Kocialski, dated 05/28/1987

Table 3c. Human Toxicology Data Requirements for Biomite ™ [1] (0.417% Farnesol and 0.167% Nerolidol) (40 CFR § 158.2050)			
Guideline .	Results	Toxicity Categories	Accession No.
Acute oral toxicity (rat) (870.1100)	LD_{50} = 5242 mg/kg (males); LD_{50} = 3753 mg/kg (females)	III[2]	45262003
Acute dermal toxicity (rat) (870.1200)	LD_{50} >5050 mg/kg (males and females)	IV	45262004
Acute inhalation toxicity (rat) (870.1300)	LC_{50} > 2.64 mg/L (males and females)	IV	45262005
Primary eye irritation (rabbit) (870.2400)	Corneal opacity & conjunctivitis symptoms cleared by day 10 post-instillation	II	45262006
Primary dermal irritation (rabbit) (870.2500)	Very slight to well defined erythema & edema clearing by day 14 posttreatment	III	45262007
Dermal sensitization (guinea pig) (870.2600)	Treated and naive control animals showed no sensitivity symptoms 24 & 48 hrs after the challenge dose	Not a sensitizer	45262008

1 Biomite™ contains 0.417% Farnesol, 0.167% Nerolidol, 0.417% Geraniol, and 0.417 % Citronellol as its active ingredients. Active ingredients collectively comprise 1.43% of the end-use product by weight.

2 Based on female LD_{50}.

TABLE 4. Non-target organism toxicity requirements for Farnesol and Nerolidol (40 CFR 158.2060)			
Guideline .	Results	Toxicity Categories	Accession No.
Avian Acute Oral Toxicity (850.2100)	>2000 mg/kg (Mallard duck) >2000 mg/kg (Bobwhite quail)	Practically Non-toxic	264426
Avian Dietary Toxicity (850.2200)	>5000 ppm (Mallard duck) >5000 ppm (Bobwhite quail)	Practically Non-toxic	
Freshwater Fish LC50 (850.1075)	=1.8 ppm (Rainbow trout)	Moderately Toxic	
Freshwater Invertebrate Toxicity (850.1010)	=2.2 ppm (Daphnids)	Moderately Toxic	
Non-target Plants (850.4000)	See Non-Target Plant Summary above	No known adverse effects	Not Applicable
Non-target Insects (850.3020; 850.3030; and/or 850.3040)	See Non-Target Insect Summary above		

VIII. Appendix B.

Stirrup M® is tank-mixed in water or an emulsified vegetable oil with a registered miticide. The product may be applied by manually-operated, ground, or aerial spray equipment at rates of up to 6 oz/A.

Biomite^{TM} is tank-mixed in water with a registered miticide. The product may be applied at up to 8 qts/A on food crops and 12 qts/A on ornamentals

IX. Appendix C.

REFERENCES

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