US Environmental Protection Agency
Office of Pesticide Programs

BIOPESTICIDES REGISTRATION ACTION DOCUMENT

Suggested Format for Acute Toxicity Studies

CITRONELLOL (PC Code 167004)

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U.S. Environmental Protection Agency
Office of Pesticide Programs
Biopesticides and Pollution Prevention Division
Citronellol
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BIOPESTICIDES REGISTRATION ACTION DOCUMENT TEAM

Office of Pesticide Programs:

Biopesticides and Pollution Prevention Division

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I. Executive Summary

A. IDENTITY

The technical grade active ingredient (TGAI) is citronellol, a colorless to pale yellow oily liquid with a sweet, rose, leather, musty, floral odor. The end-use product is BIOMITE™, which contains three active ingredients registered for use in other pesticide products, in addition to the new active ingredient, citronellol. BIOMITE™ is manufactured by an integrated process.

The product chemistry data submitted by the registrant satisfy the requirements for product identity.

B. USE/USAGE

The end-use product BIOMITE™ is to be used for mite control on agricultural crops, ornamental plants, and in professional landscape settings.

C. RISK ASSESSMENT

No unreasonable adverse effects on humans or the environment are anticipated from aggregate exposure to citronellol. This includes all anticipated exposures for which there is reliable information.

1. Human Health Risk Assessment

a. Toxicological Endpoints

The Agency reviewed information submitted by the registrant to identify toxic endpoints in the following studies: acute oral, acute dermal, acute inhalation, primary eye irritation, primary dermal irritation, and dermal sensitization. The end-use product was placed in Toxicity Category IV for acute dermal and inhalation toxicity; Toxicity Category III for acute oral and primary dermal irritation; and Toxicity Category II for eye irritation. The product was not a dermal sensitizer. A waiver was requested for mutagenicity, and the request was granted by the Agency based on studies submitted from the technical literature. Requested waivers for subchronic, chronic, oncogenic, and teratogenic effects were granted by the Agency based on the lack of toxicity and anticipated low exposure from the intended use of the product.

b. Human Exposure

The most likely human exposure to citronellol would be to agricultural applicators of the end-use product. The risks to humans are mitigated as long as the product is used according to label directions and the appropriate precautionary and first aid statements are heeded.

c. Risk Assessment

The Agency has considered citronellol in light of the relevant safety factors in the Food Quality Protection Act (FQPA) of 1996 and under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and has not identified any dietary or non-dietary exposure issues that may affect the U.S. population in general, including infants and children. The Agency has thereby determined that there is reasonable certainty that no harm will result from aggregate exposure to citronellol residues, including dietary exposures and all other exposures for which there is reliable information.

2. Ecological Risk Assessment

a. Toxicity Endpoints

No toxic endpoints were identified.

b. Ecological Exposure

Waivers were requested for ecotoxicity/nontarget organism studies and granted by the Agency based on the anticipated low rate of exposure and rapid biodegradation in soil.

c. Risk Assessment

Risk to the environment and non-target organisms is expected to be minimal since levels of citronellol resulting from use of BIOMITE™ are expected to be as low or lower than those already existing naturally in many food crops. Therefore, the Agency believes the use of BIOMITE™ according to the label use directions should not result in significant adverse effects to wildlife or the environment.

A. DATA GAPS /LABELING RESTRICTIONS

There are no data gaps. Labeling restrictions include: “For terrestrial use only,” “Do not apply with surfactants,” and “Do not apply this product through any type of irrigation system.” In addition, precautionary labeling is required to mitigate risks that may be associated with proposed uses (see “Labeling Rationale” section of this document for details).

II. Overview

A. ACTIVE INGREDIENT OVERVIEW

Common Name: Citronellol

Chemical Names: 3,7-dimethyl-6-octen-1-ol

Trade and Other Names: BIOMITE™

CAS Registry Number: 106-22-9

OPP Chemical Code: 167004

Basic Manufacturer: Natural Plant Protection
Route D'Artix - B. P. 80
64150 Nogueres, FRANCE

B. USE PROFILE

Proposed uses and application methods for BIOMITE™ include the following:

Type of Pesticide: Biochemical miticide

Use Sites: The end-use product BIOMITE™ will be used on agricultural crops, ornamental plants, and in professional landscape settings.

Target Pests: Mites (*Eotetranychus* spp., *Tetranychus* spp., and *Panonychus* spp.), including two-spotted mites, pacific mites, willamette mites, citrus rust mites, broad mites, and European red mites.

Formulation Type: Liquid

Method and Rates of Application: BIOMITE™ is applied with conventional spray equipment at a concentration of 0.37-0.59 gallons of product/100-400 gallons of water per acre on grapes, hops, stonefruits, and pome fruits; 0.37-0.59 gal/100-300 gallons of water per acre on strawberries; 0.1-0.32 gal/50-150 gallons of water per acre on cucurbits; and 0.37-0.59 gal/100-600 gallons of water per acre on ornamental plants, nursery stock, bareroot stock, container stock, bedding stock, and flowering stock, field-grown cut flowers, vegetable transplants, and nursery and landscape plants.

Use Practice Limitations: For terrestrial use only. Do not apply with surfactants. Do not apply through any type of irrigation system.

Timing: Application should occur as soon as mites are identified on the plants, or when conditions favor mite outbreaks.

C. ESTIMATED USAGE

None used yet since this will be the first registered product.

D. DATA REQUIREMENTS

The data requirements for granting this registration under Section 3(c)(5) of FIFRA have been reviewed by the Agency. The mammalian toxicology and ecological effects data requirements for citronellol have been fulfilled. Product analysis data requirements are adequately satisfied.

E. REGULATORY HISTORY

On May 23, 2000, the Agency received a Notice of Filing Petition to Establish an Exemption from the Requirement of a Tolerance (65 FR 33318) for citronellol in or on all raw agricultural commodities. No comments were received during a 30-day comment period following publication of the petition. A notice of receipt of an application for registration of BIOMITE™ , containing citronellol as an active ingredient, 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.

F. CLASSIFICATION

On April 15, 1999, the Biochemical Classification Committee determined that citronellol is classified as a biochemical pesticide due to its non-toxic mode of action as an attractant for mites.

G. FOOD CLEARANCES/TOLERANCES

An exemption from the requirement of a tolerance for residues of citronellol in or on all food commodities has been established in association with this registration**.**

III. Science Assessment

A. PHYSICAL/CHEMICAL PROPERTIES ASSESSMENT

All product chemistry data requirements for the TGAIs and end-use product are met.

1. Product Identity and Mode of Action

a. Product Identity:

Citronellol, a monoterpene alcohol, is a colorless to pale yellow oily liquid with a sweet rose, leather, musty, floral odor. It is an active ingredient in the end-use product BIOMITE™ , which is produced by an integrated system that involves the blending of 0.167% farnesol, 0.417% nerolidol, 0.417% geraniol, and 0.417% citronellol with the inert ingredients. Farnesol, nerolidol, and geraniol are registered ingredients.

b. Mode of Action:

On April 15, 1999, The Biochemical Classification Committee determined that the active ingredient citronellol appears to act as an attractant kairomone, while the other three active ingredients (Nerolidol, Geraniol, and Farnesol) in the end-use product, BIOMITE™ act as sex-specific arrestant kairomones.

2. Physical And Chemical Properties Assessment

The physical and chemical characteristics of BIOMITE™ were submitted to support the registration. They are summarized in Table 1.

TABLE 1. Product chemistry data requirements

GUIDELINE NO.	STUDY	RESULTS	MRID NO.
151B-10 151B-11 151B-12	Product identity; Manufacturing process; Discussion of formation of unintentional ingredients	The product contains 0.417 % citronellol, 0.417% geraniol, 0.417% nerolidol, and 0.167% farnesol as active ingredients. It is manufactured by an integrated process. No unintentional ingredients are formed. Acceptable data was submitted to the agency.	452620-01
151B-13	Analysis of samples	Acceptable data was submitted to the Agency	452620-01
151B-15	Certification of limits	Acceptable limits were submitted to the Agency	452620-01
151B-17	PHYSICAL/CHEMICAL PROPERTIES OF BIOMITE™		
151B-17(a)	Color	Not required	452620-01
151B-17(b)	Physical State	Liquid	452620-01
151B-17(c)	Odor	Not required	452620-01
151B-17(d)	Melting Point	N/A, product is liquid	
151B-17(e)	Boiling Point	Not required	
151B-17(f)	Density/Specific gravity	0.951 @ 20°C, 7.94 lbs/gallon	452620-02
151B-17(g)	Solubility	Not required	
151B-17(h)	Vapor pressure	Not required	
151B-17(i)	pH	5.74 (1% concentration)	452620-02
151B-17(j)	Stability	Not required	
151B-17(k)	Flammability	Flash point 93°C (Tag closed tester)	452620-02
151B-17(l)	Storage Stability	Not required	452620-01
151B-17(m)	Viscosity	16.41 centistokes @ 40°C, 33.461 centistokes @ 20°C	452620-02
151B-17(n)	Miscibility	Product is not intended to be diluted with petroleum solvents	452620-01
151B-17(o)	Corrosion Characteristics	Not corrosive	452620-01
151B-17(p)	Octanol/water partition coefficient	Not required	

B. HUMAN HEALTH ASSESSMENT

The submitted mammalian toxicity studies and the requested waivers to support the registration application and tolerance exemption petition for citronellol adequately satisfy the requirements to register a new biochemical pesticide intended for use on food commodities.

1. Toxicology Assessment

Adequate mammalian toxicology data are available to support registration of the new active ingredient, citronellol. Citronellol is widely used as a fragrance component of detergents, soaps, creams, lotions, perfumes, and aromatherapy products. It is also a component of citronella oil used in candles, sprays, oils, lotions, and towellettes as a repellent for mosquitoes and other flying insects. Citronellol is found in over 30 essential oils, as well as certain fruits, edible plants, wines, beer, and black tea. It has GRAS status (21 CFR 172.515) when used as a synthetic flavoring agent and adjuvant for direct addition to foods for humans. Citronellyl acetate, which is used as a flavoring agent, is readily hydrolyzed to citronellol in the intestines of mammals via a number of common esterases. Citronellol has been shown to undergo further metabolism (alcohol oxidation, hydration, and dydrogenation) to non-toxic polar compounds which are subsequently metabolized by glucuronidation, with the resulting glucuronide conjugates subsequently excreted in the urine. Consequently, the breakdown byproducts of citronellol are of little toxicological concern. The mode of action (attraction) of citronellol toward its target pest species is a physical, rather than a toxic action. Information submitted by the registrant indicates there is already widespread exposure to citronellol without any reported adverse effects to human health. The acute toxicity studies (Table 2), in conjunction with data/information obtained from the open literature (Table 3), demonstrate that no risks to human health are expected from the pesticidal use of citronellol, based on its already-wide usage and the expected low exposure to humans resulting from label-directed use rates.

a. Acute Toxicity

i. Acute oral toxicity (OPPTS 870.1100; 152-10; MRID 452620-03). Male and female rats (5 per sex) were dosed once with 2500 to 5500 mg/kg of BIOMITE™. All rats exhibited clinical signs of toxicity such as decreased activity, crusted muzzles, stained fur, diarrhea, soft feces, dark urine, polyuria, piloerection, ptosis, ocular discharge, respiratory chirp/gurgle, salivation, and/or withdrawn testes. The surviving rats recovered by day 9. The decedents exhibited discolored contents in the gastrointestinal tract; discolored lungs, liver, and spleen; gas in the gastrointestinal tract; lateral recumbency and nasal discharge; and/or empty intestines. Two surviving 3500 mg/kg females and 2 surviving 5500 mg/kg males had mottled livers. The acute oral LD_{50} was 5242 mg/kg for males and was 3573 mg/kg for females; the combined LD_{50} could not be calculated. Classification: Acceptable. Toxicity Category III based on the LD_{50} in female rats.

ii. Acute dermal toxicity (OPPTS 870.1200; 152-11; MRID 452620-04). Male and female rabbits (5/sex/dose) received a single dermal dose of 5050 mg/kg BIOMITE™ for 24 hours. Symptoms exhibited by some rabbits included not eating, soft feces, decreased

defecation, and/or very slight edema which cleared by day 7. Necropsies were negative. The acute dermal LD_{50} was >5050 mg/kg for males and females. Classification: Acceptable. Toxicity Category IV.

iii. Acute inhalation toxicity (OPPTS 870.1300; 152-12, MRID 452620-05). Male and female rats (5 per sex) were exposed nose-only to a gravimetric concentration of 2.64 mg/L of BIOMITE™ for four hours. During exposure, 3 males and 3 females had decreased activity and by day 2 all rats had decreased activity; symptoms cleared by day 3. Respiratory gurgles were noted from all males and 3 females on day 1, and from all rats on day 2. All of the females recovered by day 4, but 1 male did not recover by the end of the study. Piloerection, diarrhea, and decreased defecation were exhibited by some of the males. Necropsies were negative. The acute inhalation LC_{50} was > 2.64 mg/L. Classification: Acceptable. Toxicity Category IV.

iv. Primary eye irritation (OPPTS 870.2400; 152-13, MRID 452620-06). One male and 2 female rabbits were dosed with 0.1 mL of undiluted BIOMITE™ in the right eye. Corneal opacity was noted on the eyes of 2 of three rabbits at 48 hours. Opacity was observed in 1 of 3 rabbits at day 4 and day 7; these symptoms cleared by day 10. Rabbits exhibited conjunctivitis from 1 hour post-dosing through day 7; symptoms cleared by day 10. BIOMITE™ was moderately irritating to the eyes of rabbits. Classification: Acceptable. Toxicity Category II.

v. Primary dermal irritation (OPPTS 870.2500; 152-14; MRID 452620-07). One male and 2 female rabbits were dosed with 0.5 mL of BIOMITE™ on clipped skin for 4 hours. Very slight erythema with very slight edema was noted at the test site on all rabbits one hour after patch removal, which persisted or intensified to "well-defined" through day 10. All skin irritation cleared by day 14. Based on the data, BIOMITE™ was moderately irritating to the skin of rabbits. Classification: Acceptable. Toxicity Category III.

vi. Hypersensitivity (OPPTS 870.2600; 152-15, MRID 452620-08). Guinea pigs were tested using the Buehler method. All animals survived and gained weight during the study. Very faint erythema was noted on 4 out of 20 animals at 24 hours after the first induction dose at the application site, which cleared by 48 hours. Faint to moderate erythema was noted on all animals 24 hours after the second induction dose at the application site. Twenty-four hours after the third induction dose, very faint (usually nonconfluent) to strong erythema was noted at the application site on the skin in all animals. The treated test and naive control animals showed no signs of reactivity at 24 and 48 hours after challenge. Classification: Acceptable. Biomite was not a dermal sensitizer to guinea pigs using the Buehler method..

vii. Other Toxicity Data. Using data obtained from the technical literature, the registrant presented acute, chronic, subchronic, and/or mutagenicity/genotoxicity data for citronellol. These data are summarized in Table 3. The Agency notes that these data from the technical literature may be used to waive the requirements for guideline studies

for acute oral toxicity, acute dermal toxicity (Toxicty Category IV), and primary dermal irritation (Toxicity category) on a technical grade (TGAI) of citronellol.

Waivers of required studies on the technical grade of the active ingredient for acute toxicity, genotoxicity, reproductive toxicity, developmental toxicity, subchronic toxicity in mammalian species, and acute toxicity to non-target species were requested by the registrant for BIOMITE^{TM}. The waivers were based on the ubiquity of citronellol in nature; the long history of its use in cosmetics, fragrances, detergents, and household cleaners; the natural occurrence in fruits and beverages; the widespread use as a synthetic flavoring agent and adjuvant; and the low anticipated exposure to humans and the environment due to the very low concentration of citronellol in the pesticide product. In addition, data on the toxicity of citronellol from publicly available technical literature was presented to the Agency (MRID 452620-10) for acute oral toxicity in the rat (Toxicity category III), acute dermal toxicity (Toxicity category IV, no species indicated), dermal irritation (moderate in humans), and mutagenicity/genotoxicity (negative in Ames assay in three *Salmonella typhimurium* strains tested at 100 μg). These data are summarized in Table 3. The Agency notes that these data from the technical literature may be used to waive the requirements for guideline studies.

Toxicity data were also submitted for citronellyl acetate (and other esters of citronellol), which is widely used as a flavoring agent. According to the World Health Organization (WHO), dietary intake of citronellol is estimated, based on the quantity of citronellyl acetate consumed in the diet (Food Additives Series 40; 49th meeting of the Joint FAO/WHO Expert Committee on Food Additives (JEFCA), 1998). The rationale for the use of citronellyl acetate toxicity data to estimate the dietary toxicity of citronellol is based on data demonstrating that citronellyl acetate is readily hydrolyzed to citronellol in the intestines of mammals, and that citronellol is further metabolized to non-toxic, polar compounds that are excreted in the urine (JEFCA 1998). Data obtained from toxicity studies using citronellyl acetate as the test substance demonstrated an acute oral Toxicity category IV in rat; no adverse effects with an oral dose of 290 mg/kg/day for 14 days and 13 weeks in mice, and no adverse effects in a chronic dietary/carcinogenicity study in rats fed 290 mg/kg/day for 103 weeks Further, based on the data submitted by the registrant for the pesticide product and the data on citronellol and citronellyl acetate from the public literature, the no adverse effects to humans would be anticipated via acute, subchronic, or chronic dietary exposures to citronellol, particularly at the low levels of citronellol in the pesticide product under consideration for registration by the Agency.

No information nor request for waiver for acute inhalation toxicity for the technical grade of citronellol were submitted; however, the very low levels of citronellol in the registered product, along with the many uses of this active ingredient as a fragrance and flavoring agent described previously in this document, no data will be required for a technical grade of the active ingredient at this time. If other products with higher concentrations of the active ingredients in BIOMITE^{TM} are submitted for registration, the Agency will consider the need for this data at that time.

b. Mutagenicity and Developmental Toxicity

Based on the data submitted from the technical literature, citronellol was not mutagenic at 100 µg against *S. typhimurium* TA 97 and TA 102 and was negative against TA 98. Waivers were requested for mammalian mutagenicity and teratogenicity and were granted by the Agency based on the low toxicity and the lack of significant residues anticipated on treated crops.

TABLE 2. Toxicity data requirements

GUIDELINE NO.	STUDY	RESULTS	MRID NO.
870.1100; 152.10	Acute oral toxicity in rats	LD_{50} = 5242 mg/kg for males, 3573 mg/kg for females. Toxicity Category III	452620-03
870.1200; 152-11	Acute dermal toxicity in rats	LD_{50} >5050 mg/kg for males and females. Toxicity Category IV	452620-04
870.1300; 152-12	Acute inhalation toxicity in rats	LC_{50} >2.64 mg/L for males, females, and combined. Toxicity Category IV	452620-05
870.2400; 152-13	Primary eye irritation in rabbits	Moderately irritating. Toxicity Category II	452620-06
870.2500; 152-14	Primary dermal irritation in rabbits	Moderately irritating. Toxicity Category III	452620-07
870.2600; 152-15	Hypersensitivity in guinea pigs, Buehler method	Not a dermal sensitizer.	452620-08

TABLE 3. Toxicity Data for Citronellol Obtained From the Technical Literature	
Data Requirement	**Result**
Oral LD_{50}	3450 mg/kg, rat
Dermal LD_{50}	>5000 mg/kg [a]
Primary skin irritation	Moderate, 16 mg/48 hours, human; Severe, 100 mg/24 hours, rabbit; Severe, 100 mg/24 hours, guinea pig
Mutagenicity/Genotoxicity	No mutagenicity at 100 µg against *Salmonella typhimurium* TA 97 and TA 102; Negative against *S. typhimurium* TA 98

[a]Species not given in MRID 452620-10.

c. Subchronic Toxicity, Immunotoxicity

Requested waivers for subchronic (90-day) oral toxicity and immunotoxicity were granted by the Agency based on the lack of toxicity and anticipated low exposure from the intended use of the product.

d. Chronic Exposure and Oncogenicity Assessment

Repeated dose studies are conditionally required if the potential for adverse chronic effects is indicated based on: 1) the subchronic effect levels established in Tier I subchronic oral, inhalation, or dermal studies; 2) the pesticide use pattern; or 3) the frequency and the level of repeated human exposure that is expected. Oncogenicity studies are required only if the active ingredient or any of its metabolites, degradation products, or impurities produce in Tier I studies any morphologic effects in any organ that could lead to neoplastic changes. None of the results of the submitted studies orscientific literature triggered the need for chronic exposure or oncogenicity testing.

e. Effects on the Endocrine System

Based on available data, no endocrine system-related effects have been identified with consumption of citronellol. It is a naturally occurring substance and a food additive in a variety of food products, is widely used as a fragrance in the cosmetic industry, an is a component of several dermally applied insect repellents.

2. Dose Response Assessment

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

3. Dietary Exposure and Risk Characterization

Consistent with section 408(b)(2)(D) of the FFDCA, EPA has reviewed the available scientific data and other relevant information in support of registration of the active ingredient, citronellol, for use as a pesticide. In this review, EPA has considered the validity, completeness, and reliability and the relationship of this information to human risk. EPA has also considered available information concerning the variability of the sensitivities of major identifiable subgroups of consumers, including infants and children.

Citronellol is a monoterpene alcohol found in over 30 essential oils, and is widely used as a fragrance component in the manufacture of perfumes, cosmetics, detergents and household cleaners. It is a naturally-occurring substance in black currants, certain other fruits, wines, beer, and black tea. This chemical is also used as a synthetic flavoring agent in alcoholic and non-alcoholic beverages, and as a spice. Citronellol is generally regarded as safe (GRAS) under Section 409 of FFDCA (21 CFR 172.515) as a synthetic flavoring agent and adjuvant which is permitted to be added directly to food for human consumption. It is also contained in approximately 25 essential oils, oleoresins and plant extracts that are GRAS under Section 409 of FFDCA (21 CFR 182.20).

Dietary exposure is expected to occur for most, if not all individuals to citronellol primarily from the consumption of fruits, beverages, food seasonings and used as a flavoring agent/adjuvant in a wide variety of foods. The end-use product, BIOMITE^{TM}, contains a low concentration of citronellol (0.42%) which is further reduced by dilution with water (no less than approximately 1:156 v/v) prior to application. Based on the extremely low application rate required to achieve the desired pesticidal effects, the Agency concluded that dietary exposure resulting from the proposed use on agricultural and green house crops will be minimal and lower than levels of citronellol currently consumed in foods where it is naturally occurring and/or present as a food additive. The potential exposure of the general US population to geraniol is estimated to be 0.20% of the World Health Organization (1998) Acceptable Daily Intake (ADI) of 0.5 mg/kg/day. Non-nursing infant exposure to geraniol was estimated to be 1.3% of the ADI. Based on these findings, it is unlikely that residues of citronellol in/on food commodities will pose any human health concerns when the product is applied according to proposed label use directions.

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

Significant additional human exposure to citronellol from its pesticidal use is not expected in occupational, residential, school and day care areas.

a. Occupational Exposure and Risk Characterization

The possibility for occupational exposure to citronellol is mitigated as long as the end-use product BIOMITE™ is used according to the label directions, which require the use of personal protective equipment and a restricted entry interval (4 hours) for treated areas.

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

No indoor residential, school, or day care uses currently appear on the proposed label. Human exposure to BIOMITE™ should not occur in these areas. In the absence of any toxicological endpoints, risk from the consumption of residues is not expected for populations in residential, school and day care, including infants and children.

5. Drinking Water Exposure and Risk Characterization

Citronellol residues in drinking water are expected to be minimal from its use as a pesticide. The pesticide product has a low use rate and the concentration of citronellol in the pesticide product is 0.42%. The product is not intended for aquatic use. Citronellol is insoluble in water and biodegrades rapidly in the soil, precluding its entry into the ground and/or surface water. Therefore, the Agency has concluded that it is highly unlikely that any residues resulting from the pesticidal use of citronellol would migrate into drinking water from natural sources.

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

FFDCA section 408 provides that EPA shall apply an additional tenfold margin of exposure for infants and children in the case of threshold effects. In this instance, based on all the available information, including a lack of threshold effects, the Agency concluded that citronellol is practically non-toxic to mammals, including infants and children. Since there are no effects of concern, the application of an additional margin of safety does not apply and the Agency has concluded that there is reasonable certainty that no harm to sensitive subpopulations, including infants and children as well as adults, will result from the use of citronellol as an active ingredient in pesticide products.

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

There is reasonable certainty that no harm will result from aggregate exposure to residues of citronellol to the U.S. population. This includes the anticipated dietary exposures and all other exposures for which there is reliable information. The Agency has arrived at this conclusion based on the low level of toxicity and the widespread exposure to citronellol without any adverse effects on human health. The risks from aggregate exposure via oral, dermal and inhalation exposure are a compilation of three low exposure scenarios and are negligible. Since there are no threshold effects of concern, the provision requiring an additional margin of safety does not apply. Therefore, EPA has not used a margin of exposure (safety) approach to assess the safety of citronellol.

8. Cumulative Effects

Section 408(b)(2)(/d)(v) of the FFDCA requires that, when considering whether to establish, modify, or revoke a tolerance, the Agency consider the “available information” concerning the

cumulative effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity."

EPA does not have, at this time, available data to determine whether citronellol has a common mechanism of toxicity with any other substances. Its mode of action is as a repellent, which is considered by the Agency as a non-toxic mode of action on target pest species. Further, citronellol does not appear to produce a toxic metabolite produced by other substances. Therefore, for the proposed food uses the Agency has not assumed that citronellol has a common mechanism of toxicity with other substances. When used as proposed, BIOMITE™ is not expected to result in citronellol residues at levels that are of toxicological concern. The information submitted indicates there is already widespread exposure to citronellol without any reported adverse effects to human health. Because of its low inherent toxicity and low agricultural use rates, no cumulative effect with other toxins is anticipated.

9. Risk Characterization

The Agency has considered human exposure to citronellol 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 BIOMITE™ when label instructions are followed.

C. ENVIRONMENTAL ASSESSMENT

1. Ecological Effects Hazard Assessment

The registrant requested waivers for avian oral toxicity, avian dietary toxicity, freshwater fish toxicity, nontarget insect toxicity, and honeybee toxicity data requirements. The Agency has granted waivers of these data requirements based on the low toxicity, the low rate of exposure expected from label-directed use rates, and the anticipated ready biodegradability in soil.

2. Environmental Fate and Ground Water Data

The need for environmental fate and groundwater data (Tier II, (40 CFR Section 158.690(d)(2)(vii through xv)) was not triggered because the acute toxicity studies did not trigger any additional Tier I studies. Risk is minimal due to the low toxicity and exposure rate, and the expected ready biodegradation in soils.

3. Ecological Exposure and Risk Characterization

A potential for exposure exists for nontarget wildlife with terrestrial spray applications. However, the Agency believes that due to citronellol's low toxicity, the environmental risk may be characterized as minimal when the product is used according to label directions.

D. EFFICACY DATA

No efficacy data are required to be submitted because no public health uses are involved.

IV. 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.

To satisfy criterion "A" above, citronellol is not expected to cause unreasonable adverse effects when used according to label instructions. Criterion "B" is satisfied by the current label and by the data presented in this document. It is believed that these new pesticidal active ingredients will not cause any unreasonable adverse effects and will help to control mites, satisfying Criterion "C". Criterion "D" is satisfied by the data submitted and the low exposure to the product when used according to the label directions.

Therefore, citronellol is eligible for registration. The uses are listed in Table 4, Appendix A.

B. REGULATORY POSITION

1. Unconditional Registration

Based on data submitted, the Agency has determined that citronellol is eligible for unconditional registration under Section 3(c)(5) of FIFRA. The Agency foresees no adverse effects to human health or the environment from the use of this active ingredient in accordance with the label directions.

2. CODEX Harmonization

There are no CODEX maximum residue levels for citronellol.

3. Nonfood Registrations

There are no non-food issues at this time.

4. Risk Mitigation

There are no significant risk issues, and as such, mitigation measures for dietary risk, occupational and residential risk, or ground and surface water contamination are not required. Risk to nontarget organisms will be mitigated by appropriate label precautions.

5. Endangered Species Statement

Currently, the Agency is developing a program (The Endangered Species Protection Program) to identify all pesticides whose use may cause potential adverse impacts on endangered and threatened species and their habitats. To aid in the identification of threatened and endangered species and their habitats, several companies have formed an Endangered Species Task Force (EST) under the direction of the Corp Life America. Moreover, the EST will assist in providing species location information at the subcounty level, and particularly if an endangered species occurs in areas where pesticides would be used. This information will be useful once the Endangered Species Protection Program has been implemented.

The Agency has no evidence to believe that any endangered or threatened species will be adversely affected by products containing citronellol when used according to the product label directions. In this regard, label language specific for endangered or threatened species is not imposed at this time for such products.

C. LABELING RATIONALE

It is the Agency's position that the labeling of BIOMITE™ complies with current pesticide labeling requirements.

1. Human Health Hazard

a. Worker Protection Standard

Any product whose labeling reasonably permits its use on an agricultural plant on any farm, forest, nursery, or greenhouse must comply with the labeling requirements of PR Notice 93-7, ''Labeling Revisions required by the Worker Protection Standard (WPS),'' and PR Notice 93-11 "Supplemental Guidance for PR Notice 93-7," which reflect the requirements of EPA's labeling regulations for worker protection statements (40 CFR part 156, subpart K). These labeling revisions are necessary to implement the Worker Protection Standard for Agricultural Pesticides (40 CFR part 170) and must be completed in accordance with, and within the deadlines specified in PR Notices 93-7 and 93-11. Unless otherwise specifically directed, all statements required by PR Notices 93-7 and 93-11 are to be on the product label exactly as instructed in those Notices. After October 23, 1995, except as provided in PR Notices 93-7 and 93-11, all products within the scope of those notices must bear WPS PR Notice complying labeling when they are distributed or sold by any person. The labels and labeling of all products must comply with EPA's current regulations and requirements as specified in 40 CFR 156.10 and other applicable notices. Labeling must also conform to Worker Protection Safety standards concerning re-entry into sprayed fields. End-use products containing citronellol must comply with WPS, and as such

have the appropriate language as required by the standard. For uses of this product that are covered by the Worker Protection Standard (WPS), worker entry into treated areas is not allowed during the restricted entry interval of 4 hours or until the spray has dried. The PPE requirement for early entry to treated areas that is permitted under the WPS and that involves contact with anything that has been treated, such as plants, soil, or water, is coveralls, waterproof gloves, shoes plus socks, and protective eyewear.

b. Non-Worker Protection Standard

There are no non-WPS human health hazard issues.

c. Precautionary Labeling

The Agency has examined the toxicological data base for BIOMITE™ end-use product and concluded that the proposed precautionary labeling (i.e. Signal Word, Statement of Practical Treatment and other label statements) adequately mitigates any risks associated with the proposed uses. Precautionary labeling for end-use products containing this active ingredient is:

> "**WARNING. Causes substantial but temporary eye injury. Harmful if swallowed. Do not get in eyes or on clothing. Wear protective eyewear (goggles, face shield, or safety glasses). Wash thoroughly with soap and water after handling. Remove contaminated clothing and wash before reuse."**

d. Spray Drift Advisory

An advisory statement is contained in the DIRECTIONS FOR USE statement: "Do not apply this product in a way that will contact workers or other persons, either directly or through drift."

2. Environmental Hazards Labeling

The precautionary labeling for end-use products containing citronellol is:

> **"Do not apply directly to water, or to areas where surface water is present, or to intertidal areas below the mean highwater mark. Do not contaminate water when cleaning equipment or disposing of equipment washwater. "**

3. Application Rate

The end-use dilution is applied as a spray or fog at a rate of 100 to 150 gallons/acre, depending on the maturity of the plants being treated. When the product is applied in a drench or root application, the application rate is increased.

D. LABELING

Product name: BIOMITE™

Active Ingredients:
Citronellol (3,7-dimethyl-6-octen-1-ol).....0.417%
Geraniol (2-trans-3,7-dimethyl--2,6-octadien-1-ol).....0.417%
Nerolidol (3,7,11-trimethyl-1,6,10-dodecatrien-3-ol).....0.417%
Farnesol (3,7,11-trimethyl-2,6,10-dodecatrien-1-ol).....0.167%
Other Ingredients.....98.582%

Total 100.000%

Signal word is "WARNING".

The product shall contain the following information:
- Product Name
- Ingredient Statement
- Registration Number
- Signal Word (WARNING)

V. Actions Required by Registrants

There are no data requirements, label changes or other responses necessary for the reregistration of the end-use product since the product is being registered after November 1984 and is, therefore, not subject to reregistration. There are also no existing stocks provisions at this time.

VI. Appendix A

Table 4 lists the use sites for the product. The label for the product is also attached.

Table 4. Use Sites	
BIOMITE™ Use Sites: Agricultural crops, ornamental plants, and professional landscape settings.	**Official date registered**: