BIOPESTICIDES REGISTRATION ACTION DOCUMENT

Heptyl Butyrate
PC Code 100247

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

(June…, 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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BIOPESTICIDES REGISTRATION ACTION DOCUMENT TEAM

Office of Pesticide Programs:

Biopesticides and Pollution Prevention Division

Biochemical Pesticides Branch (BPB)

Driss Benmhend	Regulatory Action Leader
Linda Hollis	Branch Chief
Jacob Moore	Chemist

I. EXECUTIVE SUMMARY:

The new active ingredient heptyl butyrate is a colorless liquid ester that is naturally found in fresh apples and plums and therefore, humans have been regularly exposed to this active ingredient through consumption of these fruits. It is intended for use in traps to attract several species of yellow jackets and wasps.

The Biopesticides and Pollution Prevention Division (BPPD) has reviewed the data required to support the registration of this biochemical active ingredient, under Section 3(c)(5) of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA). Product chemistry data requirements were satisfied by acceptable guideline studies. In lieu of human health studies, the registrant requested data waivers from the requirements for all guideline studies and submitted a compendium of information in support of the data waivers. The registrant also provided adequate justification for waiving data requirements based on the proposed use pattern, which would result in no exposure to the active ingredient. Ecological effects data requirements for heptyl butyrate are fulfilled by acceptable guideline studies and additional data/information from the scientific literature sufficient to support data waivers for the remaining Tier I and Tier II requirements.

Based on the data available to the Agency, it has been determined that no unreasonable adverse effects to the U.S. population and the environment will result from the use of the active ingredient when label instructions are followed and good agricultural practices are employed. Laboratory studies indicate that the active ingredient has low toxicity following oral, inhalation or dermal exposure. Moreover, no significant human exposure to heptyl butyrate is expected since the compound will be used in traps at very low rates.

Based on data and acceptable rationales for waiver requests waivers submitted by the registrant, there is no reason to believe that any nontarget organisms, including honeybees and other beneficial insects, would be attracted to or adversely affected by the use of heptyl butyrate in a wasp trap.

Efficacy data submitted on the end use product were reviewed and showed support to the claims of product performance against yellow jackets and wasps.

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

II. ACTIVE INGREDIENT OVERVIEW

Common Name: Heptyl Butyrate

Chemical Names: Heptyl Butyrate

Trade & Other Names: Heptyl Butyrate

CAS Registry Number: 5870-93-9

OPP Chemical Code: 100247

Type of Pesticide: Hornets, wasps and yellowjackets attractant.

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

III. REGULATORY BACKGROUND

On June 16, 2008, the Agency received an application from Bull Run Scientific, VBT to register heptyl butyrate as an active ingredient in an end-use products (EP) containing up to 99.8% heptyl butyrate. A notice of receipt of the application for registration for heptyl butyrate as a new active ingredient was published in the Federal Register on March 16, 2009 (74 FR 11098), with a 30 day comment period. No comments were received as a result of this publication.
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A. Classification

On April 15, 20081, the Biochemical Classification Committee determined that heptyl butyrate can be classified as a biochemical pesticide due to its nontoxic mode of action to target pest, natural occurrence in the environment, and history of exposure to humans and the environment demonstrating minimal toxicity.

B. Food Clearances/Tolerances

Currently, this active ingredient is not registered for use on food or feed commodities, and the applicant has not filed a petition for a tolerance (nor a tolerance exemption) for heptyl butyrate. As a result, a tolerance or exemption from the requirement of a tolerance is not relevant.

IV. RISK ASSESSMENT

A. Active Ingredient Characterization

The new active ingredient, heptyl butyrate, will be formulated into an end use product (EP) for use as an attractant for yellow jackets. The technical grade active ingredient (TGAI) is a colorless liquid that is naturally found in fresh apples and plums. Heptyl Butyrate is a food

grade ester that has a nontoxic mode of action against the target pest. Yellow jackets are attracted to its fruity smell.

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

All product chemistry data requirements for registration of heptyl butyrate have been satisfied.

B. Human Health Assessment

1. Toxicology

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 is available to support registration of heptyl butyrate. All toxicology data requirements for heptyl butyrate 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 cites from information from the database ChemIDPlus Lite, for the acute oral (OPPTS 870.1100) and acute dermal (OPPTS 870.1200) toxicity. The acute oral has a minimal lethal dose (LDLo) of 5000 mg/kg in rats, and the dermal toxicity has a LD_{50}>5000 mg/kg in rabbits. The substance is in Toxicity Category IV for acute oral, acute dermal, acute inhalation toxicity, and dermal irritations. The substance is not a dermal sensitizer. Some potential exists for eye irritation. In lieu of submitting new eye irritation data, a Toxicity Category III category language will used on the product label.

For more information regarding the acute toxicity data requirements, refer to Table 3 in Appendix A.

b. Sub-chronic Toxicity

Subchronic data is required to determine a no-observed-effect-level (NOEL) and toxic effects (if any) associated with repeated or continuous exposure to a test substance for a period of 90 days.

The Agency received and accepted the registrant's waiver requests for 90-day Feeding Study (OPPTS 870.3100); 90-Day Dermal Study (OPPTS 870.3250); 90-Day Inhalation Study (OPPTS 870.3465); and Immune Response (OPPTS 880.3550).

The data requirement for 90-day Feeding Study (OPPTS 870.3100) is not applicable because the product will not be used on food commodities, and no repeated sub-chronic oral exposures are expected. Moreover, Tier I acute toxicity studies show toxicity category IV for all routes of exposure.

The waiver rational for a 90-Day Dermal Toxicity Study (OPPTS 870.3250) was accepted because the product will be used in traps and is not likely to result in prolonged skin exposure. Furthermore, heptyl butyrate is found abundantly in nature, and has low toxicity.

The 90-Day Inhalation Toxicity Study (OPPTS 870.3465) waiver request was accepted because the use pattern of the product in traps, is not expected to result in repeated inhalation exposure at a concentration which is likely to be toxic.

For more information regarding the subchronic data requirements, refer to Table 3 in Appendix A

c. Developmental Toxicity and Mutagenicity

Request to be waived from submitting the data required for Developmental toxicity and Mutagenicity (OPPTS 870.3700) which were supported by valid scientific rationales, are acceptable. The Agency concluded that human's are regularly exposed to heptyl butyrate found abundantly in fresh apples and plums. No negative effects of heptyl butyrate have been reported because of its low toxicity. Moreover, the active ingredient is not a mutagen nor is it related to any known classes of mutagens. For more information regarding this data requirements, refer to Table 3 in Appendix A.

e. Effects on the Endocrine System

EPA is required under the FFDCA, as amended by 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 were scientific bases for including, as part of the program, 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. When the appropriate screening and/or testing protocols being considered under the Agency's Endocrine Disrupter Screening Program (EDSP) have been developed and vetted, heptyl butyrate may be subjected to additional screening and/or testing to better characterize effects related to endocrine disruption.

2. Dose Response Assessment

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

3. Drinking Water Exposure and Risk Characterization

Based on the proposed use pattern, no significant exposure is expected from use of heptyl butyrate in the environment when used according to label instructions.

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

a. Occupational Exposure and Risk Characterization

Occupational exposures are not a concern based on the use pattern, low to no potential for exposure due to trap design, and because heptyl butyrate is naturally occurring in the environment and possesses a nontoxic mode of action when used as an attractant at a low concentration. The application method of heptyl butyrate inside a water-soluble pouch that is placed within a trap poses no significant concern for dermal, eye, and inhalation exposures.

The product label will bear the signal word "Caution." No reentry interval is required in conjunction with the use of the EP.

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

The Agency is not concerned about the potential exposure to children because the end use product containing heptyl butyrate is intended for use in enclosed traps. In addition to the low potential for exposure, heptyl butyrate's low toxicity will cause no unreasonable adverse effects in case of accidental exposures.

5. Risk Characterization

The Agency considered human exposure to heptyl butyrate 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 heptyl butyrate when label instructions are followed.

C. ENVIRONMENTAL ASSESSMENT

1. Ecological Hazards

Based on the natural occurrence of heptyl butyrate in fresh apples and plums and the fact that heptyl butyrate is not expected to cause adverse effects on nontarget organisms, adequate rationales for waiving nontarget toxicology data were submitted to support registration of heptyl butyrate. All nontarget toxicology data requirements for heptyl butyrate have been satisfied.

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

2. Environmental Fate and Ground Water Data

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

3. Ecological Exposure and Risk Characterization

The active ingredient is intended for formulation of end use products which be placed in insect traps for residential or agricultural use. When used according to the proposed label directions, no direct exposures are expected for nontarget organisms. Moreover, the active ingredient is used at a low concentration as an attractant, and is not expected to accumulate in the environment. Given these characteristics of heptyl butyrate, nontarget exposure and ecological effects studies were waived.

4. Endangered Species Assessment

Based on the fact that this chemical is not toxic to non-target organisms and on its use pattern and use instructions, EPA has determined it will have "No Effect" on any currently listed threatened or endangered species or any designated critical habitat.

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).

A series of field trials were conducted to evaluate the efficacy of products containing heptyl butyrate. The studies submitted and reviewed showed that heptyl butyrate is more effective than control traps on capturing various yellowjacket species. Field trials of 17 to 64 days duration were conducted in Washington and Pennsylvania to compare the efficacy of reusable and disposable yellowjacket traps containing heptyl butyrate (99.8, 63.9, or 18.9%) to that of control traps without heptyl butyrate. Approximately every three weeks, the reusable traps were emptied and re-baited, and the disposable traps were collected and replaced with new disposable traps. Although no statistical analysis was provided, the traps containing heptyl butyrate appeared to be more effective than the control traps in attracting a variety of yellowjacket species. No honeybees or other beneficial insects were attracted to the traps.

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 heptyl butyrate. 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, heptyl butyrate is eligible for registration for the labeled uses.

B. Regulatory Decision

The data submitted fulfill the requirements of registration of products containing heptyl butyrate for use to attract ten species of yellowjackets (*Vespula pensylvanica, V. atripilosa, V. sulphurea, V. consobrina, V. acadica, V. squamosa, V. vidua, V. vulgaris, V. maculifrons,* and *V. germanica*). Refer to Appendix B for product-specific information.

1. Conditional/Unconditional Registration

All data requirements are fulfilled and EPA has determined that unconditional registration of heptyl butyrate 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 heptyl butyrate, 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 heptyl butyrate and determined that these data are sufficient to satisfy current registration data requirements. No additional data are required to be submitted to the Agency at this time. For new uses and/or changes to existing uses, additional data may be required.

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

A. Reporting of Adverse Effects

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

B. Reporting of Hypersensitivity Incidents

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

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

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

TABLE 1. Product Chemistry Data Requirements for *Active Ingredient* (40 CFR § 158.2030)

OPPTS Guideline No.	Study (MRID 474519-07 through 474519-11)	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 n 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 1. Physical and Chemical Properties for Yellowjacket Attractant Study (MRID 474519-07 through 474519-11)			
Guideline Reference No./Property		**Description of Result**	
830.6302	Color	Colorless	
830.6303	Physical State	Liquid	
830.6304	Odor	Sweet-green, slightly tea-like odor	
830.6313	Stability	Stable for 36 months when stored in its original packaging, tightly sealed in cool (46-90°F) and dry location out of direct heat and light.	
830.6314	Oxidation/Reduction: Chemical Incompatibility	Not applicable, the product is not intended to contact strong oxidizing or reducing agents.	
830.6315	Flammability	Flash point = 195°F	
830.6317	Storage Stability	A field efficacy study showed that the product was still effective, and hence stable, after 12 years of storage under commercial warehouse conditions.	
830.6319	Miscibility	Not applicable, the product is not an emulsifiable liquid to be mixed with petroleum solvents	
830.6320	Corrosion Characteristics	No corrosion of EVOH plastic barrier tubes was seen after 12 years of storage under commercial warehouse conditions.	
830.6321	Dielectric Breakdown Voltage	Not applicable, the product is granular and not for use around electrical equipment	
830.7000	pH	5.6±0.1 at 21°C (1% w/v aqueous solution)	
830.7100	Viscosity	1.7 cP at 25.0°C	
830.7200	Melting Range	Not applicable, product is a liquid	
830.7220	Boiling Range	225-226°C	
830.7300	Density/Relative Density/Bulk Density	0.8600-0.8640 g/mL	
830.7370	Dissociation Constant in Water	Waiver requested. Based on the chemical structure, the product does not contain any ionizable protons, and no significant dissociation of protons in water is anticipated. No significant environmental exposure is anticipated.	
830.7550	Partition Coefficient	Log Kow = 4.3019	
830.7840	Water Solubility	Insoluble in water	
830.7950	Vapor Pressure	0.0972 mm Hg	

Table 3. Human Toxicology Data Requirements for heptyl Butyrate (40 CFR § 158.2050)

Study Type/OPPTS Guideline	LD_{50}/LC_{50}/Results	Toxicity Category	MRID
Acute Oral Toxicity/OPPTS 870.1100	> 5000 mg/kg	IV	474519-13
Acute Dermal Toxicity/OPPTS 870.1200	> 5000 mg/kg	IV	474519-14
Acute Inhalation Toxicity/OPPTS 870.1300	> 5.43 mg/L	IV	474519-13
Acute Eye Irritation/OPPTS 870.2400	Mildly irritating	III	474519-13
Acute Dermal Irritation/OPPTS 870.2500	Non-irritating	IV	474519-14
Skin Sensitization/OPPTS 870.2600	Not skin sensitizer	IV	474519-14

Nontarget Organism Toxicity Requirements for *active ingredient* (40 CFR § 158.2060) MRID: 474519-12

VIII. Appendix B.

For product specific information, please refer to…*add in link.*

IX. Appendix C.

Include link to Scientific Term Glossary