



US Environmental Protection Agency Office of Pesticide Programs

4-Allyl Anisole (PC Code 062150)

4-allyl anisole
BIOPESTICIDES Registration Action Document

BIOPESTICIDES REGISTRATION ACTION DOCUMENT

**U.S. Environmental Protection Agency
Office of Pesticide Programs
Biopesticides and Pollution Prevention Division
4-Allyl Anisole
(PC Code 062150)**

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I. Executive Summary

A. IDENTITY

The new active ingredient 4-allyl anisole is a technical grade active ingredient, to be used in the manufacturing of end-use biochemical pesticide products. The manufacturing use product, Beetleball Technical, contains 97.5% of 4-allyl anisole (estragole).

B. USE/USAGE

Beetleball Technical will be used to formulate repellent products for the management and prevention of southern pine beetle infestations and other insects on conifers in forests.

C. RISK ASSESSMENT

The Agency recognizes that the manufacturing use of 4-allyl anisole will not only limit human exposure but also, in conjunction with the low toxicity of this compound, will limit the likelihood of having any negative adverse effect resulting from the use of 4-allyl anisole. The Agency is making its risk management decision regarding the registration of 4-allyl anisole based on the lack of environmental and low human exposure; in addition, the precautionary labeling further minimizes exposure and mitigates risks. The Agency believes that 4-allyl anisole can be used without causing unreasonable adverse effects to humans or to the environment. Based on the negligible risk concerns, 4-allyl anisole meets the criteria as specified in §3(c)(5) of FIFRA as amended, and is thus eligible for unconditional registration. No additional data are needed.

This document presents the Agency's decision regarding the registration of the new active ingredient, 4-allyl anisole, commonly known as Beetleball Technical.

D. DATA GAPS / LABELING RESTRICTIONS

There are no data gaps for registration of 4-allyl anisole. **End-use products containing 4-allyl anisole as the active ingredient must be registered with the Agency prior to distribution.**

II. Overview

A. ACTIVE INGREDIENT OVERVIEW

Common Name:	Beetleball Technical
Chemical Name:	4-allyl anisole (estragole)
Chemical Formula:	C ₁₀ H ₁₂ O
Chemical Class:	Terpineols
CAS Registry Number:	140-67-0
OPP Chemical Code:	062150
Trade Name:	BEETLEBALL Technical
Basic Manufacturer:	Taensa, Inc. 26 Sherman Court P.O. Box 764 Fairfield, CT 06430

B. USE PROFILE

The following is information on the proposed uses with an overview of use sites and application methods.

Type of Pesticide:

Biochemical, repellent/anti-aggregant

Use Sites:

Beetleball Technical Grade Product will be incorporated into end-use products to repel southern pine beetles from conifer trees in forests.

Target Pests:

Bark beetles, such as southern pine beetle (*Dendroctonus frontalis*)

Formulation Types:

Technical

Method and Rates of Application:

The Beetleball Technical label states that this product is “only for formulation into a repellent for the following use: For management and prevention of Southern Pine Beetle infestations and other insects on conifers.”

The end-use products containing 4-allyl anisole will be enclosed in a paint ball, which will be applied to conifer trees in forests.

Use Practice Limitations:

This product may be used to formulate products for any additional use(s) not listed on the BEETLEBALL Technical label if the formulator, user group, or grower has complied with U.S. EPA submission requirements regarding the support of such use(s).

C. ESTIMATED USAGE

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

D. DATA REQUIREMENTS

Recognizing the low toxicity (see Table 2), non-food use, and low expected exposure to humans from contact with end-use products containing 4-allyl anisole in point source applications (e.g., enclosed paintball), the Agency has granted data waivers for certain mammalian toxicity studies, such as hypersensitivity, subchronic (90-day) oral and inhalation toxicity, genotoxicity, immunotoxicity, and developmental toxicity which are only conditionally required for terrestrial non-food use biochemical pesticides if significant exposure is expected.

The registrant has submitted product chemistry studies and has provided citations or submitted acute toxicity studies to support the product registration. The data requirements for granting this registration under Section 3(c)(5) of FIFRA have been reviewed by the Biopesticides and Pollution Prevention Division (BPPD). Based on submitted information, the Agency foresees no unreasonable adverse effects to human health and the environment from the use of this biochemical pesticide and recommends an unconditional registration of this new active ingredient for the proposed uses.

E. REGULATORY HISTORY

On January 25, 1998, the Agency received applications from Taensa, Inc. to register 4 products containing 4-allyl anisole.

A notice of receipt of the applications for registration for Beetleball Technical, Beetleball MP, Beetleball Paintball and Beetleball Microencap was published in the Federal Register (volume 64, Number 75, pages 19356-19357) on April 20, 1999. No public comments were received on this notice. On February 2, 2001, Taensa Inc. sent a letter to the Agency requesting to withdraw the registration applications of Beetleball MP, Beetleball Paintball, and Beetleball Microencap. The request to withdraw these applications was accepted by the Agency on April 17, 2001.

F. CLASSIFICATION

4-Allyl anisole is produced naturally in conifer trees in response to infestation by beetles. Herbs such as basil, fennel and tarragon also contain high levels of 4-allyl anisole. The Agency has classified 4-allyl anisole as a biochemical pesticide based on its natural occurrence and non-toxic mode of action as a repellent. 4-Allyl anisole has been classified as GRAS (generally recognized as safe) by the FDA for use in perfumes and as flavorings in foods and liqueurs.

G. FOOD CLEARANCES/TOLERANCES

The manufacturing use and end-use products are intended for non-food use; therefore, no tolerance is required.

III. Science Assessment

A. PHYSICAL/CHEMICAL PROPERTIES ASSESSMENT

All product chemistry data requirements for Beetleball Technical (4-allyl anisole are satisfied).

1. Product Identity and Mode of Action

a. Product Identity:

The TGAI is a colorless liquid with an odor reminiscent of anise. It has a boiling point of between 214 -216 ° C and a density of 0.957 - 0.965 at 25°C. The technical is soluble in alcohol and chloroform. The technical contains 98% 4-allyl anisole.

b. Mode of Action: Anti-aggregation agent. The exact mechanism is unknown but it is proposed that 4-allyl anisole, found in conifers, either acts as a repellent when large amounts are released to signal bark beetles that too many beetles are present on a diseased tree, or that the release of the compound by an infested tree attracts parasites that attack the bark beetles.

2. Food Clearances/Tolerances

A tolerance is not needed because Beetleball Technical is intended for nonfood use.

3. Physical And Chemical Properties Assessment

The data requirements for physical and chemical characteristics that support the registration of the Beetleball Technical 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 formulation of unintentional ingredients	Satisfied requirements	447465-01 447465-02 447465-02
151B-13	Analysis of samples	Submitted data satisfy the data requirements for analysis of samples	447465-03, 454956-01

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GUIDELINE NO.	STUDY	RESULTS	MRID NO.
151B-15	Certification of limits	Satisfied requirement	447465-03
151B-16	Analytical Method	Acceptable	447465-03, 454956-01
151B-17	PHYSICAL / CHEMICAL PROPERTIES of TGAI		
151B-17a	Color	Colorless	447465-04
151B-17b	Physical State	liquid	447465-04
151B-17c	Odor	Anise-like	447465-04
151B-17d	Melting point	N/A (product is a liquid; required for solids only)	
151B-17e	Boiling point	214 - 216 ° C	447465-04
151B-17f	Density/Specific gravity	0.957 - 0.965 at 25°C	447465-04
151B-17g	Solubility	soluble in alcohol and chloroform relatively insoluble in water	447465-04
151B-17h	Vapor Pressure	0.09 mm Hg at 20°C	447465-04
151B-17i	pH	N/A (not soluble in water)	447465-04
151B-17j	Stability	not stable to excessive heat or oxidation	447465-04
151B-17k	Flash point	86°C	447465-04
151B-17l	Storage stability	N/A (not required for TGAI)	
151B-17m	Viscosity	N/A (not required for technical grade product)	

GUIDELINE NO.	STUDY	RESULTS	MRID NO.
151B-17n	Miscibility	N/A (not required for technical grade product)	
151B-17o	Corrosion characteristics	N/A (not required for technical grade product)	

B. HUMAN HEALTH RISK ASSESSMENT

1. Toxicology Assessment

The mammalian toxicity studies that are required to register a terrestrial non-food use biochemical pesticide have been submitted and cited (acute oral toxicity) and are acceptable and adequately satisfy data requirements to support registration. Submitted data indicate that the Technical Grade of the Active Ingredient (TGAI) should be classified as Toxicity Category III for acute oral and dermal toxicity, and Toxicity Category IV for acute inhalation toxicity. The TGAI was found to cause slight ocular irritation in an eye irritation study (Toxicity Category IV) and moderate irritation in a dermal irritation study (Toxicity Category III). No hypersensitivity incidents were reported.

B. HUMAN HEALTH ASSESSMENT

1. Toxicology Assessment

Acute toxicity studies were submitted to support the registration of the technical product. The results are provided below.

a. Acute Toxicity

The registrant cited the acute oral toxicity study and submitted all other toxicity studies which were classified as acceptable. The submitted results indicated acceptable acute toxicity studies for the TGAI. The acute oral LD₅₀ in rats was >1230 mg/kg (Toxicity Category III); the acute dermal LD₅₀ in rabbits was >2020 mg/kg (Toxicity Category III); the acute inhalation LC₅₀ in rats was > 2.64 mg/L (Toxicity Category IV); 4-allyl anisole caused slight ocular irritation in rabbits which cleared by 48 hours post-instillation (Toxicity Category IV) and caused moderate dermal irritation in rabbits (Toxicity Category III). No hypersensitivity incidents were reported to the manufacturer, and MSDS states the active ingredient is not a sensitizer. Acute toxicity data submitted are summarized in Table 2.

Table 2. Acute Toxicity Data requirements for the TGAI:

GUIDELINE NO.	STUDY	RESULTS	MRID NO.
TIER I			
152-10	Acute oral toxicity	LD50 >1230 mg/kg in rats (Toxicity Category III)	Cited in information from manufacturer
152-11	Acute dermal toxicity	LD50 >2020 mg/kg in rabbits (Toxicity Category III)	447465-05
152-12	Acute inhalation toxicity	LC50 >2.64 mg/L in rats (Toxicity Category IV)	447465-06
152-13	Primary eye irritation	slightly irritating to rabbit eyes (Toxicity Category IV)	447465-07
152-14	Primary dermal irritation	moderately irritating to rabbit skin (Toxicity Category III)	447465-08
152-15	Dermal sensitization	*Waived	
152-16	Hypersensitivity incidents	No incidents of hypersensitivity reported	447465-09
152-17	Genotoxicity	*Waived	
152-18	Cellular immune response	*Waived	

* The Registrant requested a data waiver. Data waivers were granted based on the use pattern and lack of toxicity associated with the active ingredient as documented in peer reviewed scientific literature.

b. Mutagenicity and Developmental Toxicity

Based on low toxicity and low expected exposure, the Agency has granted data waivers for certain mammalian toxicity studies, such as hypersensitivity, subchronic (oral, dermal and inhalation) immunotoxicity, mutagenicity and developmental toxicity. These studies are only required for

registration of a terrestrial non-food use biochemical pesticide, when significant exposure is expected.

c. Subchronic Toxicity

No subchronic toxicity studies are required for the active ingredient. Refer to section III (B) (1) (b) above.

d. Chronic Exposure and Oncogenicity Assessment

Chronic and oncogenicity studies are not required. A review of peer reviewed scientific literature supplied by the registrant indicates the carcinogenic risk of the compound is considered minimal. The basis of the minimal risk classification is that once the compound is metabolized it is rapidly detoxified in rodents. In animal studies, it has proved to have weak carcinogenic effects in the liver at doses several hundred times the estimated human daily intake. Metabolism studies, however, indicate that the side-chain oxidation at high doses in rats do not occur in humans at doses up to 250 mg/day.

e. Effects on the Endocrine Systems

The Agency is not requiring information on the endocrine effects of this compound at this time. BPPD has considered, among other relevant factors, available information concerning whether this biochemical may have an effect in humans similar to an effect produced by a naturally occurring estrogen or other endocrine effects. There is no known evidence that this active ingredient acts as an endocrine disrupter in humans. No adverse effects to the endocrine system are known or expected.

2. Dose Response Assessment

No toxicological endpoints are identified.

3. Dietary Exposure and Risk Characterization

Beetleball Technical demonstrates low acute toxicity (Table II). The study results indicated no significant signs of toxicity in rats. No additional data or other information is required to support the registration of 4-allyl anisole.

4. Occupational and Residential Exposure

Human exposure and risk to 4-allyl anisole is expected to be minimal in occupational, residential, school and day care settings from the manufacturing use product and end-use products because of the use in formulation of pesticide products and the use in forests.

a. Occupational Exposure and Risk Characterization

Based on the use pattern, the potential for dermal, eye and inhalation exposure to pesticide handlers is expected to be low. No adverse health effects to workers are expected from the use of Beetleball Technical. Because of a low acute toxicity, worker exposure data are not required.

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

No indoor residential, school or day care uses currently appear on the label. No residential, school or day care exposure will occur from the use of Beetleball Technical as a manufacturing use product, nor from the forestry use of any end-use products containing 4-allyl anisole as the active ingredient.

5. Drinking Water Exposure and Risk Characterization

The Agency does not anticipate exposure to residues of 4-allyl anisole in drinking water or accumulation in the aquatic environment, due to the paintball application method and forestry only use.

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

The Agency has concluded that due to the forestry use, the potential for exposure to 4-allyl anisole residues from this use does not pose a dietary risk to sensitive subpopulations including infants and children.

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

Submitted data confirm the low oral, dermal and inhalation toxicity of this active ingredient. Based on this information, and because of its natural occurrence, nontoxic mode of action, and forestry use, the Agency has concluded that aggregate exposure to 4-allyl anisole over a lifetime will not pose appreciable risks to human health.

8. Cumulative Effects

4-Allyl anisole is not toxic and rapidly metabolized and therefore would not be expected to have cumulative effects from common mechanisms of toxicity.

9. Risk Characterization

The Agency has considered 4-allyl anisole in light of the relevant safety factors and 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 this compound when label instructions are followed.

C. ENVIRONMENTAL ASSESSMENT

1. Ecological Effects Hazard Assessment

The results from an acute oral avian toxicity study indicate that the technical product is minimally toxic to bobwhite quail. Since Taensa, Inc. currently plans to limit production to Technical Grade Beetleball, a waiver was granted for an avian dietary study. However, any new end-use product should be re-evaluated as to the need for a dietary avian study, based on the formulation and use pattern.

2. Environmental Fate and Ground Water Data

Exposure assessments of this type of product (biochemical pesticide) are not performed unless significant human health or ecological effects issues arise in the Tier I studies for either of these disciplines (40 CFR §158.690 (c) and (d)). Since Tier II studies were not triggered, there is no requirement for environmental fate data.

3. Ecological Exposure and Risk Characterization

Beetleball Technical mimics a naturally occurring compound, and has a target-specific, non-toxic mode of action. Based on the use pattern and low toxicity, transport and exposure in the environment is expected to be very limited and to pose minimal risk to non-target terrestrial and aquatic species.

Table IV. Non-Target Toxicity Data - Tier I Guideline Requirements for Beetleball Technical:

Guideline No.	Study	Result	MRID
154-6	Avian acute oral	LD ₅₀ >2,075 mg/kg	44746511
154-7	Avian dietary	Waived (registrant requested waiver; not required for technical grade product)	N/A
154-8	Freshwater fish LC ₅₀	Waived (registrant requested waiver; not required for technical grade product)	N/A

D. EFFICACY DATA

Registrants are required to conduct and have available, upon request, efficacy studies to support the registration of biochemical pesticides. The Agency is not requiring the submission and review of efficacy studies to support this active ingredient at this time since 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 criteria “A” above, 4-allyl anisole products are not expected to cause unreasonable adverse effects when used according to label instructions. Criteria “B” is satisfied by the current label and by the data presented in this document. It is believed that the components of 4-allyl anisole products will not cause any unreasonable adverse effects, will act as a repellent of bark beetles as claimed satisfying Criteria “C”. Criteria “D” is satisfied in that the toxicological properties of this product are less toxic than any other conventional pesticide product currently in use.

Therefore, 4-allyl anisole is eligible for registration. Registered use is listed in Table 4, Appendix A.

B. REGULATORY POSITION

1. Conditional/Unconditional Registration

Based on the data submitted, BPPD recommends that 4-allyl anisole is eligible for registration under Section 3(c)(5) of FIFRA. BPPD foresees no unreasonable adverse effects to human health or the environment from the use Beetleball Technical.

2. Tolerance Reassessment

A tolerance (or exemption) is not required for 4-allyl anisole since Beetleball Technical and any resulting end-use product are not intended for food use.

3. CODEX Harmonization

There are no Codex harmonization considerations, since a tolerance or exemption from the requirement of a tolerance is not required for the currently registered nonfood uses.

4. Nonfood Re/Registrations

There are no nonfood issues at this time, other than any addressed within this document.

5. Risk Mitigation

Since there are no risk issues identified for 4-allyl anisole, mitigation measures are not required at this time for dietary risk, residential risk, risks to nontarget organisms (plants and wildlife), or ground water contamination.

6. Endangered Species Statement

Based on the use pattern and the results of toxicity and exposure studies, the Agency has determined that this action will have no effect on listed species.

C. LABELING RATIONALE

It is the Agency's position that the labeling for Beetleball Technical products containing 97.5% 4-allyl anisole comply with the current pesticide labeling requirements.

1. Human Health Hazard

a. Worker Protection Standard

This product does not come under the provisions of the Worker Protection Standards (WPS).

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 4-allyl anisole and concludes that the proposed precautionary labeling (i.e. Signal Word, Statement of Practical Treatment and other label statements) adequately mitigate the risks associated with the proposed use.

Technical Grade Active Ingredient Product Precautionary Labeling: for Beetleball Technical, the following labeling is required:

"Keep out of Reach of Children"

"Caution"

First aid:

"Is Swallowed: Call a physician or Poison Control Center. Drink 1 or 2 glasses of water and induce vomiting by touching back of throat with finger, or, if available, by administering syrup of ipecac. If person is unconscious, do not give anything by mouth and do not induce vomiting."

"If on Skin: Wash with plenty of soap and water. Get medical attention."

"If Inhaled: Remove victim to fresh air. If not breathing, give artificial respiration, preferable mouth-to-mouth. Get medical attention."

"If in Eyes: Flush eyes with plenty of water. Get a physician if irritation persists".

Precautionary Statements:

"Hazards to Humans and Domestic Animals"

"CAUTION"

"Harmful if swallowed, absorbed through skin, or inhaled. Causes moderate eye irritation. Avoid contact with skin, eyes, and clothing. Avoid breathing vapor. Remove contaminated clothing and wash clothing before reuse. Wash thoroughly with soap and water after handling."

d. Spray Drift Advisory

No spray drift advisory statement is necessary for this use.

2. Environmental Hazards Labeling

Technical Grade Active Ingredient Environmental Hazards Labeling:

" Do not discharge effluent containing this product into lakes, streams, ponds, estuaries, oceans or other waters unless in accordance with the requirements of a National Pollutant Discharge Elimination System (NPDES) permit and the permitting authority has been notified in writing prior to discharge. Do not discharge effluent containing this product to sewer systems without previously notifying the local sewage treatment plant authority. For guidance, contact your State Water Board or Regional Office of the EPA."

3. Application Rate

Manufacturing use or formulating registered pesticides products only.

D. LABELING

Product name: Beetleball Technical
Active Ingredient:

4-Allyl anisole	97.5%
Other Ingredients	2.5%

Total	100.00%
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Signal word is "Caution ".

The product shall contain the following information:

- Product Name
- Ingredient Statement
- Registration Number
- "Keep Out of Reach of Children"
- Signal Word (Caution)

V. Actions Required by Registrants

Reports of incidences of adverse effects to humans or domestic animals under FIFRA, Section 6(a)2 and incidents of hypersensitivity under 40 CFR Part 158.690(c), guideline reference number 152-16. There are no data requirements, label changes and 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. Non-food Use Site Registration/Reregistration

<p>Beetleball Technical Grade</p> <p><u>Use Sites</u> For incorporation into end-use products.</p>	<p>Official date registered:</p>
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