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Study Title

Reduced-Risk Rationale for Hexaflumuron
in a Termite Baiting System

Data Requirement

None

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Performing Laboratory

None

Project Study ID

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STATEMENT OF NO DATA CONFIDENTIALITY CLAIMS*

No claim of confidentiality is made for any information contained in this study on the basis of its falling within the scope of FIFRA S 10(d)(1)(A), (B), or (C).

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*The above statement supersedes all other statements of confidentiality that may occur elsewhere in this report.

GOOD LABORATORY PRACTICE COMPLIANCE STATEMENT

The GLP requirements specified under the Code of Federal Regulations, Title 40, part 160, are not applicable to this study.

Signature: _____ Date: 8-10-93

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The criteria for flagging studies stipulated in the Code of Federal Regulations, Title 40, Part 158.34, do not apply to this study.

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INTRODUCTION AND PRODUCT OVERVIEW

Hexaflumuron is proposed for use in a termite baiting system which incorporates key concepts of an Integrated Pest Management Program.

1. A monitoring device without pesticide is placed in an underground bait station situated at various intervals around the structure to be protected. These devices are checked periodically for the presence of termites. If there are termites feeding on the monitoring device, they are replaced with the baiting devices.

2. The bait matrix (composed of approximately [redacted] and 0.1% active ingredient) is enclosed in a plastic tube with small holes just large enough for a termite to enter. This tube is placed into the underground bait station only after termites are detected. Once the population is suppressed or eradicated and no further feeding occurs, the bait tubes are replaced with the monitoring devices.

With this system, active ingredient is utilized only <u>when</u> needed, and only <u>where</u> needed.

The current technology for termite control has been in use for over half a century. It entails placing approximately 12-16 pounds of active ingredient in the soil around an average structure to form a barrier to foraging termites. In contrast, the bait system would utilize milligrams of active ingredient and would suppress or eradicate the foraging population.

The baiting system will not totally replace barrier treatments, but the impact is expected to be significant. Chemical termiticides applied as a soil barrier prior to construction of the building continues to be a sound and effective protection technique; however, no barrier lasts forever, thus the bait would likely be applied as post-construction to enhance the effectiveness of the barrier treatment. Traditionally, a loss of the chemical soil barrier would necessitate reapplying the liquid termiticide to the soil around the structure. Successful utilization of the baiting system has the potential to significantly impact the amount of post-construction liquid chemical barrier product used by changing the control technique emphasis from prophylactic applications to spot-type treatments. The baiting system could also reduce the potential

for misapplication when treating sensitive areas such as near ponds and lakes or around structures with wells.

Efficacy data submitted in support of the hexaflumuron registration package (MRID #42648525), reported that 2.5 grams of active ingredient eradicated 5 separate colonies of termites totaling an estimated 7.5 million individuals.

The economic need for termite control is significant. Termites attack approximately 2 million houses each year resulting in an estimated three quarters of a billion dollars in damage. For most, a house is the largest investment one will make in a lifetime.

Prior to addressing the separate items listed in the Reduced-Risk Initiative, it is important to understand several key points concerning the formulation, active ingredient, and delivery system.

1. The bait matrix contains a nominal 0.1% of the 98.5% pure active ingredient.
2. The bait matrix is a semi-solid material with roughly the same consistency as cookie dough.
3. The bait matrix is placed in a plastic tube and has no direct contact with non-target animals or the environment.
4. The plastic tube containing the bait matrix is placed in a bait station just below the soil surface.
5. The bait matrix is used only when there is termite activity, otherwise a non-chemical monitoring device is used.
6. There is virtually no exposure to any organism other than the target pest. In addition, the cellulose based matrix and subterranean station placement further serve to make the matrix species specific.

A. Human Health

1. Acute Toxicity

The acute toxicity was determined for the technical grade active ingredient, 62719-EUU. This compound is approximately 98.5%

pure. Hexaflumuron acts as an insect growth regulator which inhibits the synthesis of chitin in the insect exoskeleton. It is because of this mode of action that there is virtually no mammalian toxicity. Please refer to MRID #'s 42648514 - 20 for the following results:

a. Acute Oral - No mortality at 5000 mg/kg.
b. Acute Dermal - No mortality at 2000 mg/kg.
c. Acute Inhalation - No mortality at 7.0 mg/l.
d. Eye Irritation - All signs resolved by 24 hours post treatment.
e. Dermal Irritation - One animal with slight irritation at 72 hours, clear by day 7.
f. Dermal Sensitization - Negative.

Because of these results, in addition to the semi-solid/enclosed nature of the formulation containing a nominal 0.1% hexaflumuron and the absence of toxic inerts, a waiver has been requested for acute studies on the end use formulation (62719-EUG). A waiver was also requested for acute neurotoxicology study (81-7) because hexaflumuron is not a nerve poison. A European study (summarized in MRID # 42648520) reported that hexaflumuron did not produce delayed neuropathy in hens even at 5000 mg/kg body weight.

2. Reproductive, Developmental, and Mutagenic Properties.
Tests to determine chromosomal aberrations, CHO/HGPRT mutations, and bone marrow aberrations were all negative (MRID #'s 42648521-24). Waivers have been asked for reproductive and developmental studies on the basis of the enclosed matrix design. A summary of European studies (MRID # 42648520) reports that in a two-generation rat reproduction study, hexaflumuron had no effect on fertility, reproductive performance or fetal development.

3. Oncogenic effects.
Waivers were requested for chronic and oncogenic studies based on the bait station design and non-dusting nature of the formulation. There is very little chance for human exposure. European data (MRID # 42648520) determined hexaflumuron to be non-oncogenic.

B. Environmental Fate and Effects

1. Mammalian Acute Toxicity

Covered in previous section A.

2. Avian Toxicity

Based on the bait station design and underground placement, there is virtually no opportunity for avian exposure. Waivers have been requested for these studies; however, summaries of European data were submitted (MRID #'s 42648506-10).

a. Dietary Toxicity for Bobwhite Quail -
LD_{50} calculated to be 900 mg/kg for 5 days.

b. Acute Toxicity for Bobwhite Quail -
There was no mortality at the 2000 mg/kg limit test.

c. Dietary Toxicity for Mallard Ducks -
It was determined that the LC_{50} is in excess of 5200 ppm. There were no deaths at the limit dose following a 5 day study.

d. Acute Toxicity for Mallard Ducks -
There was no mortality at the 2000 mg/kg limit test.

3. Avian Reproductive Toxicity

This study is not considered necessary for the product and has not been conducted.

4. Fish and Aquatic Invertebrate Toxicity

Hexaflumuron has a low water solubility (27 ppb) and a strong binding affinity for the [redacted] in the matrix (Kd = 147-1326). Hexaflumuron has virtually no potential for leaching from the matrix even if the bait matrix tube were inadvertently thrown into a water source without its protective wrapping. The bait matrix enclosure would further minimize the exposure potential even in this extreme potential. On these bases, test waivers have been requested; however, summaries were submitted (MRID #'s 42648511-13).

a. Acute Toxicity for Bluegill Sunfish -
There was no mortality to fish exposed to 100 mg/l of hexaflumuron added directly to water.

b. Acute Toxicity for Rainbow Trout -
One fish died at concentrations up to 500 mg/l of hexaflumuron in a dimethyl sulphoxide (DMSO) solvent. The LC_{50} is in excess of 500 mg/l which is more than 10 times the maximum solubility of hexaflumuron in water.

Note: All existing liquid barrier termiticides are toxic to fish. The hexaflumuron baiting system would represent a greatly reduced-risk treatment near wells or bodies of water.

c. Toxicity to Daphnia magna
The EC_{50} was calculated to be 0.11 *u*g/l.

5. Honeybee Toxicity, Effects on Terrestrial Plant Growth, and Effects on Aquatic Plant Growth.
The formulation and delivery system of the product obviate the need for studies in these categories.

6. Potential Exposure to Non-Target Organisms.
The hexaflumuron baiting system is extremely pest specific. It is placed underground and contains a cellulose food source which is attractive and palatable only to termites. Ants and other subterranean organisms would have very little chance of being effected.

7. Drift Potential, Environmental Persistence and Mobility In Soil and Water.
Because the product is not applied to water, has no potential for drift, does not come in contact with the soil, and is removed when no longer needed - persistence and mobility in soil and water are not a concern. In addition, the low water solubility, high Kd, and non-leaching properties (MRID #42648527) ensure that the only movement of hexaflumuron in the environment will be in the termite gut.

8. Bioaccumulation Potential
Termites have very few predators, however, with a K_{ow} calculated to be 5.462 (MRID #42648505), this is not a concern.

C. Other Hazards

1. Ozone Depletion Potential
There are no ozone depleting products used in either the manufacture or formulation of hexaflumuron.

2. Chemical and Physical Properties
Please reference MRID #'s 42648501-06. The end use formulation is approximately [redacted] thus it is stable, non-flammable, non-corrosive, and non-explodable.

D. Risk Discussion

Consider the example of a residential structure in a high termite pressure area. If termites are detected in the structure, typically a pest control company would seek to reestablish the chemical barrier in the soil. This has been a successful tactic for more than 50 years and would still be advisable as a pre-construction treatment of a new structure; however, it represents a large amount of active ingredient in a small volume of soil. In the given example, a Pest Control Operator would dig a trench around the structure, apply the liquid termiticide, and mix soil back into the trench. Termiticide could also be injected through long rods deep into the soil to reach the foundation footing. Other rod application sites would include: under concrete slabs; through cinder block walls or other areas where trenching or direct access to soil is difficult. On average, 16 pounds of active ingredient are applied to the soil around the structure.

The hexaflumuron baiting system would utilize non-chemical monitoring devices placed around a structure. Once termites attacked these devices, the bait matrix tube would replace the monitoring devices. Each tube contains 150 milligrams of active ingredient.

While difficult to estimate due to the numerous variables involved, on average a typical structure would utilize approximately 10-20 bait sticks. Using the highest estimate, a total of 3 grams of hexaflumuron would be used which represents an estimated 2400 fold decrease in active ingredient when compared to the barrier treatments. In addition, hexaflumuron is utilized only when there is termite activity. Liquid termiticide could be utilized as a spot application in this example to treat the point of termite entry into the structure and negate further damage. This would entail significantly less dilution than would be required if the objective were to reestablish a barrier around the entire structure.

The hexaflumuron baiting system has another advantage in that it serves to suppress or eradicate the foraging termites. This should enhance the effectiveness of any barrier treatment by reducing the termite pressure. It is important to note that this system is being tested in each of the major termite pressure states and against both economically important species of termites (the native subterranean and Formosan species).

In summary, the hexaflumuron baiting system is utilizing the termite biology and behavior as a pest management weapon. It poses virtually no risk to any species other than the termites themselves.

E. Pest Resistance Management

Termites have evolved an elaborate caste system. There exist soldiers, workers, and a queen. Worker termites are essential to the colony because they forage for food and feed the queen and soldiers who are unable to feed themselves. Workers are sterile and incapable of reproduction, thus, the potential for resistance is extremely low. Hexaflumuron is a slow acting toxicant which eventually prevents a successful molt or shedding of the termite exoskeleton. This slow action is necessary to allow a large number of workers to feed on the hexaflumuron matrix. There follows a collapse in the number of workers followed by a collapse of the colony simply because there aren't enough workers to successfully support the dependent castes.

On the bases stated in this document, DowElanco believes hexaflumuron fully meets the criteria for consideration as a reduced-risk pesticide.