UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

DEC 11 1985

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: EPA Registration No. 45167-1, 5F3255.
Margosan-O (Neem Extract), Used as an Insect Antifeedant Extract for Lepidopterous Insects.
Accession No. 252097 Caswell No. 594A

FROM: William Woodrow, Ph.D.
Section VII, Toxicology Branch
Hazard Evaluation Division (TS-769C)

ABK for William Woodrow 11/19/85

TO: Willie Nelson, PM Team No. 17
Insecticide/Rodenticide Branch
Registration Division (TS-767C)

THRU: Albin B. Kocialski, Ph.D., Supervisory Pharmacologist
Section VII, Toxicology Branch
Hazard Evaluation Division (TS-769C)

A.B.K. 11/19/85

Petitioner: Vikwood, Ltd.
1221A Superior Avenue
Sheboygan, WI 53801

Action Requested:

Mr. Robert Larson of Vikwood, Ltd. requests that an exemption from the requirement of tolerances be granted for Margosan-O, an insect antifeedant extract, when Margosan-O is used on RAC (Raw Agricultural Commodities).

Recommendations:

1. The request for registration and exemption from the requirement for tolerances by Mr. Larson of Vikwood, Ltd. for Margosan-O used on RAC (Raw Agricultural Commodities) is not toxicologically supported. The

following data deficiencies and data gaps should be corrected and submitted:

a. The acute inhalation toxicity experiment must be repeated. The acute inhalation toxicity study previously submitted (see Woodrow memo of April 20, 1984, attached) did not determine the actual aerosol concentration animals were exposed to.

b. A 90-day feeding study using one mammalian species must be submitted.

c. A teratogenicity study using one mammalian species must be submitted.

NOTE: Subsequent to the Agency/Vikwood meeting on February 19, 1982, to discuss toxicity data requirements for Margosan-O, the 40 CFR Part 158 Data requirements for pesticide registration was published Wednesday, October 24, 1984. This document lists a 90-day subchronic feeding study and a teratogenicity study as requirements.

2. Previously reviewed data (See Woodrow memo of April 20, 1984).

a. Acute oral toxicity of Margosan-O, rat.

LD_{50} > 5 g/kg
Toxicity Category IV
Classification: Core Minimum Data

b. Acute dermal toxicity of Margosan-O, rabbit.

LD_{50} > 2.08 g/kg
Toxicity Category III
Classification: Core Minimum Data

c. Primary skin irritation of Margosan-O, rabbit.

P.I. Index = 4.74, a moderately irritating substance.
Toxicity Category III
Classification: Core Minimum Data

d. Acute inhalation toxicity of Margosan-O, rat.

Nominal LC_{50} > 43.9 mg/L
Toxicity Category - Not appropriate
Classification: Supplementary Data
(The actual cloud concentration that the animals were exposed to was not determined.)

e. Primary eye irritation of Margosan-O, rabbit.

The MMTS (maximum mean total score) for unwashed eyes was 4.33; for irrigated eyes, 3.3, which indicated a minimally irritating substance.
Toxicity Category III
Classification: Core Minimum Data

f. Immune response of Margosan-O in the rat.

Margosan-O does not elicit an immune response in the rat.
Classification: Core Minimum Data

g. Sensitization study using Margosan-O, guinea pig.

Margosan-O is not a sensitizing agent.
Classification: Core Minimum Data

h. Mutagenicity study using Margosan-O (Ames test).

Margosan-O did not exhibit any mutagenic potential using the Ames test.
Classification: Acceptable Study

3. No additional toxicity studies were submitted with the current application.

4. The product label was designed to serve for an Experimental Use Permit. The product manager should advise Mr. Larson concerning proper precautionary statements. The submitted subject label CAUTION signal word is appropriate, however, a number of statements must appear on the product label:

a. Keep out of reach of children (this warning must appear an the front label panel).

b. Avoid contact with skin, eyes, or clothing. In case of contact immediately flush eyes or skin with plenty of water.

c. Additional cautions may or may not be warranted depending upon resolution of the acute inhalation study.

d. The phrase NON-TOXIC must be deleted from the label as it is considered a claim for the safety of the pesticide (refer to 40 CFR 162.10). Also delete the phrase ". . . toxicological studies have shown no negative effects from exposure to the Azadirachtin extract . . . ."

FORMULATION: (CONFIDENTIAL)

Product Label

	by wt.
Active ingredient	
Azadirachtin	0.3%
Inert ingredient	99.7%
	100.0%

The inert ingredients [redacted] have been cleared under CFR 40 §180.1001(c).

BACKGROUND INFORMATION:

Margosan-O contains an active ingredient called Azadirachtin (a tetranortriterpenoid) that is obtained by alcoholic extraction of ground "Neem" nuts from the Indian tree named Azadirachta indica. Mr. Larson, of Vickwood, Ltd., states that the active ingredient acts as an insect antifeedant, and is requesting that Margosan-O be granted exemption status for crop use. The Agency has determined that Azadirachtin is to be designated a "biochemical" pesticide and therefore toxicity testing requirements for Margosan-O may be limited to the following studies.

Tier 1 Biochemical Tests:

Acute oral toxicity
Acute dermal toxicity
Acute inhalation toxicity
Primary eye inhalation
Primary dermal inhalation
Hypersensitivity study
Study to detect genotoxicity
A 90-day feeding study using 1 mammalian species
A teratogenicity study using 1 mammalian species