UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

DATE: November 21, 1977

SUBJECT: Giv-Gard DXN (Dimethoxane) EPA Registration #824-7
Caswell #363

11/21/77 WHD E 11/22/77
INSB 11-28-77

FROM: William Dykstra, Ph.D
TOX/RD WH-567

TO: James H. Banks, PM #33

Thru: Martin Rogoff, Ph.D
Pesticide Science Officer

Product Manager: James H. Banks, PM #33

Action Type: Resubmission with DATA

Recommendations:

1. The active ingredient of the formulation is 6-acetoxy-2,4-dimethyl-m-dioxane (Dimethoxane) which according to the open literature produces ~~malignant~~ tumors, predominantly in the liver of male Wistar rats may after its oral administration. ~~I recommend that~~ This evidence ~~should~~ trigger RPAR criterion 162.11. Enclosed is a copy of W. H. O., IRAC Monograph, volume 15, 1977, wherein the reference to the original report by Hoch-Ligeti etal (J. Nat. Cancer Inst. 53, 791-794, 1974) was reported.

2. In the 13-week tolerance test with subcutaneously applied dimethoxane on rats, the no effect level is 10 mg/kg/day which is the intermediate level in this study.

Review: 13-Week Tolerance

Test with Subcutaneously applied RO 07-0055 (Dimethoxane) on Rats (Hoffman - Roche and Co, Basel, Switzerland; Roche rpt #B-85, 711; Hoffman-La Roche Corporation, 6/22/77).

Dimethoxane was applied subcutaneoulsy to groups (16 male and 16 female) of Fü-Albino (SPF) rats at dosages of 3.0, 10.0, and 30.0 mg/kg/day. The 7 days per week for 13 weeks as a 3 ml/kg volume of application. A phase of recovery was not included in the test. The clinical chemistries and hematological studies were carried out on 8 animals per group and sex. Histological preparations of the organs were made and examined from all rat used in the test.

Results:

Body weight: A 5-6% reduction in weight gain was observed in the 30 mg/kg/day and 10 mg/kg/day groups of male rats compared to the controls. Female body weights were comparable to the controls.

Hematology: Negative

Clinical Chemistries: Negative

Histopathology: Negative

Mortality: control (2 animals); 3 mg/kg/day (1 animal)

Toxic Symptoms:

Dose (mg/kg/day)	Animal	Symptom	Week
30	1	Loss of Hair	2
30	1	Conjunctivities	5
30	1	Colds, sneezing	6
30	1	redding skin	6.7
10	1	Conjunctivitis	5
10	1	Colds, sneezing	6
Control	1	bleeding mouth, colds	3,6

Organ/Body weight: No significant differences between control + experimentals.

Conclusion: The no - effect level appears to be 10 mg/kg/day from the results submitted. This is the intermediate dose level in this study. The examination of the toxic signs of the high dose level revealed a more frequent toxic reaction in this group in comparison to the controls.