UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

Coberly

DATE: November 29, 1976.

SUBJECT: EPA Reg. No. 824-7 (Giv-Gard DXN). Addition of toxicity study to product file

FROM: Edwin R. Budd/Toxicology Branch

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TO: James Banks/PM #33

CONCLUSION:

The submitted study was reviewed and found to be acceptable. Add study to registration file for the product Giv-Gard DXN (EPA Reg. No. 824-7).

IDENTIFICATION OF STUDY:

Study entitled "13-Week Tolerance Test with Subcutaneously Applied RO 07-0055 (Dioxin) on the Dog". Conducted in research laboratories of F. Hoffman-LaRoche and Co., Basel, Switzerland. Roche Report #B-85,710, dated 3/30/76. Original report in German; translated.

EXPERIMENTAL PROCEDURE:

RO 07-0055 (Dioxin, Giv-Gard DXN, brand of Dimethoxane, 6-acetoxy-2,4-dimethyl-m-dioxane--presumably the 92% technical product) was subcutaneously administered to Swiss "beagle" dogs 7 days/week for 13 weeks. The mean age of the dogs was 7 3/4 months and the mean weight was 11.6 kg. Food and water were given ad lib. The test material was diluted in saline (?) to 0.5, 1.0 and 3.0 % concentrations and injected in 0.1 ml/kg volumes so as to yield the following 4 dosage groups: 0 (control), 0.5, 1.0 and 3.0 mg/kg/day. 4 male and 4 female dogs per dosage group. The following parameters were observed or measured in all dogs: signs of toxicity, mortality, acceptance of food, body weights (weekly), rather complete hematological examinations (0, 2, 6 and 13 weeks), rather complete clinical chemistries (0, 2, 6 and 13 weeks), BSP excretion rate (0, 5, and 11 weeks), urinalysis (5 and 11 weeks), electrocardiograms (0 and 13 weeks) and eye examinations (13 weeks). At 13 weeks, all dogs were sacrificed and gross necropsies were performed on all of them. Organ weights (11 organs) were recorded. 33 tissues from all dogs were subjected to histopathological examination.

RESULTS:

There were no mortalities. The following differences were observed between control and test animals:

Body Weights--1 mg/kg/day dogs gained about 2 fold more weight than all other groups during the 13 week test period. The difference was not dose-related and is considered to be toxicologically insignificant. The remaining groups

gained equivalent amounts of weight (on a % basis).

Hematology----There was a tendency towards increased erythrocyte counts, increased hemoglobin contents, increased packed cell volumes and increased band cells, monocytes and eosinophils in differential counts in the 3 mg/kg/day dogs at 6 and 13 weeks. No other differences in hematological parameters were observed between control and test animals.

Clinical Chemistries--There was a tendency towards increased plasma bilirubin and decreased serum potassium in the 1 and 3 mg/kg/day dogs at 6 and 13 weeks. Both appeared to be dose-related. No other differences in clinical chemistries were observed between control and test animals.

Organ Weights--For the 3 mg/kg/day dogs, absolute weights for all organs weighed were about 10% less than in all other groups. Since body weights for this group were also about 10% less than in all other groups at the beginning and end of the study, calculations of organ/body weight ratios would probably not indicate a significant effect in this group--except perhaps in uterus weights. Organ/body weight ratios were not presented. There were no differences in absolute organ weights between controls and the other test groups.

No differences were observed between control and test animals in acceptance of food, BSP-retention time, urinalysis, electrocardiograms, eye examinations, gross necropsies or histopathological examinations (poorly reported). Local reactions were not observed at the sites of injections. There was no statistical analyses presented for any of the data in this report.

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GIVAUDAN

GIVAUDAN CORPORATION - 125 DELAWANNA AVE., CLIFTON, N.J. 07014

GIV-GARD DXN

(BRAND OF DIMETHOXANE)

BACTERIOSTAT/FUNGISTAT

ACTIVE INGREDIENT:

6-acetoxy-2, 4-dimethyl-m-dioxane.....92%

INERT INGREDIENTS 8%

Giv-Gard DXN® (Brand of Dimethoxane) is a microbial growth inhibiting agent to be used as directed in Givaudan Corporation's Technical Bulletin 27A.

CAUTION: Harmful if swallowed! Do not get in eyes, on skin or on clothing. In case of contact, immediately flush skin or eyes with water. If irritation persists, get medical attention. Do not reuse empty drum. Return to drum reconditioner or destroy by perforating or crushing and burying in a safe place away from water supplies.

NON-WARRANTY: Our recommendations for use of this product are based upon tests believed to be reliable. The use of this product being beyond the control of the manufacturer, no guarantee, expressed or implied, is made as to the effects of such or the results to be obtained if not used in accordance with directions and established safe practice. The buyer must assume all responsibility, including injury or damage, resu from its misuse as such, or in bination with other mater.

*U.S. PAT. 3,167,477 EPA REG. NO.

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ACCEPTED
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