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[DICLORAN]

Carcinogenicity Study-Rat (83-2a)

EPA Reviewer: P. V. Shah, Ph.D
Registration Action Branch 1/HED (7509C)

P.V. Shah Date 4/17/01

EPA Secondary Reviewer: Guruva Reddy, D.V.M., Ph.D
Registration Action Branch 1/HED (7509C)

Date 4/17/01

DATA EVALUATION RECORD- SUPPLEMENTAL
See TXR N0. 007922 for Original DER

NOTE:
This study was previously reviewed and classified as supplementary data. However, the format for the executive summary and the first page of the **DER** were different from the current format. This is to update the format and, at the same time, to add needed data to the **DER** for the ease of evaluating this study.

STUDY TYPE: Carcinogenicity Study- Feeding Rat
OPPTS 870.4200 [§83-2a]

DP BARCODE: D241078

SUBMISSION NO.: S541375

PC CODE: 031301

TOX. CHEM. NO.: 311

MRID NO: 00086903

TEST MATERIAL (PURITY): DICLORAN (unspecified purity)

COMPOSITION/SYNONYM(S): 2,6-dichloro-4-nitroaniline; DCNA; Botran™

CITATION: Lessel, B. (1974). Two-year Feeding Trial in Rats on Dicloran (2,6-Dicloran-4-nitroaniline). Unpublished study received Nov..17, 1981 under 1023-36; submitted by Upjohn Co., Kalamazoo, Mich; CDL: 070501-AF. MRID No. 00086903. Unpublished study.

SPONSOR: Upjohn Company, Kalamazoo, Michigan.

EXECUTIVE SUMMARY:

In a carcinogenicity study (MRID# 00086903), Boots-Wistar rats (25/sex/group) were administered via diets for 2 years with dicloran (unspecified purity) at dose levels of 0 or 1000 ppm (mean compound intake 0, or 58.6 mg/kg/day for males and 0, or 71.4 mg/kg/day for females, respectively). The rats were weighed three times each week for the first three months, and then once weekly for the remainder of the experiment. Hematological examinations were performed on two cages (10 rats) of males and females in each group at 3, 6, 12 and 24 months. Animals that died or were killed when moribund were autopsied and any grossly abnormal organs were removed for microscopic examination. Animals that survived for two years were killed, and

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from each liver, kidneys and spleen were weighed and various other organs taken for histopathology.

There was no difference in daily food consumption expressed relative to body weight between dosed and control groups of rats. Mortality and life span of animals in the dosed group was no different from that in the control group. In the two year study duration, 15 males and 7 females died from the treatment group and 15 males and 11 females died from the control group. Body weight gain was similar between treated rats and control groups.

There were no remarkable differences in hematological parameters measured between the dosed group and the control group. There was no statistically significant differences between the liver, kidney and spleen weights of the dosed and control groups.

Histological examination revealed minor abnormalities in organs but occurred both in the dosed and control groups. Neoplastic changes were seen in animals of both groups. In the dosed group, neoplastic changes were as follows: two males had reticulum cell sarcomata, one male had alveolar carcinoma, one had an embryoma of the left kidney and a fifth male had an adrenal adenoma, three females had undifferentiated tumors of the kidney, renal pelvis and a thorax, another female had adeno-carcinomas in undifferentiated tissue, probably uterine and fifth had a fibrosarcoma in the vagina. The incidence of tumors was similar in the two groups which indicates the treatment did not have a carcinogenic effect.

In conclusion, the administration of dicloran at 1000 ppm in diets to rats for two years did not have carcinogenic effect. The dosing was not adequate for carcinogenicity testing.

This study is classified as **Unacceptable/Guideline** and **does not satisfy** the guideline requirement for a carcinogenicity study (83-2(a)) in the rat. This study can not be upgraded to acceptable because only one dose level was used and other deficiencies.

COMPLIANCE: No Signed and dated GLP, Quality Assurance and Data Confidentiality statements were provided.