US EPA ARCHIVE DOCUMENT

1/18/83

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

002409

MEMORANDUM

OFFICE OF PESTICIDES AND TOXIC SUBSTANCES

TO: Henry Jacoby (21)
Registration Division (TS-767)

THRU: Orville E. Paynter, Ph.D.
Chief, Toxicology Branch
Hazard Evaluation Division (TS-769)

SUBJECT: Review of Rabbit Teratology Study of Ronilan (Vinclozolin). PP#1E2457; Tox. Chem. 323C; Acc. No. 070400

Registrant: BASF Wyandotte

Recommendation:

It is recommended that this study be core classified as Core-Minimum Data. The NOEL for maternal toxicity is 300 mg/kg/day (HDT) and the NOEL for fetotoxicity is 80 mg/kg/day. A teratogenic potential is not suggested in this study.

Review of Data:

Teratology, Rabbits. Conducted by Huntingdon Research Centre, Huntingdon, England, September 4, 1981 (Identification Number 80/232) and submitted by BASF.

(A preliminary study of non-pregnant does found overt clinical toxicity and weight loss at 900 mg/kg. Slight lethargy and friable liver (in 2/6 animals) were noted in the 300 mg/kg group. No indication of toxicity was noted in lower dose groups.)

Vinclozolin technical was suspended in 1.0% methylcellulose and administered by gavage at dose levels of 0, 20, 80 and 300 mg/kg/day to pregnant Zealand White rabbits on days 6 through 18 of gestation. Fifteen females per dose level were used. Animals were sacrificed on day 29 of gestation by cervical dislocation. All animals were weighed on days 1, 6, 10, 14, 19, 23 and 29 of gestation and observed daily for signs of toxicity. After sacrifice on day 29, dams were necropsied and the number of corpora lutea, live young, fetal deaths, fetal weights,

1/2

002409

fetal external abnormalities and uterine weight were recorded. Live young were examined externally, killed by Pentobarbitone Sodium injection and "dissected to examine for visceral abnormalities". Fetuses were then skinned and fixed and "heads were sliced through the line of the frontoparietal suture and the brain examined for visible abnormalities" after which carcasses were cleared and stained for skeletal examination.

Results:

Four mortalities occurred during the study (two animals at 300 mg/kg/day, one at 80 mg/kg/day and one in the control group). Three of these mortalities appeared attributable to intubation error and no mortalities or other maternal toxicity could be associated with Vinclozolin at the dose levels used in this study. Pregnancy rates, number of live young, embryonic deaths and rate of implantations were similar in all groups.

Although the post-implantation loss (%) appears to increase with dose, and the mean litter and fetal weights appear to decrease with dose, it must be noted that a relatively small number of litters are available at each dose (10-13) and the elucidation of compound related effects on litter parameters is therefore difficult. However, the data does suggest an effect on post-implantation loss, litter weight and mean fetal weight in the high dose group. The submitted historical data appears to be less appropriate, for comparison purposes, than the concurrent control data for two reasons:

1) The historical data base appears to have been generated from animals receiving various test compounds as well as true controls.

2) The historical data base covers a very large interval of time (5 years).

	Live Young	Resorption and Abortions Per Litter	Post-Implantation Loss (%)	Litter Wt. (g)	Mean Fetal Weight (g)
0 mg/kg/day	8.5	.45	3.9	371.1	49.0
20 mg/kg/day	7.9	.62	7.6	351.8	44.9
80 mg/kg/day	7.5	.46	6.2	332.7	45.0
300 mg/kg/day	8.0	.80	10.2	323.6	41.4
Historical	8.3	Unknown	10.4	332.9	41.3

A total of 3 major malformations of fetuses were observed (2 in the control group and 1 in the high dose group). The incidence of minor visceral and skeletal anomalies and variations were also similar in all groups. Furthermore, a pattern of characteristic skeletal or visceral anomalies related to compound administration was not apparent.

Core Classification: Core-Minimum

The NOEL for maternal toxicity is 300 mg/kg/day (HDT) and the NOEL for fetotoxicity is 80 mg/kg/day. A teratogenic potential is not suggested in this study.

Gary J. Burin FDC 1/18/83

Gary J. Burin, Toxicologist
Toxicology Branch
Hazard Evaluation Division (TS-769)

TS-769:th:TOX/HED:GJBurin:12-21-82:card 1