3-10-93

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

MAR 10 1993

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM:

Subject: EPA ID # 007969-00053, 007969-0062, 007969-0085 & 007969-57. Vinclozolin; 6(a)(2) Data on Summary Effects of Vinclozolin (MRID# 42577-00) for a Preliminary Report for Oncogenicity Study in Mice (MRID# 42577-01).

PC Code: 113201.
Tox. Chem. No.: 323C.
DP Barcode: D186218, D186219, D186222 & D186225.
Case: 037677, 032049, 044332 & 011409.
Submission No.: S432311, S432312, S432313 & S432315.
Action: 405 6(a)(2) adverse data.

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Thru: Karen Hamernik, PhD. K. Hamernik 3/9/93 KB 3/9/93
Acting Section Head, Section
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Health Effects Division (H7509C).

CONCLUSIONS: The 6(a)(2) data submitted is a summary report (MRID# 425775-00) of a preliminary report of an oncogenicity study in mice (MRID# 425775-01). When the final report is submitted, a detailed Data Evaluation Record (DER) will be prepared. The study report tends to confirm effects demonstrated by a previous chronic study in rats. The rats appear to be more sensitive than the mouse to these antiandrogenic effects of vinclozolin. This 6(a)(2) data does not appear to alter the existing RfD or effects noted after vinclozolin administration. However, since only summary reports have been reviewed, a final evaluation can only be

made after reviewing the final report on the mouse study and other studies submitted as preliminary reports.

The summary letter (MRID# 425775-00) stated that vinclozolin was administered in the feed to 50 (main groups) and 10 (satellite groups) C57B1/6N mice at 0, 15, 150, 3000 or 8000 ppm for 18 months. Mortality was 60% in males and 48% in females at 8000 ppm. Mortality was 6 to 22% in males and 6 to 24% in controls and other dosed groups, respectively. Body weight reductions were 23% in males and 18% in females at 8000 ppm and 18 months. At 3000 ppm, body weights were reduced by 11% in males and 7% in females. The report indicated that the MTD had been exceeded at 8000 ppm and that 3000 ppm was an adequate MTD.

Liver masses were seen in female mice at 8000 ppm, but none in males at 8000 ppm or females at 3000 ppm or less. It is noted that an interim report on a chronic toxicity study in 20 rats/sex/group, demonstrated liver carcinogenicity (9/20) in males at 4500 ppm, but not in females at the 24 months sacrifice. The 4500 ppm dose level in rats was also considered by the report authors to be above the MTD.

Epididymal, seminal vesicle and prostate weights in the mice were reduced and adrenal weights were increased at 18 months at 3000 and 8000 ppm. Ovaries were enlarged at 8000 ppm at 18 months. The effects were reasonably attributed to the antiandrogenic effects of vinclozolin. The rat appears to be more sensitive than the mouse to the antiandrogenic effects of vinclozolin.

6(a)(2) Summary Data (425909-00) on the effects of Vinclozolin on a preliminary oncogenicity study in mice(425909-01)/D186218, D186219, D186222 & D186225/B:\VINCLV43.23C\CMSONCOM.6a2/ DANDERSON/2/24/93.*