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

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DEC 17 1993

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM:

SUBJECT: Review of Tumor Comparison Data for Atrazine, EPA Reg. No. 100-529. MRID # 42777201.

D 191726
S 441577
Chemical No 080803
Tox Chem No. 063
MRID 42777201

TO: Venus Eagle
PM # 71
Reregistration Branch
SRRD (H7508W)

FROM: Henry Spencer, Ph.D. 11/12/93
Pharmacologist
Review Section 3
Toxicology Branch 1
Health Effects Division (H7509C)

THRU: Karen Hamernik, Ph.D. 12/1/93
Section Head
Review Section # 3
Toxicology Branch 1
Health Effects Division (H7509C) KR 12/8/93

ACTION: The registrant, Ciba-Geigy, has submitted for review, a compilation of two, 2-year, long term studies in each of both the Sprague Dawley and the Fischer 344 rats with Atrazine as the test material. This compilation is reported in the following review.

CONCLUSIONS:

1/ The purpose of the submitted document was to "present results of statistical analysis of data from selected parameters from combined as well as individual studies for each strain and to compare strain differences evident

from the analyses".

2/ The statistical analysis of the data can not be verified at this time since individual animal supporting data did not accompany the submission.

3/ The results alluded to in this submission: increased mortality at 400 ppm, tumor occurrences (earlier onset) in mammary tissue in Sprague Dawley compared to that of the F-344 rat and that pituitary tumor occurrences were unaffected by treatment in SD rats will be addressed in the review of the final summary document covering the carcinogenicity of Atrazine in the rat, to be supplied by the registrant in the near future.

4/ The submission is based on two year studies for the Fischer 344 rat: HWA Report 483-277 and HWA Report 483-279 & for the Sprague Dawley rat: HWA Report 483-275 and HWA Report 483-278.

5/ Core Grade: Supplemental information. This submission cannot be upgraded. No additional information from the registrant is required.

REVIEW:

This submission reviews findings from a 24 month feeding (hormone) study with interval sacrifices at 1,3,9,12,15,18 and 24 months of ten animals each for both the Sprague Dawley and Fischer 344 rats. Also, each rat strain was studied in a 24 month feeding oncogenicity study without interval sacrifices where the test material was 97% Atrazine in the diet at 0, 70, and 400 ppm for the Sprague Dawley rat and in the diet at 0,10,70,200,400 ppm for the Fischer 344 rat. Only data on female rats are reported in this submission.

Parameters reported in this submission included the 1. mortality, 2. body weight and weight gains, 3.tumor incidences of the pituitary gland, mammary tissue, uterus and ovary.

RESULTS:

1. Mortality was noted to be increased in the SD rats at the highest dose tested (400 ppm). Mortality rates in the Fischer 344 rats were not significantly different from controls.

2. The SD rats were reported to exhibit reduced mean body weight gains of 12 % in the period of 0-13 weeks at 400 ppm but not at 70 ppm in the oncogenicity study and a 17% reduction at the top dose in the hormonal study when compared to their respective control groups. The Fischer 344 rats also showed reduced weight gains at the top doses of 200

and 400 ppm of atrazine when compared to their controls. Supportive individual animal data were not submitted in this report.

3/ Tumor occurrences are reported by the authors of this summary to show no significant increase in SD rats of total tumors (fibroadenomas/carcinomas) in the mammary tissues, while exhibiting an earlier onset of those tumors at dosages of 400 ppm (a reduced latency) than those occurring in controls.

4/ No differences in either reduced latency or total tumors were reported for the F-344 female rats at any dose level compared to controls.

5/ Pituitary tumors, ovarian, or uterine tumors were reported to not be increased in either strain of rat following two years of exposure to up to 400 ppm of atrazine in the diet in the 4 studies examined.

6/ Only summary data were presented which are unable to be verified at this time. The results of body weight gains and tumor incidences are reported for separate studies and as a combined data set.

7/ Core Grade: Supplemental information. Cannot be upgraded. No additional information from the registrant is required.