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

AUG 1 1988

MEMORANDUM

OFFICE OF PESTICIDES AND TOXIC SUBST

SUBJECT: EPA ID: 100-529: Atrazine: Reevaluation of slides for rat chronic feeding/oncogenicity study (Sprague Dawley).

TO: **Robert Taylor (PM 25)**
Registration Division (TS-767C)

FROM: Marion P. Copley, D.V.M., D.A.B.T. Marion Copley 7/26/88
Section VI, Toxicology Branch
Hazard Evaluation Division (TS-769C)

THRU: Judith W. Hauswirth, Ph.D., Section Head
Section VI, Toxicology Branch
Hazard Evaluation Division (TS-769C) Judith W. Hauswirth 7/27/88

Tox. Chem No.: 63
Proj. No.: 8-0898
Record No.: 223805

CONCLUSIONS:

This reevaluation of the slides resulted in similar mammary tumor counts to the original submission. Therefore, the original DER will not be altered. The refinement of the tumor diagnosis has no impact on the scientific interpretation of this study.

BACKGROUND:

Atrazine was associated with increased oncogenicity (mammary tumors) in a Sprague Dawley 2 year chronic feeding/ oncogenicity study (reviewed in 1987). There was no associated oncogenicity in the mouse oncogenicity study. A registration standard was completed in 1983. A FRSTR is currently scheduled for early 1989.

CURRENT ACTION:

Ciba-Geigy has submitted a re-evaluation of the pathology data for the rat combined chronic feeding/oncogenicity study (#410-1102). This evaluation was conducted to further characterize the oncogenic effect of Atrazine and determine if there was any progression of tumors from benign to malignant.

1/4

COMMENTS:

Discussion of the study is in the attached DER supplement.

The contractor should be careful when compiling summary tables such as 1 and 2. There were several discrepancies from the individual histology incidence tables. At the high dose in table 1, there were 10 (not 9) mammary tumor bearing animals in the histopathology incidence table (HIT) resulting in 40 %. In table 2, the HIT had 33 mammary tumor bearing animals not 30, resulting in 50 %. There were 46 (not 45) and 55 (not 54) tumors for 500 ppm and 1000 ppm, respectively in the histopathology incidence table resulting in 71 and 90 %.

Tox. Br. recommends that the registrant be sent a copy of the DER-Supplement to update their files.

COPLEY\PC6\ATRAZINE\MEMO1.218, PROJ 8-0898, #63, 7/22/88

Reviewed by: Marion P. Copley, D.V.M., D.A.B.T. 7/24/87
Section VI, Tox. Branch (TS-769C)
Secondary reviewer: Judith W. Hauswirth, Ph.D. 7/27/87
Section VI, Tox. Branch (TS-769C)

DATA EVALUATION REPORT - SUPPLEMENT (histopath.)
Original DER, see doc. 005940

STUDY TYPE: 2-yr chronic/onco - rats (83-5) TOX. CHEM NO: 63

MRID NO.: 406293-02 (Orig Acc. 262714-262727; MRID 00158930)

TEST MATERIAL: Atrazine technical

SYNONYMS: 2-Chloro-4-ethylamino-6-isopropylaminotriazine

STUDY NUMBER: EPL report # 140-040 (original study 410-1102)

SPONSOR: Ciba-Geigy

TESTING FACILITY: Experimental Pathology Laboratories, Inc.

TITLE OF REPORT: Supplement to two-year chronic feeding/oncogenicity study in rats administered atrazine

AUTHOR(S): Jerry Hardisty

REPORT ISSUED: Oct. 1, 1987

CONCLUSION:

No change from the original DER. This reevaluation of the slides resulted in similar mammary tumor counts to the original submission. Therefore, the original DER will not be altered. The refinement of the tumor diagnosis has no impact on the scientific interpretation of this study.

RESULTS AND DISCUSSION:

The overall tumor reanalysis was similar to the earlier reading of the slides. The tumors that were increased over controls at 12-13 months were tubulo papillary carcinomas with some compact tubulo carcinomas (both non-invasive). At two years, there was a slight increase in fibroadenoma NOS and proliferative fibroadenoma. Most of the increased incidence at two years was due to tubulo papillary carcinomas with some compact tubulo carcinomas (both non-invasive).

The results of this report were for the most part in agreement with the original report. The Zwieten's expanded mammary tumor classification indicated that the compound,

"while enhancing the overall mammary tumor incidence, also produced additional epithelial proliferation, dedifferentiation and less frequently, malignant transformation in mammary fibroadenomas. Not withstanding, the foregoing observations concerning malignant progression in fibroadenomas, most of the malignant tumors diagnosed in this study appeared to arise de novo from normal appearing mammary gland. . .

Both tubulo papillary and compact tubular carcinomas were recognized, with the former being more frequently diagnosed."

The contractor should be careful when compiling summary tables such as 1 and 2. There were several discrepancies from the individual histology incidence tables. At the high dose in table 1, there were 10 (not 9) mammary tumor bearing animals in the histopathology incidence table (HIT) resulting in 40 %. In table 2, the HIT had 33 mammary tumor bearing animals not 30, resulting in 50 %. There were 46 (not 45) and 55 (not 54) tumors for 500 ppm and 1000 ppm, respectively in the histopathology incidence table resulting in 71 and 90 %.

COPLEY\PC6\ATRAZINE\CHRONC1.218, PROJ 8-0898, #63, 7/22/88