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

MAR 11 1992

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

SUBJECT: Cyanazine; Historical Control Data on 2-Year Rat Study; ID # 100101; Support of Reregistration

Tox.Chem No.: 188C
MRID No.: 421384-01
HED Project No.: 2-0969
Submission No.: S409418

TO: Walter Waldrop, PM # 71
Reregistration Branch
Special Review and Reregistration Division (H7508W)

FROM: William Dykstra, Ph.D., Toxicologist
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THRU: Roger Gardner, Section Head, Toxicologist
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ACTION REQUESTED: Review additional historical control data on mammary gland tumors from Haskell Lab and historical control data on non-neoplastic lesions of concern in 2-year rat study.

CONCLUSIONS: The historical control data from Haskell Lab adequately addressess the concerns of TB-I regarding the incidences of non-neoplastic lesions observed in the 2-year rat study. With respect to males, the range of incidences in the historical data for granulocytic hyperplasia of bone marrow was 0-69.6%, which encompassed the 23% incidence at the high-dose, (individual incidences were 0, 69.6, 24.2, 26.2, 22.5, 1.8, 40.3, and 43.5%) and the range for extramedullary hematopoiesis of the spleen was 0-

63.0%, which overlapped the 56% incidence at the high-dose (individual incidences were 0, 46.3, 7.5, 55.7, 4.8, 41.1, 12.3, and 63.0%).
In females, the historical range for demyelination of the sciatic nerve was 0-40.6%, which encompassed the high-dose incidence of 18% (individual incidences were 0, 0, 3.2, 10.1, 3.3, 40.6, 6.7, and 36.1%)
The issue of non-neoplastic lesions is resolved. There were no compound-related non-neoplastic lesions in the 2-year cyanazine rat study.

With respect to Haskell Lab's reassessment of the incidences of malignant mammary gland tumors (adenocarcinomas and carcinosarcomas), the previous range was 10.1-22.7%, whereas now the range is 10.8-23.2%.
This slight shift in the range does not change the interpretation of the original conclusion that cyanazine is a mammary gland carcinogen.
The incidences calculated in the study by HED statisticians were 9, 11, 22, 32, and 24%, for the 0, 1, 5, 25, and 50 ppm groups, respectively.

Based on the submission of these historical control data, the 2-year rat study is upgraded to core-guideline data.

Review: Supplement No. 1 to 2-year rat Study; Author: M.S. Bogdanffy; Lab Project No. 23-90; pages 1-12 (MRID No. 421384-01)

2