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

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NOV 25 1992

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

SUBJECT: Maneb - UPDATE Chronic Toxicity Study in Dogs

TO: Terri Stowe
PM Team Reviewer (71)
SRRD/RB (H7508W)

FROM: Linda L. Taylor, Ph.D. *Linda Lee Taylor 11/18/92*
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Health Effects Division (H7509C)

THRU: K. Clark Swentzel *K. Clark Swentzel 11/19/92*
Section II Head, Toxicology Branch II
Health Effects Division (H7509C)

and

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Chief, Toxicology Branch II/HFAS/HED (H7509C)

Registrant: ELF ATOCHEM North America, Inc.
Chemical: manganese ethylene-1,2-bisdithiocarbamate;
ethylene thiourea

Synonym: Maneb
Caswell No.: 539
Case No.: 818618
Submission No.: none
Identifying No.: 014505
DP Barcode: none
MRID No.: 422516-01

Comment: The chronic oral toxicity study in dogs, entitled: "52-Week Oral Toxicity (Feeding) Study with MANEB TECHNICAL in the Dog", was reviewed earlier this year and classified Core supplementary, pending submission of the results of the neuropathological examination of the sciatic nerve. Although neural tissue had been retained and embedded in resin blocks for possible future histopathologic examination, problems were encountered and further examination of the neural tissue was not possible. The company asked for a meeting (held 11/18/92) to discuss alternative means to satisfy the data requirement (for a chronic dog study, with special attention paid to the types of lesions associated with the neurological observations noted in the previous dog study) and

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proposed that they would perform the neurotoxicity screening battery in rats. In preparation for this meeting, TB II in discussions with Bill Sette, had determined that the neurotoxicity studies would be required for this EBDC at this time since the neuropathological examination of the dogs was not possible.

CONCLUSION

The chronic dog study can be upgraded to minimum, contingent on Atochem's commitment to perform the necessary neurotoxicity studies in rats. TB II recommends that the Registrant perform acute and 90-day neurotoxicity studies, as described in the 1991 Neurotoxicity Screening Battery, with the additional assay of brains from at least 3 rats/sex/dose for NTE (neurotoxic esterase) [according to the procedure described in the appropriate 1991 guideline or more recent revisions (O'Callaghan, et al., 1991)].

The NOEL for the chronic dog study can be set at 50 ppm (1.53 $\sigma\sigma$ /1.71 $\rho\rho$ mg/kg) and the LEL is 200 ppm (6.36 $\sigma\sigma$ /7.18 $\rho\rho$ mg/kg), based on decreased body-weight gain/food consumption, changes in hematology/clinical chemistry parameters indicative of thyroid toxicity/anemia, increased thyroid weight, and follicular (thyroid) hyperplasia.

Classification: core-Minimum, but the neurotoxicity screening battery is required for Maneb and should include an assay of the brains for NTE.

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