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CASWELL FILE

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

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SEP 30 1992

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

SUBJECT: 6(a)(2) Data - Preliminary Findings from a 21-Day Oral Range-Finding Study in Rats

TO: Stowe/Waldrop, PM 71
SRRD (H7508W)

FROM: Byron T. Backus, Ph.D., Toxicologist Byron T. Backus 9-28-92
Toxicology Branch 2
HED (H7509C)

THROUGH: K. Clark Swentzel K. Clark Swentzel 9/30/92
Section Head, Review Section II
Toxicology Branch 2
HED (H7509C)

and Marcia van Gemert 9/30/92

Marcia van Gemert, Ph.D., Branch Chief
Toxicology Branch 2
HED (H7509C)

DP Barcode: D182594 Submission: S425298

Case: 818616

Chemical No. 014503 Disodium ethylenebis(dithiocarbamate)

Tox. Chem. 585

Action Requested:

"Please review the 6(a)(2) submission (MRID 42378801) for GLN 82-1. Please send a copy of the review and the status of the tox. requirements for Nabam to: Terri Stowe."

Background:

This material (MRID 423788-01) consists of a letter from Jellinek, Schwartz, & Connolly, Inc. which presents preliminary findings from a 21-day oral rat range-finding subchronic study (preliminary to what will presumably be a 90-day subchronic study in rats). As noted in the cover letter: "The range-finding study doses were 0, 0.1, 1, 10, 100, and 500 mg/kg/day of Aquatreat® DN-30, the technical material, which is a 32.97-percent aqueous solution of

nabam. The effects observed in the range-finding study included increased thyroid weights, thyroid hypertrophy, and changes in thyroid hormone levels at 100 and 500 mg/kg/day. These are all effects that have previously been observed with nabam and other EBDC compounds, and do not occur at lower doses in this study compared to the other subchronic studies. However, the exposure period was shorter than it was in previous studies."

Discussion:

From an examination of these preliminary (unaudited) data, the following statistically significant effects of exposure to the test substance at the highest dose (500 mg/kg/day) were observed at 21 days in both males and females: 1) decreased levels of mean T4 (also present, but not statistically significant, at 100 mg/kg/day); elevated mean TSH; elevated mean thyroid weight; and increased mean liver-to-body weight ratio. The findings are consistent with previous observations on other EBDCs and Nabam.

Comments and Recommendations:

1. The 6(a)(2) findings of this study are not surprising, as liver and/or thyroid effects have been observed in previous studies involving dietary exposure to Nabam, other EBDCs, and ETU. Although the statement is made in the cover letter that: "the exposure period was shorter than it was in previous studies," this is the first 21-day oral study on Nabam that the Agency has received.

2. Toxicology Branch 2 recommends no regulatory action on the basis of these 6(a)(2) findings. It is noted that there were no indications of effects at the three lower dose levels (0.1, 1, and 10 mg/kg/day) in this 21-day study. The major questions are whether a NOEL for Nabam will be defined in the 90-day rat feeding study, and how this NOEL will relate to human exposure.

3. Toxicology Branch 2 recommends that the list of toxicology data requirements for Nabam should not be changed on the basis of the findings from this preliminary 21-day study. However, we have also received a copy (MRID 424377-01) of the final report of a rabbit developmental toxicity study (also designated as 6(a)(2) data) conducted at Wil Research Laboratories. This material has not yet been reviewed, and so no recommendations can be presently made on the findings of this study.