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

MEMORANDUM JAN 31 1983

TO: Richard Mountfort (23)
Registration Division (TS-767)

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

THRU: Orville E. Paynter, Ph.D.
Chief, Toxicology Branch
Hazard Evaluation Division (TS-769)

SUBJECT: Review of Comments on Thidiazuron Mouse Dominant Lethal Study; Reg. No. 2139-122; Acc. No. 248401; CASWELL#659A

Registrant: Nor-Am Agricultural Products
350 West Shuman Blvd.
Naperville, Illinois 60566

Background Information:

In my review of August 2, 1982, I noted that, although the results of this study were not conclusive, a weak dominant lethal effect was suggested. I requested individual animal data from the sponsor and classified the study as Supplementary Data. The sponsor has recently submitted additional comments and individual animal data. This information is reviewed below.

Recommendation/Discussion:

Because the conduct of the study was acceptable and the reporting is now complete, it is recommended that the study be upgraded to "Adequate".

The additional information is suggestive of a weak dominant lethal effect but is still not conclusive. Additional mutagenicity testing, using different assay methods, may clarify the mutagenic potential of Thidiazuron.

The comments of the registrant regarding the apparent positive response include those made in the original submission. Because those comments were addressed in detail in my review of August 2, 1982, they will not be discussed again.

Both the historical data and the individual animal data suggest a weak dominant lethal effect in the high dose group. The mean percent of implant loss (i.e. dead implants/total number of implants) was .04, 04, .05, .098 and .22 for the vehicle control,

100, 200, 400 mg/kg and positive control groups, respectively. The historical data showed mean percent implant losses of .08, 0.053, .055, .044, .085 and .057. Thus the percent implant loss for the 400 mg/kg group was greater than either the concurrent control group or the 6 historical control groups. The individual animal data showed that the animals with high rates of implant loss were not limited to a few females which, as contended by the registrant, biased the findings. The number of females with greater than 10% implant loss during week 1 were 7, 8, 5, 17 and 35 for the vehicle control, 100, 200, 400 mg/kg and positive control groups, respectively. Thus the number of females having high rates of implant loss was clearly greater in the high dose group than in the control or low and mid dose groups, albeit less than the positive control group.

Gary J Burin 1/14/83

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