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

FEB 22 1995

CERTIFIED MAIL SC-673

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

Ms. Judith Ball
UNIROYAL Chemical Company, Inc.
74 Amity Road
Bethany, CT 06525

Subject: Naptalam Registration Standard Data
Low Volume Minor Use Waiver Request Package and
Toxicology Reviews

Dear Ms. Ball:

The Agency has performed a complete assessment of available naptalam toxicology data. The Agency's findings are summarized below. Please consult enclosed reviews for details.

In our letter dated May 5, 1994 addressing Uniroyal's low volume minor use waiver request package for Naptalam, we indicated that the data for Guidelines 83-1(a) and 83-2(a) combined chronic toxicity/oncogenicity in rats were to be reviewed by the RfD/Peer Review Committee. They have reviewed the existing data for rat, mouse, and dog and determined that the existing data for Guidelines 83-1(a) and 83-2(a) combined chronic toxicity/oncogenicity in rats (MRID No. 00077053, 41838801, and 42784001) satisfy guideline requirements. The chronic toxicity study in dogs (MRID No. 41057501) was also found to satisfy guideline requirements. A copy of this September 7, 1994 review is enclosed.

However, major deficiencies were found when the carcinogenicity study in mice (MRID No. 00119003) was reassessed. This study was found unacceptable and does not satisfy data requirement Guideline 83-2(b), oncogenicity in mouse. Naptalam is currently registered as a low volume/ minor use chemical. A new mouse study is not required at this time based on the current use and/or exposure profile. Should the exposure or use profile expand in the future a new mouse study may be required. Naptalam is currently classified as a "Group D" carcinogen based on the inadequacy of the data available.

The subchronic oral toxicity data for rats and dogs (MRIDs 00106276 and 00106277) were also found unacceptable. These data do not need to be repeated because there are acceptable chronic toxicity data available to address these requirements.

The rat teratology study, MRID 00106320, was reassessed and found to be core supplementary. Several deficiencies were noted that need to be addressed in order to satisfy Guideline 83-3(a). Please consult the enclosed S. Dapson review dated June 22, 1994 for details. Upgrade data to address these deficiencies must be submitted within 6 months of receipt of this review. If data are not available to upgrade this study, Uniroyal must submit a new rat teratology study within 2 years of receipt of this letter.

In our May 5, 1994 letter, EPA requested that for the technical formulation, Uniroyal submit a new study for Guideline 81-3, acute inhalation in rat and any available studies for Guidelines 81-4 and 81-5, primary eye and dermal irritation. In response to these requests, Uniroyal stated that highly concentrated Alanap technical does not exist and that workers are not exposed to the Alanap 40% Technical Concentrate. Uniroyal has proposed that the acute studies be conducted with the 23.7% product, Alanap-L. In addition, studies performed with an Alanap end-product for Guidelines 81-4 and 81-5 were submitted.

This proposal to conduct the acute studies with the 23.7% product is unacceptable because the acute toxicity studies should be conducted with the same concentrated material with which the chronic toxicity studies were conducted. The primary eye and dermal irritation studies, MRIDs 00060408 and 00078530, do satisfy Guidelines 81-4 and 81-5 for the formulation specific requirements for Alanap-L but do not adequately address generic data requirements.

eye
skin irritation w/MCPA?

Uniroyal must commit in writing to submit a new acute inhalation study with concentrated naptalam. The results of this study must be submitted within a year of receipt of this letter. As stated in our previous letter, data for Guidelines 81-4 and 81-5 may be required in a future Data Call-In.

Uniroyal has requested a time extension to respond to the data deficiencies noted in our May 5, 1994 letter because Uniroyal needed to know the results of the scheduled RfD/Peer Review evaluation of Naptalam before committing economic resources to support this chemical. The RfD/Peer Review Committee results have been provided.

Uniroyal submitted detailed protocols for Uniroyal's proposed bridging studies to fulfill Guidelines 85-1 and 171-4(a). These protocols currently are in review. You explained when you met on January 24th with the chemical review manager, Susanne Cerrelli that Uniroyal needed an Agency review of these protocols before commencing these studies. The due dates for Guidelines 85-1 and 171-4(a) data are respectively, 6 months from receipt of a protocol review for 85-1 and one year from receipt of a protocol review for 171-4(a).

Within 30 days of receipt of this letter, the Agency requires that Uniroyal address data gaps that were identified in this letter and recent toxicology reviews. Specifically, you must:

(1) Disclose when Uniroyal will submit the micronucleus study for Guideline 82-4(b) that Uniroyal has elected to repeat.

(2) Commit in writing to submit a new acute inhalation study (Guideline 81-3) performed with naptalam concentrate. This study must be submitted with in a year of receipt of this letter.

(3) Commit in writing to submit the additional data necessary to upgrade your rat teratology study (MRID 00106320) or commit to repeat the study. These upgrade data must be submitted within 6 months of receipt of this letter.

Failure to respond adequately within the time frames provided in this letter may result in the issuance of a Notice of Intent to Suspend affecting all products containing naptalam. Questions concerning these reviews should be directed to Susanne Cerrelli at (703) 308-8077.

Sincerely,

Esther Saito

Esther Saito, Chief
Reregistration Branch
Special Review and
Reregistration Division (7508W)

Enclosures