



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

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OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

SUBJECT: Methylene bis (thiocyanate): Amendment to Developmental Study in Rats MRID No. 411719-01.

Project No: 2-1144
MRID No.: 421627-00
PC No.: 068102
ID No.: 068102-001448
Submission No.: S409995
BARCODE No.: D173379

TO: Barbara Briscoe/Betty Crompton, PM # 51
Registration Division (H7505C)

THRU: Roger Gardner, Section Head *K/B for*
Review Section 1
Toxicology Branch I
Health Effects Division (H7509C)

FROM: Nguyen Bich Thoa, Ph.D. *08/19/92*
Review Section 1
Toxicology Branch I
Health Effects Division (H7509C) *K/B 9/1/92*

Registrant: Buckman Labs. International Inc.

ACTIONS REQUESTED

Review Amendment to Developmental Study in Rats entitled "Developmental Toxicity (Embryo/Fetal Toxicity and Teratogenic Potential) Study of Methylene Bis (Thiocyanate) administered Orally via Gavage to Crl:CD(SD)BR Presumed Pregnant Rats" (MRID No. 411719-01) for possible upgrading.

CONCLUSIONS

TB is satisfied with the correction of reporting errors on table 20 and considers the number of high dosage group litters exposed to the test substance on days 6 to 15 of gestation (17 litters) to be adequate for a meaningful evaluation of the developmental toxicity data. The study entitled "Developmental Toxicity (Embryo/Fetal Toxicity and Teratogenic Potential) Study of Methylene Bis (Thiocyanate) administered Orally via Gavage to



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Crl:CD(SD)BR Presumed Pregnant Rats" (MRID No. 411719-01) has now satisfied the toxicological data requirements for a developmental toxicity study in rodents (83-3) and can be upgraded from a core classification of supplementary to Minimum. The NOEL for maternal toxicity in rats is 3mg/kg/day and the LOEL is 6 mg/kg/day (highest dose tested), based on slightly decreased maternal body weight gain and a small increase in the incidence of rales. The developmental NOEL is >6 mg/kg/day.

BACKGROUND

A developmental toxicity study in rats entitled "Developmental Toxicity (Embryo/Fetal Toxicity and Teratogenic Potential) Study of Methylene Bis (Thiocyanate) administered Orally via Gavage to Crl:CD(SD)BR Presumed Pregnant Rats" (MRID No. 411719-01) was reviewed by TB in 1991 and the following conclusions were made:

The NOEL for maternal toxicity in rats is 3 mg/kg/day; the LOEL is at 6 mg/kg/day (highest dose tested) and is based on slightly decreased maternal body weight gain and a small increase in the incidence of rales (a sign also observed at higher dose levels in range-finding studies). No developmental toxicity was noted at 1 or 3 mg/kg/day dose levels but discrepancies in reporting preclude a final conclusion about the NOEL for developmental toxicity in this study. The classification of this study as supplementary can be upgraded with an acceptable explanation of discrepancy in the number of animals reported as partially dosed (5 as shown in tables of individual maternal data and 11 as indicated in table 20 of fetal data.

The following response is quoted from the submitted Amendment:

Table 20 (Fetal Anomaly Data - Litter Incidence) - High dosage group litters 883, 884, 885, 886, 887, and 888 were incorrectly footnoted as being from dams administered the test substance on days 6 to 14 of gestation, rather than days 6 to 15 of gestation. Therefore, the total number of high dosage group litters exposed to the test substance on days 6 to 15 of gestation was 17, rather than 11".

The registrant has also revised table 20 to reflect the correct number of high dosage litters from dams administered the test substance on days 6-14 or 6-15 of gestation. The revised table 20 was included in the submitted Amendment.