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CASWELL FILE 010374

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

JUL - 9 1993

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Barium Metaborate - Final Report of a 28-Day Range-finding and Subchronic Toxicity/ Neurotoxicity Study in Rats; **6(a)(2)**

TO: Barry O'Keefe
PM Team Reviewer (72)
Reregistration Branch, SRRD (H7508C)

FROM: Linda L. Taylor, Ph.D. Linda Lee Taylor 7/7/93
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THRU: K. Clark Swentzel K. Clark Swentzel 7/8/93
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and

Marcia van Gemert, Ph.D. Marcia van Gemert 7/8/93
Chief, Toxicology Branch II/HFAS/HED (H7509C)

Registrant: Buckman Laboratories International, Inc.
Chemical: Barium metaborate
Synonym: Busan 11-M1
Case No.: 818581
Caswell No.: 071
Submission No.: S439869
Identifying No.: 011101
DP Barcode: D190748
MRID No.: 427478-01 and 427242-01
Action Requested: Please review MRID 42747801 for guidelines 82-1(a) and 82-5(b) [Combined Oral Subchronic Toxicity and Neurotoxicity]. In conjunction, please review MRID 42724201 for guidelines 82-1(a) and 82-5(b) [Dietary Range-finding study].

Comment: The Registrant submitted both study reports under FIFRA 6(a)(2). The same grounds were cited for this submission under 6(a)(2) as were used earlier this year with their submissions of preliminary results from both studies, namely that the effects noted had not been previously reported for this chemical.

Both studies have been reviewed, and the DER's are attached. The range-finding study is classified Acceptable; it does not satisfy

the guideline requirements (82-1/82-7) for a subchronic toxicity/ neurotoxicity study nor was it intended to. The combined study is classified Core Minimum, and it satisfies the guideline requirements [82-7/82-1] for a subchronic toxicity study in rodents and a 90-day neurotoxicity study.

1) A 28-Day Dietary Range-Finding Study of Busan 11-M1 in Rats. Under the conditions of the study, administration of Busan 11-M1 to rats at dose levels of 0, 1000, 5000, 10000, and 15000 ppm for 28 days resulted in reduced body weight/gains in rats of both sexes at the 15000 ppm dose level throughout the study and to some extent in males at the 10000 ppm dose level, with concomitant decreases in food consumption. Other findings include decreases in several hematology and clinical chemistry parameters and dose-related decreases in liver and kidney weights, which were statistically significant only in males. There were apparent dose-related decreases in testes and ovarian weight, and relative brain weights were increased in both sexes at the highest dose tested. A no-effect dose (NOEL) can be set at 5000 ppm (459 mg/kg) for males/10000 ppm (984 mg/kg) for females, and the LEL at 10000 ppm (881 mg/kg) for males/15000 ppm (1285 mg/kg) for females, based on reduced body-weight/gain/food consumption, gait abnormalities, changes in hematology and clinical chemistry parameters, decreased testes, liver, and kidney weights in males, decreased ovarian weight, and increased relative brain weight in both sexes. The dose levels chosen for the definitive subchronic/neurotoxicity study were 1000, 5000, and 10000 ppm.

2) A Combined Oral Subchronic (13 Week) Toxicity and Neurotoxicity Study of Busan 11-M1 in Rats. Under the conditions of the study, administration of Busan 11-M1 via the diet to rats for 90 days at dose levels of 0, 1000, 5000, and 10000 ppm resulted in reduced body weight/gains in rats of both sexes at the high-dose level throughout the study and to some extent in females at the mid-dose level, with concomitant decreases in food consumption. Other findings include decreases in several hematology [RBC, HGB, HCT; high-dose level (both sexes)] and clinical chemistry [total protein, cholesterol, globulin; mid- and high-dose males] parameters, decreased liver and testes weights (absolute and relative) and decreased relative (to brain) kidney weight in the high-dose males, increased relative brain weight in females at the mid-dose level and in both sexes at the high-dose level, increased relative (to body) kidney weight in the high-dose females, and small and/or soft testes with aspermatogenesis in males at the high-dose level. Additionally, there was an absence of spermatocytes in the epididymal tubules at the high-dose. With regard to the neurotoxicity phase of the study, there were no differences in brain weight or brain dimensions in the rats perfused at necropsy, and no treatment-related neuropathological lesions were observed between the high-dose and control rats at the microscopic examination of perfused tissues. An apparent treatment-related decrease in one of the parameters of the functional

observational battery (forelimb grip strength) was observed in the high-dose males at week 3, and a small stimulatory effect (increased ambulatory activity) was noted at week 3 in the mid-dose females and in both sexes at the high dose. A no-effect dose (NOEL) can be set at 1000 ppm (70 mg/kg ♂♂/80 mg/kg ♀♀), and the LEL can be set at 5000 ppm (349 mg/kg ♂♂/406 mg/kg ♀♀), based on reduced body-weight/gain in females; clinical chemistry parameters in males; increased ambulatory activity in females, and decreased relative liver weights in males. An apparent decrease in forelimb grip strength was observed in the high-dose males at week 3. The dose levels tested are adequate.

No regulatory action is required at this time.