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

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OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

SUBJECT: Barium Metaborate - Final Report of a Range-finding Acute 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 11/4/92
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THRU: K. Clark Swentzel K. Clark Swentzel 11/4/92
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and

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Registrant: Buckman Laboratories International, Inc.
Chemical: Barium metaborate
Synonym: Busan 11-M1
Case No.: 818581
Caswell No.: 071
Submission No.: S428350
Identifying No.: 011101
DP Barcode: D180239
MRID No.: 425012-01

Action Requested: Please review this final range-finding acute neurotoxicity study on an expedited schedule; as per direction of the 6(a)(2) screening team. Guideline 81-8-SS, MRID 42501201.

Comment: The Registrant submitted this final report under FIFRA 6(a)(2). The same grounds were cited for this submission under 6(a)(2) as were used for the DRAFT report, namely that the effects noted had not been previously reported for this chemical. As pointed out by TB II in a cover memo (dated 7/22/92) to the review of the DRAFT, the results of this range-finding study had been brought to the Agency's attention previously with the submission of the protocol and dose selection for the acute neurotoxicity study on Busan 11-M1 and again with the submission of the DRAFT final

report (DER dated 7/20/92). The current submission is the FINAL report of the study (dated September 16, 1992). It fails to address the issues raised in the review of the DRAFT report (copy appended). Review of the SAME data three times under EXPEDITED review seems a waste of time and resources. Additionally, it would appear that 40 CFR § 153.66 (b)(2) exempts information previously submitted to the Agency from being subject to 6(a)(2).

The current FINAL report does not appear to differ significantly from the DRAFT. Based on the data in the final report, a revised table of body-weight gains is provided below (replaces the table in the DER of the DRAFT report on pages 10-11). Additionally, the DER did not note that dosing mixtures were prepared one day prior to the day of dosing.

Mean Body-Weight Change (g)

Days/Dose (mg/kg)	12.5	25.0	50.0	100.0	150.0	200.0	400.0	600.0
MALES								
-1-0	16	13	15	12	14	14	15	12
0-7	58	55	56	58	51	60	41	19
7-8	10	6	7	5	6	8	6	10
0-8	68	60	62	63	57	68	47	29
-1-8	83	73	77	75	70	81	62	41
FEMALES								
-1-0	7	3	8	2	9	11	8	8
0-7	27	25	20	35	21	19	-	-
7-8	-2	-4	5	-1	6	11	-	-
0-8	25	21	25	34	27	30	-	-
-1-8	31	25	32	40	36	40	-	-

Under the conditions of the study, administration of a single dose of Busan 11-M1 via gavage to rats at dose levels of 12.5, 25, 50, 100, 150, 200, 400, and 600 mg/kg resulted in death at the 400 and 600 mg/kg dose levels in females only and several clinical signs indicative of neurological involvement, which included gait abnormalities, reduced/absent forelimb/hindlimb grasp reflex, and reduced/absent surface righting reflex. A no-effect dose was observed at 25 mg/kg. Dose levels of 175, 200, and 250 mg/kg were administered similarly to clarify selection of a benchmark dose level and to estimate the time of peak neurologic effect for the subsequent acute neurotoxicity study. It was determined that the peak effect was reached at 3-5 hours post dose, and the benchmark dose level was estimated to be 200 mg/kg. Doses of 25, 50, 100 and 200 mg/kg were selected for the acute neurotoxicity study with Busan 11-M1 in rats, and the time to peak effect was estimated to be ≈ 4 hours following dosing.

CONCLUSION

This study is a range-finding study, which does not satisfy any guideline requirement per se (nor was it intended to). The purity of the test material and analysis of the test material formulations were not provided in either the DRAFT or FINAL report, nor does the

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cover letter to the FINAL report from the Registrant provide this information. Although it appears that no analyses were performed to verify the doses administered (page 12 states that unused portions of the dose preparations were discarded), this was a range-finding study and such information is not critical at this point. However, the purity of the test material (Busan 11-M1) should be reported for this study. This study is classified not acceptable, but it may be upgraded with the submission of information on the test material purity.

This range-finding study demonstrates that Busan 11-M1 causes neurotoxic effects in rats following acute exposure at dose levels greater than 25 mg/kg. This endpoint will be more thoroughly investigated in the definitive acute neurotoxicity study.

NOTE: The "bean sheet" indicated (Bill Burnam) that this study would be reviewed on an expedited basis within 60-90 days. The date of the "bean sheet" is 11/2/92, and the Administrative Due Date is 11/27/92.

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