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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM:

Subject: EPA ID 129006: Response to Sponsor's Comments Guinea Pig Sensitization Test (Buehler Method) (81-6) with DPX-43898-26 (Fortress 5G™). MRID# 425592-09.

Barcode: D208376. ToxChem No.: 663P.
MRID No.: 425592-09. PC No.: 129006.

From: David G Anderson, PhD 10/5/94
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HED (7509C)

Thru: Karen Hamernik, PhD 10/18/94
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CONCLUSIONS: The dermal sensitization study in Guinea Pigs (MRID# 412906-26) should be upgraded to acceptable. With the sponsor's responses to question about the test method, the study (MRID# 412906-26) is acceptable for a Guideline (81-6) dermal sensitization study in Guinea Pigs. The sponsor's responses are adequate and acceptable.

In addition, Table III (appended) should be substituted for Table III in HED Doc.# 008330.

BASES FOR THE CONCLUSIONS: Supplement 1 referenced below was submitted (requested) in clarification of the Dermal Sensitization Test (MRID# 412906-26) reviewed in HED Doc.# 008330.

> Brock, JW (June 6, 1989) Closed Patch Dermal Sensitization Study (Buehler Method) with DPX-43898-26 in Guinea Pigs. Study conducted (Haskel Lab No. 142-89, Med Res.No. 4581-661) by E.I. du Pont de Nemours Co., Inc. for E.I. du Pont de Nemours Co., Inc. Supplement 1 to HLR 142-89, MRID# 412906-26. MRID# 425592-09. 12 Pages.

The EPA reviewer requested (a) information of the criteria for a positive dermal sensitization and requested that (b) Table IV of the report be corrected for incidences of sensitization at 24 and 48 hours. (c) In addition, the sponsor was requested to explain the method of application of the test material.

(a) Response: The criteria for positive dermal sensitization response is a positive incidence in 1 or more animals as indicated by a graded response higher than that observed in naive controls. In general a response at challenge would have to be greater than a mild response of 1 in naive controls. In general it is a grade 2 response or greater. If a grade 2 or greater response is seen in the negative controls, the reactions of the test group that exceed the most severe negative control reaction are also considered indicative of sensitization.

(b) Response: Table IV of the submitted report was corrected and was included in the submission. The data in Table IV should also replace the data in Table III in the original DER. The submitted clarification by the sponsor of the definition of a positive dermal sensitization response also indicates the data in Table III of the original DER should be changed. A corrected Table III is appended.

(c) Response: The "neat" granular material was measured out in a 15 ml centrifuge tube graduated in 0.1 ml unit to 1 ml. The volume measured was 0.4 ml and weighed approximately 0.28 g. The measure test material was placed in the Hill Top Delivery System and moistened with solvent to facilitate contact with the animals skin.

TABLE III

INCIDENCE AND SEVERITY RESPONSES AT CHALLENGE

	24 hour		48 hour	
Test article	Incidence	Severity	Incidence	Severity
Test (80% ethanol)	2/10	1.0	2/10	1.1
Test (distilled water)	0/10	0.4	0/10	0.1
Neg. control (80% ethanol)	1/5	0.2	1/5	0.2
Neg. control (distilled water)	1/5	0.2	0/5	0.0
Neg. control (0.1% DCNB)	0/5	0.0	0/5	0.0
Pos. control (0.1% DCNB)	5/5	3.0	5/5	2.4