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

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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: V9360-27 (ACCENT®): Registrant's Responses to the Agency's Questions Concerning the Chronic Oral Toxicity Study in Dogs and the Acute Inhalation Study in Rats

Caswell No.: 359J
HED Project No.: 0-1325
MRID No:: Not applicable
Record Nos.: 264848, 264849 and 264852
Identifying Nos.: 352-LGU, 352-LGL and 9F3763

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TO: R. Taylor/C. Giles PM 25
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and

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Registrant: E. I. Du Pont de Nemours & Company
Wilmington, DE

Action Requested: Review the Registrant's responses to the Agency's questions concerning the chronic oral toxicity study in dogs and the acute inhalation study in rats.

RECOMMENDATION:

1. Chronic Dog Study - It is considered that a NOEL of 5,000 ppm (LOEL of 20,000 ppm) has been attained (based on relative liver and kidney weights) and it is therefore recommended that this study be upgraded from Core Supplementary to Core Minimum.

2. Acute Rat Inhalation Study - The Registrant has responded to the Agency's request in an acceptable manner. It is therefore recommended that this study be upgraded from Core Supplementary to Core Minimum.

QUESTIONS, RESPONSES AND REPLIES

1. Chronic Dog Study (MRID No.: 413601-02; DER No. 007943, 5/21/90)

The original review of this study indicated a classification of Core Supplementary because a NOEL had not been attained in female dogs (decrease in body weight gain: 250 ppm LDT = -28% from control value; 5,000 ppm = -40%; and 20,000 ppm HDT = -28%).

The Health Effects Division RFD/Peer Review Committee met on June 14, 1990. The recommendation was made that because of the material submitted by the Registrant (May 23, 1990 from T. E. Catka to R. J. Taylor - copy attached) and a re-evaluation of the body weight data, the decrease in body weight gain appearing in females should not be the criterion used in establishing the NOEL in this study. This Committee recommended that the NOEL be 5,000 ppm (middle concentration tested) based upon a statistically significant increase ($p<0.05$) in the relative liver and kidney weights of males administered 20,000 ppm (no effect observed in females). [A copy of the dog DER is attached.]

2. Acute Rat Inhalation Study (MRID No. 413601-05; DER No.; 007943, 5/21/90)

Agency's Recommendation - "This study is to be considered SUPPLEMENTARY because no rationale was provided for not being able to generate 25% of the particles that are smaller than 1 um in diameter." "This study may be upgraded to CORE MINIMUM provided the response to the above is acceptable, even though the particle sizes were considered too large. This is based upon the relatively low toxicity of the chemical and an apparent problem with the physical nature of the test material."

Registrant's Response - "In order to generate the concentrations necessary for the conditions of this test, the delivery rate of the test material to the generation system was at its maximum. There is a characteristic self-limiting or maximum feed rate at which the jet mill begins to clog and a decrease in generation efficiency is experienced. In pre-test trials (as detailed in HLR 704-89), the airflows to the jetmill were altered to vary the degree of milling and separation. As airflows were increased, reduced particle sizes were achieved; however, the coincident decreases in total particulate concentrations resulted."

"The physical or chemical properties of DPX-V9636 may have contributed to the inability to generate atmospheres with a combined total particulate concentration greater than 5000 mg/m^3 and a particle size distribution where 25% of the particles were less than 1 um. The

[redacted]

Agency's Reply and Conclusion - The rationale provided by the Registrant is satisfactory and it is recommended that the study be upgraded to Core Minimum.

INERT INGREDIENT INFORMATION IS NOT INCLUDED