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TFR-5614

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MEMORANDUM

JUL 28 1986

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: Endosulfan-Acute Delayed Neurotoxicity in the Hen-
Registrant Response to 9/18/86 Review

TO: George LaRocca, PM 15
Registration Division (TS-767)

FROM: Margaret L. Jones
Review Section III
Toxicology Branch (TS-769)

THROUGH: Marcia Van Gemert, Ph.D., Head
Review Section III
Toxicology Branch

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and Theodore M. Farber, Ph.D., Chief
Toxicology Branch

Theodore M. Farber 7/24/86

Chemical: Endosulfan

Tox. Chem. No: 420

Registration No: 172671

Registrant: American Hoechst

Accession No: 260675

Tox. Project No: 1803

Action Requested: Respond to comments on the September 18, 1985 review of Acute Delayed Neurotoxicity Study in the Hen using Endosulfan. The registrant disagreed with the conclusions of the Data Evaluation Report.

Conclusions: The September 18, 1985 letter from Mr. LaRocca to Mr. Dorr gives an excellent summary of the review of the subject neurotoxicity study and the Agency requirements for acute delayed neurotoxicity testing.

The registrant response does not change the deficiencies in the original study. The Pesticide Assessment Guidelines, Subdivision F, (October, 1982) state that [§81-7 (b)(5)(ii)] "Histopathology. All animals should be subjected to microscopic examination." None of the animals dying on test were examined due to "the problem of artefact caused by autolysis."¹

1. Test Report A 32153, p. 35.

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Since testing took place at the LD₅₀ it seems this problem should have been anticipated and provision made to preserve animals as they die, particularly for animals dying after the challenge dose. In addition, the revised study submitted with the registrant response does not appear to correct the arithmetical discrepancies noted in Tables 4 and 8 in the original report.

Classification: Core Supplementary

Once again, the only appropriate compounds which should be used in acute delayed neurotoxicity testing are organophosphates or metabolites and degradation products thereof or compounds which are structurally related to substances known to cause acute delayed neurotoxicity. Endosulfan does not belong to this category of compounds and no further testing in this category is required at this time.