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

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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

Caswell # 889

MEMORANDUM

SUBJECT: Trifluralin: Consultant's Review of Cardiomegaly
Found in Rabbit Teratology Studies.

FROM: Stephanie P. April, Ph.D. *Stephanie P. April 5/8/85*
Review Section III
Toxicology Branch
HED (TS-769)

TO: Richard Mountfort, PM-23
Registration Division (TS-767)

THRU: Clint Skinner, Ph.D., Section Head
Review Section III
Toxicology Branch
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Clint Skinner
5-14-85
5/15/85

Theodore M. Farber, Ph.D., Chief
Toxicology Branch
HED (TS-769)

The registrant for Trifluralin (EL-152), Eli Lilly and Company, requested that Mildred S. Christian, Ph.D. of Argus International Incorporated, 955 Horsham Road, Horsham, Pa. 19044 act as a consultant to review the rat and rabbit teratology studies for this compound. This request was stimulated by a rare finding of "cardiomegaly" in one litter of each of two rabbit teratology studies.

Dr. Christian's findings and evaluation are in concurrence with the conclusions of toxicology branch (Memorandum April to Mountfort, April 26, 1985).

There were two rabbit teratology studies because the first one did not provide an adequate number of litters in the test groups including controls to make an adequate assessment of teratogenic potential due to low fertility.

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In the first experiment the initial observation was ventricular hypertrophy with dual apex and wavy ribs. The hearts were somewhat larger and the ventricle was somewhat thicker. This variation has been observed in the same laboratory previously in New Zealand white Dutch Belted rabbits and is, therefore, probably genetic in nature.

In the second experiment the affected two animals in one litter had multiple other malformations which were developmental in nature. The cardiomegaly was compensatory reflecting physiological changes such as hypoplasia of the lung and morbidity of the littermates rather than a direct developmental effect.

These effects occurred at dose levels where there was excessive maternal toxicity and maternal morbidity.

Neither of these two findings are indicative of any risk to humans nor of a chemically induced teratogenic effect.

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