

SEP 13 1984
SEP 18 1984

MEMORANDUM

SUBJECT: Trifluralin, Intrim Report of Teratology Study
Submitted in Accordance with Sec 6(a)(2).

TO: Richard F. Montfort PM-23
Registration Division (TS-767)

FROM: Robert P. Zendzian PhD, Acting head
Review Section III
Toxicology Branch
HED (TS-769)

9/17/84
WJB
9-17-84

THROUGH: William Burnam, Chief
Toxicology Branch

Compound Trifluralin

Tox Chem #889

Registration #1471-70

Registrant Elanco

Action Requested

Under the provisions of §6(a)(2) of FIFRA the Registrant has submitted an intrim report of two teratology studies of Trifluralin in rabbits. These studies show cardiomegaly, an unusual abnormality, in several pups at the high dose in each study.

Recommendation

Toxicology Branch Recommends the following;

1) No further registration actions should be approved on Trifluralin until the final reports of the two teratology studies are received and evaluated.

2) When submitting the final reports the Registrant should include historical control data on the incidence of abnormalities found in pups of the same strain of rabbits used in the Trifluralin studies.

3) The registrant should provide, to the extent possible, information from the scientific literature or a recognized expert(s) in teratology on the 'meaning' of cardiomegaly in the rabbit and its possible connection to human teratogenesis.

Background

The Registrant has submitted the following document:

Intrim Report on Two Teratology Studies in Rabbits Given Trifluralin (Compound 36352), J.K. Markham, W.D. Johnson, D.R. Brannon, J.L. Emmerson & M.E. Amundson, Lilly Research Laboratories, Studies B02283 and B01784, Aug 1984

The studies are standard teratology studies in the rabbit. The first study utilized doses of 0, 100, 225, 500 and 800mg/kg/day. Maternal toxicity was reported at the two highest doses. Because of low fertility in the control group the study was repeated omitting the highest dose and utilizing five more females per dose.

"At doses of 500mg/kg/day or greater, maternal and fetal toxicity was marked as indicated by abortions, anorexia, and decreased percentages of live fetuses. In study B02283 three littermates had cardiomegaly and wavy ribs [500mg/kg/day]. In study B01784 two littermates had cardiomegaly, hypoplastic lungs and thymus, and spade ribs [500mg/kg/day]." The report does not consider this a teratogenic effect and states "Cardiomegaly, which has been observed in our control rabbit population at a low incidence, was not observed at doses as large as 225mg/kg/day." Neither individual litter/pup data nor was historical control data was presented.

Based on the small amount of information presented it is impossible to determine the validity and toxicological meaning of these observations.

I judge the study # B022