MEMORANDUM

SUBJECT: Trifluralin, Intrrim 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)

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 intrrim 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 teratogenisis.
Background

The Registrant has submitted the following document:


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 littersmates had cardiomegaly and wavy ribs [500mg/kg/day]. In study B01784 two littersmates 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 # B002