

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

DATE: January 21, 1980

CASWELL#706A

SUBJECT: EPA Reg.#11273-EE; -ER; Propetamphos; Addition to validation Review on
IBT#651-06763 - Delayed Neurotoxicity Study on VEL 4283 (propetamphos) in hens.

FROM: William Dykstra
Toxicology Branch (TS-769) *WMD 1/21/80*

TO: William Miller
Product Manager#16

THRU: M. Adrian Gross, Chief
Toxicology Branch (TS-769)

William S. Butler for M. Adrian Gross

Conclusion:

"Although the clinical and histopathological data are negative, it is concluded that this study should be considered an invalid estimate of the neurotoxic potential of VEL 4283 (propetamphos) in hens. To this reviewer, the survival of only 2 hens in the LD₅₀ group does not constitute a data base adequate to definitely show that VEL 4283 is not neurotoxic in hens"; from memo of 12/17/79 from L. Anderson to Branch Chief, Lab Audits and Regulatory Analysis, SPRD.

TOX/HED:th:RD Initial CFRICK:1-21-80

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1/21/80

DATE: December 17, 1979

SUBJECT: Addition to Validation Review on IBT Study No. 651-06763 -Delayed Neurotoxicity Study on VEL4283 (Propetamphos) in Hens.

FROM: Larry Anderson, Ph.D. Toxicology Branch/HED (TS-769) *Larry Anderson*

TO: Branch Chief Lab Audits and Regulatory Analysis SPRD (TS-769)

THRU: M. Adrian Gross, Ph.D. *M. Adrian Gross* Chief, Toxicology Branch/HED (TS-769)

Discussion

According to the attached 10/12/79 memo, this study previously was concluded to be invalid relative to the deficiencies stated therein. However, reconsideration of this conclusion was deemed feasible pending submission of data from the histopathologic examination of wet tissues indicated by the registrant to have been retained. These results are now available and are discussed below.

Microscopic evaluation of spinal cord and sciatic nerve from birds in the control and each of the 3 treatment groups revealed no signs of induction of delayed neurotoxicity by the test material. It is evident that tissues from all birds on study (10/dosage group) were available for examination.

The 3-treatment groups consisted of birds given 1/2 the LD₅₀, the LD₅₀, or 2 X the LD₅₀. The discussion herein will focus on the LD₅₀ which is normally the dosage of concern in delayed neurotoxicity studies.

Histologic evaluation of tissues was recommended to provide a more precise estimate of neurotoxic potential of VEL 4283 under the conditions of this study. Of particular concern to this reviewer was the possibility of overlooking a positive neurotoxic effect due to failure to examine tissues microscopically.

Although the clinical and histopathologic data are negative, it is concluded that this study should be considered an inadequate (invalid) estimate of the neurotoxic potential of VEL 4283 in hens. To this reviewer, the survival of only 2 birds in the LD₅₀ group does not constitute a data base adequate to definitely show that VEL 4285 is not neurotoxic in hens. It should be noted that all birds given 2X the LD₅₀ died within 30 minutes following initial dosing.