



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

CASWELL #623A

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: Oryzalin; Conference with Elanco Representatives 10/10/85
CASWELL NO. 623A

FROM: R. Bruce Jaeger, Section Head
Review Section #1
Toxicology Branch/HED (TS-769) *RB*
11/17/85

TO: Robert J. Taylor, PM #25
Herbicide/Fungicide Branch
Registration Division (TS-767)

Please note the copy of the 10/17/85 letter from Elanco which is their understanding of the conference between EPA and Elanco concerning the ongoing 6 month dog study.

Their letter does not accurately reflect TB's understanding of what was discussed at that meeting. EPA attendees did not say this "study would be acceptable", implying that it would satisfy toxicology data requirements pursuant to 40 CFR §158.135. TB attendees noted the Agency's concern for the anti-thyroid effect of oryzalin, demonstrated in the rat, and which was presently undergoing peer review within OPP. TB requested that functional evaluations of the thyroid be performed in the ongoing dog study (e.g. T₃, T₄, PBI, etc.). However, Elanco stated the study was too far along to provide any useful information since no baseline data had been originated. TB also requested that a thorough histological evaluation be performed on the thyroid glands from all animals.

The original concern over the ongoing study centered around the absence, thus far, of a demonstrated or observable effect at the highest dose level. Elanco representatives were fearful the study would be rejected on that basis. They noted their concern over the Branch's position on the MTD for other compounds.

TB stated that they should consider adding the necessary clinical measurements for the remainder of the study even though there are no baseline data for each (i.e., each dog cannot serve as its own control for T₃, T₄ or T peroxidase). TB voiced no

particular concern for the dose increase proposed, provided they get an effect. However, if there is no thyroid effect or insufficient data to assess an anti-thyroid effect it will provide inadequate data. TB recommended they consider a 90 day study at doses of 0, 50, 250, 500 mg/kg b.wt. to look at thyroid effect specifically. TB also stated the dose selection in the ongoing dog study may have been somewhat on the low side (i.e. high dose of 50 mg/kg b.wt. produced minimal effects in the 90 day study; a 1966 study). TB asked, relevant to that, if their manufacturing process or grade of oryzalin had changed since the generation of the 1966 data. They responded that it had not.

I believe the above responses are a more accurate reflection of the concern and conversation which took place at the 10/10/85 conference referred to in Elanco's letter (attached).

Attachment

TS-769:JAEGER:s11:X73710:11/7/85

Card 7

DR. JAeger

Elanco Regulatory Services
Elanco Products Company
A Division of Eli Lilly and Company



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October 17, 1985

Mr. Robert J. Taylor
Product Manager (25)
Office of Pesticide Programs (TS-767-C)
Environmental Protection Agency
401 M Street, S.W.
Washington, D.C. 20460

Dear Mr. Taylor:

Re: EPA Conference of October 10, 1985 Regarding Oryzalin
One-Year Dog Study

On October 10, 1985, a conference was held to discuss a one-year dog study that is currently being conducted with oryzalin. Attendees were as follows:

Elanco Products Company

Dr. J. L. Emmerson
Dr. W. H. Jordan
Dr. K. E. McNeill

EPA

Dr. J. Chen
Dr. B. Jaeger
Mr. J. Yowell

The purpose of the conference was to review the progress of the above study and to discuss the apparent lack of an effect at six months into the study. We proposed that the current 250 mg/kg dose be increased to 500 mg/kg and that the study be terminated at the originally-planned termination date; i.e., at the end of twelve months. The EPA attendees agreed to this proposal and stated that the study should be acceptable if this dose change resulted in a significant toxic effect and if a no-effect level were present.

If this does not accurately reflect your understanding of this meeting, please let us know immediately.

Sincerely,

ELANCO PRODUCTS COMPANY

K. E. McNeill
Product Registration Manager
Elanco Agrichemicals Regulatory Services Division

KEM:dln