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2-Year Chronic Feeding Study in Dogs with Atrazine 80W.
Woodard Research Corp., Oct. 27, 1964.
Submitted 7/29/66.
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Material Tested:

Atrazine 80W (purity unknown). PC 080803

Animal Tested:

Purebred beagles from R.E. Sanders Corp, Richmond, Va. and Animals for Research, Lorton, Va. No age given. Acclimated for 3 weeks.

Methods:

4/sex/dose were given 0, 15, 150 or 1500 ppm in the diet and were dividually housed, given food once a day during the week, and double portions on Saturday and none on Sunday. At week 35 the beef supplement was halved. Due to the initial addition of beef (90g) the ppm values were 10.3, 103, 1030 ppm for the different groups. From 36 weeks to the termination the ppm values were 14.10, 141.5, and 1415.

Physical exams were made weekly. Food consumption, clinical effects and behavioral changes were checked daily. The animals were given the antihelmenthic, tetrachlorethylene at 58 and 85 weeks.

Blood values for ESR, Hct, Hgb. and WBC (differential) were obtained. Clinical chemistry values for BUN, SAP, and SGOT plus urinalyses were obtained on weeks 4, 8, 13, 22, 26, 39, 53, 65, 78, 91, 104. Thirty different tissues including prostate and or uterus were observed histologically.

Results:

No deaths occurred in the study. Wt. losses were noted in both males and females at 1500 ppm but not at lower dosages excepting 1 male at 15 ppm. An LEL for this effect is 1500 ppm and NOEL = 150 ppm (141.5 ppm).

Clinical signs:

Sacral area and rear limb muscular tremors occurred at 1500 ppm in 5/6 animals after 6 months. One male (150 ppm) experienced severe neuromuscular spasms. Watery lacrimation occurred in 3/6 high dose, 3/6 mid dose and 2/6 low dose. LEL = 15 ppm (LDT) (14.1 ppm).

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At the highest dosage (1500 ppm) a reduction in food intake and variability in Hct and Hgb values with time are seen. Blood chemistry and urinalysis results were not markedly different from controls.

Relative organ wts. appear to be increased in thyroids of females at 1500 ppm; increased for hearts of females at 1500 and 150 ppm. Liver wts are increased in females at 1500 ppm and 150 ppm while adrenals appear enlarged at 1500 ppm.

Ovaries, appear enlarged at 1500 ppm while testes are equivocally decreased in wt. at 1500 ppm. Prostatic wts, appear slightly decreased at 1500 ppm while uterine wts. are increased. Brain wts. appear to be slightly increased as does the pituitary at 1500 ppm in females.

Comment:

With the changes seen in pigmentation of the spleen (the RBC scavenging organ) one might suspect that the Hgb-Hct changes to be compound induced. However, upon closer scrutiny, one notes changes in Hct which are in obvious error in conjunction w/Hgb. i.e. the MCHC. Time sequences showing marked changes in all groups suggest poor feeding/watering practices and/or poor quality control of methodolgy in Hgb-Hct analysis.

Conservatively: For increased relative organ wts. a NOEL for liver and heart in females is 15 ppm. A NOEL for increased/decreased relative organ wts. of adrenals, prostate and testes in males is 150 ppm.

Toxicology Branch considers this study to be supplementary due to the above questions on hematology and lack of stated purity. These may be rebutted with submission of the daily individual animal feeding and observation records, methodology of hematology and statements of sample purity used.

The question of the watery lacrimation should be addressed by the registrant since that is considered a cholinergic effect as are the neuro-muscular effects reported unless other causes were apparent but unreported.

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