8-8-69

UNITED STATES GOVERNMENT

Memorandum

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
Public Health Service
FOOD AND DRUG ADMINISTRATION

SC-330

TO : Dr. H. Blumenthal, Chief
Petitions Review Branch, DPT (SC-970)

DATE: August 8, 1969

FROM : Dr. Eleanor L. Long
Pathology Branch, DPT/Sci (SC-940)

P-144-69

SUBJECT: Daconil (tetrachloroisophthalonitrile). Also called DAC-2787.

PESTICIDE PETITION NO. 9F0743

Diamond Shamrock Company
Painesville, Ohio
(AF 25-202)

File: PP# 9F0743

I have reviewed slides and data on Daconil on 2 previous occasions. On August 6, 1969, a conference on this fungicide was held between Dr. Herbert Blumenthal, Dr. O. G. Fitzhugh, Dr. H. R. Richardson, Mr. Drew Baker, and myself from the Food and Drug Administration and several representatives from Diamond Shamrock Co. and Hazleton Laboratories, Inc. (which is performing the animal studies on the compound). Because of a dispute regarding the no-effect level in the animals autopsied after one year of treatment in the latest dog feeding study (Project 200-206) in which Hazleton maintained that it was 60 ppm (the lowest level tested), while I stated that its description of the lesions indicated that there was some renal toxicity at this level, Dr. R. W. Voelker, the Hazleton pathologist who interpreted the slides, and I studied the slides in question together. We both agreed that there was moderate to marked vacuolation of the cells lining the tubules of the inner cortex in the kidneys of the high-dose (120 ppm) males but not in those of the 60 and 0 ppm males. In the case of the females, however, a similar type of vacuolation was found at all 3 dosage levels, control as well as treated, the amount being approximately equal at each level. In both sexes, at 120 ppm, the renal tubules showed a slight to moderate increase in pigment in comparison with the controls, in which it was minimal; in this respect there did not seem to be a significant difference between the controls and the low dosage group. Although tubular hypertrophy had been described for 2 of the 60 ppm males in Hazleton's description, Dr. Voelker agreed with me that this had been due to overreading and that the lesion was not really present.

In view of the above findings, both Dr. Voelker and I concluded that the no-effect level of Daconil for the dog after oral administration for one year was 60 ppm. Dr. Voelker agreed that Hazleton's description of the data did suggest an effect at this level, and explained that after complete study of

SEP 9 REC'D

the slides he had decided that there was no significant difference between the 60 ppm and control groups, but had neglected to correct his original written description.

Eleanor L. Long

Dr. Eleanor L. Long

cc: Dr. Leo Friedman (SC-900)
Dr. Richardson (SC-940)
Dr. Long (3)

ELLong:vo d-8-8-69