UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

CB

Rec'd Chem Br. JUL 3 1974

SUBJECT: Daconil (2,4,5,6-Tetrachloroisophthalonitrile) and 4-Hydroxy Metabolite (4-Hydroxy-2,5,6-Trichloroisophthalonitrile). Review of Report of Microscopic Study of Slides from Rats Fed 4 PPM and 0 PPM Daconil in Study 200-205 by Simon Koletsky, M.D.

DATE: July 3, 1974

FROM:

TO: Mr. Lee TerBush
Acting Chief
Coordination Branch
Registration Division (HM-567)

Copy file: PP#1230 Schmitt

Pesticide Petition No.: 2F1230 - Diamond Shamrock Chemical Company
300 Union Commerce Building
Cleveland, Ohio 44115

This is my 7th review of Daconil. During a conference on January 17, 1974 (see memo of February 1, 1974) at which Dr. Kent Davis, Staff Assistant (Pathology) to the Director of the Registration Division, and I met with 2 representatives of Diamond Shamrock Chemical Company, Milton Eisler, Ph.D., Director of Toxicology, and Klaus L. Stemmer, M.D., Pathologist and Associate Professor of Environmental Medicine, Department of Environmental Health, College of Medicine, University of Cincinnati, Dr. Stemmer (in spite of his report of March 12, 1974) admitted that he agreed with Dr. Davis and me that the microslides of the kidneys of some of the rats on the lowest dose of Daconil fed, 4 ppm, in 2-year rat study 200-205 showed changes not found in the controls which were possibly related to treatment. When Drs. Stemmer and Eisler then offered to do another, more thorough 2-year rat study in which they stated that the pathologic examination, including technical preparation of tissue for microscopy, would receive the utmost care, Dr. Davis and I agreed that this might clarify the issue. Instead of beginning another experiment such as this, Dr. Eisler submitted the microslides of the kidneys from the 4 ppm and 0 ppm rats in the study in question, 200-205, to another pathologist, Simon Koletsky, M.D., of Case Western Reserve

University, Cleveland, Ohio. Though I respect Dr. Koletsky as a pathologist, I cannot accept his conclusion that the changes at 4 ppm are artefacts unrelated to treatment, as he has given no reasons other than those we have already considered (as indicated in my 6th review of February 28, 1974) and seems unaware of the serious renal pathology clearly induced by higher levels of Daconil in both the dog and the rat. As has been stated before, the burden of proof of the absence of an effect must lie with the manufacturer, and no such proof has yet appeared in regard to Daconil rat study 200-205.

Statements in COB memo of 1/10/74 (Jesse E. Mayes) to Dr. Eisler have not been changed by the present submission.

Eleanor L. Long, M.D.
Pathologist
Toxicology Branch
Registration Division (HM-567)

Eleanor L. Long

cc: Dr. Rogoff
CB ✓
EEB
Division File
Branch Reading File
PP# 2F1230

R/D Init:CHWilliams:7/2/74
ELLong:sss:7/3/74
Init:CHWilliams CHW 7/3/74