CASWELL FILE

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

OCT 15 1991

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM:

Subject: EPA ID# 282778 - AC 303,630. Review of doses for chronic rodent toxicity study.

Shaughnessy No.: 129093
EPA Record No.: S401891
HED Project No.: 1-2471

From: Guruva B. Reddy, D.V.M., Ph.D.
Section 4
Toxicology Branch I
Health Effects Division (H7509C)

10/10/91

To: Dennis H. Edwards, Jr.
Product Manager 19
Registration Division (H7505C)

Thru: Marion P. Copley, D.V.M., D.A.B.T. Marion P. Copley
Section Head
Section 4, Toxicology Branch I
Health Effects Division (H7509C)

The Toxicology Branch I has evaluated the dose selection for an 18 month mouse study using the following studies: A 28-day mouse feeding study and limited data from 90-day mouse study. Detailed reviews of these submissions have not been conducted. The submission is in response to our meeting with registrant on July 23, 1991. Regarding the selection of the doses to be tested in mice, we expressed reservations and wanted to evaluate the 28-day mouse study to determine the adequacy of dose selection. We have no objection to the 240 ppm level representing the highest dose proposed for testing (0, 20, 120, and 240 ppm), even though body weight gains and mortality in 28-day and 90-day mouse feeding studies, did not conclusively support 240 ppm as the MTD. However, the presence of spongiform-myelopathy in almost all males and females at 320 ppm and one male at 160 ppm leads us to believe that these changes are severe enough to indicate toxicity of the chemical and higher doses may compromise the study.

In addition, we raised no objection to the rat dose.

Table I

Summary of Selected Percent Body Weight Change and Mortality[a]

Interval (Weeks)	Dose (ppm) 80	160	240	320	480
		90-Day Study (% Body Weight)			
		Males			
4	-19	-5	-	-43 (5)[c]	-
8	30	31	-	26	-
13	-14	1	-	-26	-
		Females			
4	5	-22	-	-33 (5)[c]	-
8	17	21	-	8	-
13	-2	-17	-	-29	-
		28-Day Study (% Body Weight)[b]			
		Males			
4	-	-16(0)[c]	-30(20)	-24(0)	-50(20)
		Females			
4	-	-24(0)	0(0)	-30(20)	-74(60)

[a] N = 20
[b] N = 5
[c] Mortality (%)