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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

Subject: Telone II - Qualitative Risk Assessment,
Mouse ($B_6C_3F_1$) Inhalation Study
caswell no. 324A

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Summary

The qualitative risk assessment of telone II was based upon a 2-year inhalation chronic/oncogenicity study in $B_6C_3F_1$ mice exposed to 0, 5, 20, and 60 ppm concentrations of vapor.

The statistical evaluation of these data indicated that neither male nor female mice had mortality differences with incrementatal doses of telone II.

In male mice, there was a significant dose related trend in lung bronchiolcaveolar adenomas and also a significant difference in the pair-wise comparison of control and the 60 ppm concentration group. In addition male mice had a significant difference in lacrimal gland cystadenomas in the pair-wise comparison of controls and the 20 ppm concentration group.

In female mice there was a significant difference in mesenteric lymphnode lymphosarcoma in the pair-wise comparison of control and the 5 ppm concentration group.

Background

A 2-year inhalation chronic toxicity/oncogenicity study in $B_6C_3F_1$ mice was conducted by Dow Chemical (study no. M-003993-009) and reported in July, 1987.

The study design allocated groups of 70 males and 70 females, each in a random manner to four exposure groups of 0, 5, 20 and 60 ppm target concentrations of telone II vapor. Exposure to the vapor occurred for 6 hours/day, 5 days/week (excluding holidays) for 2 years. Ten mice/sex/exposure level were predesignated for 6 and 12 month interim sacrifices.

Table 1. Telone II, $B_6C_3F_1$ Mouse, Experimental Design of the Inhalation Study

	Main Study(24 months) Number of		Interim Sacrifice at 27 and 53 weeks	
Dose (ppm)	Males	Females	Male	Female
0	50	50	10	10
5	50	50	10	10
20	50	50	10	10
60	50	50	10	10

Survival Analysis

In both male and female mice there were no statistically significant mortality differences with increments of telone II vapors (Tables 2 and 3 respectively).

The statistical evaluation of mortality in the mouse was based upon the Thomas, Breslow and Gart computer program.

Table 2. Telone II - Mouse Inhalation Study, Male Mortality Rates+ and Cox or Generalized K/W Test Results

Dose(ppm)	1-27	27[a]	28-52	Week 53[a]	53-78	79-105[b]	Total
0	2/70	10/10	1/58	8/8	0/49	3/49	6/52 (12)
5	0/70	10/10	0/60	10/10	1/50	4/49	5/50 (10)
20	1/70	10/10	1/59	9/9	0/49	4/49	6/51 (12)
60	0/70	10/10	0/60	10/10	0/50	3/50	3/50 (6)

+ Number of animals that died during interval/ Number of animals alive at the beginning of the interval.

( ) percent

a Interim sacrifice at week 27 and 53.

b Final Sacrifice at week 106.

Note: Time intervals were selected for display purposes only.
Significance of trend denoted at Control.
Significance of pair-wise comparison with control denoted at Dose level.

If * then $p<.05$ and if ** then $p<.01$.

Table 3. Telone II - Mouse Inhalation Study, Female Mortality Rates[+] and Cox or Generalized K/W Test Results

	Week						
Dose(ppm)	1-27	27[a]	28-52	53[a]	53-78	79-105[b]	Total
0	0/70	10/10	0/63	10/10	0/50	8/50	8/50 (16)
5	1/70	10/10	0/59	10/10	2/49	3/47	6/50 (12)
20	0/70	10/10	0/60	10/10	1/51	1/49	2/50 (4)
60	1/70	10/10	0/60	10/10	1/50	8/49	10/50 (20)

[+] Number of animals that died during interval/ Number of animals alive at the beginning of the interval.

( ) percent

a Final Sacrifice at week 106

Note: Time intervals were selected for display purposes only.
Significance of trend denoted at Control.
Significance of pair-wise comparison with control denoted at Dose level.

If * then $p<.05$ and if ** then $p<.01$.

Tumor Analysis

Male mice had a significant (p=.001) increasing trend in lung bronchioloalveolar adenomas with increasing concentrations of telone II vapors and also a significant (p=.009) difference in the pair-wise comparison of controls and the 60 ppm vapor concentration group. In addition, the males had a significant (p=.004) difference in lacrimal gland cystadenoma in the pair-wise comparison of controls and the 20 ppm vapor concentration group (Table 4).

Female mice had a significant (p=.010) difference in mesenteric lymphnode lymphosarcoma in the pair-wise comparison of controls and the lowest (5 ppm) vapor concentration group of telone II (Table 5).

Since there was no statistical evidence of differential survival with incremental concentrations of telone II vapors, the above tumor rate statistical analysis was based upon the Cochran- Armitage Trend test and the Fisher Exact test for the pair-wise comparison of controls and each vapor concentration group.

Table 4. Telone II - Male Mice Neoplastic Tumor Rates[+] and Cochran-Armitage Trend Test and Fisher's Exact Test Results

Tumor	Dose(ppm) 0	5	20	60
Lung Bronchioloaveolar Adenoma	9/57 (16)	6/51 (12)	13/49 (27)	22[a]/60 (37)
p=	0.001**	0.374	0.132	0.009**
Lacrimal Gland Cystadenoma	1/57 (2)	6/60 (10)	10/58 (17)	5[b]/60 (8)
p=	0.301	0.065	0.004**	0.116

[+] Number of tumor bearing animals/ Number of animals at risk (excluding those that died before 52 weeks).

( ) percent

a first lung adenoma observed at week 80.
b first cystadenoma observed at week 85.

Note: Significance of trend denoted at Control.
Significance of pair-wise comparison with control denoted at Dose level.

If * then $p<.05$ and if ** then $p<.01$.

Table 5. Telone II - Female Mice Neoplastic Tumor Rates[+] and Cochran-Armitage Trend Test and Fisher's Exact Test Results

Tumor	Dose(ppm) 0	5	20	60
Mesenteric Lymphnode Lymphosarcoma	3/57 (5)	11[a]/49 (22)	5/47 (11)	6/55 (11)
p=	0.407	0.010**	0.256	0.227

[+] Number of tumor bearing animals/ Number of animals at risk (excluding those that died before 52 weeks).

( ) percent

a first lymphosarcoma observed at week 71.

Note: Significance of trend denoted at Control.
Significance of pair-wise comparison with control denoted at Dose level.

If * then $p<.05$ and if ** then $p<.01$.

References

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