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

OFFICE OF
PREVENTION, PESTICIDES, AND
TOXIC SUBSTANCES

TXR No. 0054586

MEMORANDUM

DATE: May 18, 2007

SUBJECT: **Pyroxsulam:** Qualitative Risk Assessment Based On CD-1 (Crl:CD1(ICR)) Mouse Carcinogenicity Dietary Study

P.C. Code: 108702

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BACKGROUND

A carcinogenicity study in CD-1 (Crl:CD1(ICR)) mice was conducted by Dow Chemical Company, Midland, Michigan, for Dow AgroSciences, Indianapolis, Indiana, and dated December 15, 2005 (Study ID No. 031015, MRID No. 46908406).

The study design allocated groups of 50 mice per sex to nominal dose levels of 0, 10, 100 and 1000 mg/kg/day of Pyroxsulam in the diet for 79 weeks. Actual doses were 0, 10, 100 and 932 mg/kg/day for males. There were no compound-related tumors in the females so only analyses of the males are presented in this document.

ANALYSES

Survival Analyses

There were no statistically significant incremental changes in mortality with increasing doses of Pyroxsulam in male mice (Table 1).

Tumor Analyses

Male mice had a statistically significant trend for liver carcinomas at $p < 0.05$. There were statistically significant pair-wise comparisons of the 10 and 1000 mg/kg/day dose groups with the controls for liver adenomas, and liver adenomas and/or carcinomas combined, all at $p < 0.05$. The statistical analyses of the tumors in the male mice were based upon Fisher's Exact Test for pair-wise comparisons and the Exact Test for trend (Table 2)

Table 1. Pyroxsulam – CD-1 (Crl:CD1(ICR)) Mouse Study (MRID 46908406)

Male Mortality Rates[a] and Cox or Generalized K/W Test Results

	Weeks			
Dose (mg/kg/day)	1-26	27-52	53-79[f]	Total
0	0/50	1/50	9/49	10/50 (20)
10	1/50	3/49	6/46	10/50 (20)
100	0/50	2/50	8/48	10/50 (20)
1000	0/50	2/50	10/48	12/50 (24)

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

[f]Final sacrifice at week 79.

( )Percent.

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 $p < 0.05$. If [**], then $p < 0.01$.

Table 2. Pyroxsulam – CD-1 (Crl:CD1(ICR)) Mouse Study (MRID 46908406)

Male Liver Tumor Rates[+]
and Fisher's Exact Test and Exact Test for Trend Results

	Dose (mg/kg/day)			
	0	10	100	1000
Adenomas (%)	5/49 (10)	13/46 (28)	9[a]/49 (18)	14/48 (29)
p =	0.06696	0.02300*	0.19363	0.01716*
Carcinomas (%)	1/49 (2)	0/46 (0)	2[b]/49 (4)	4/48 (8)
p =	0.02622*	1.00000	0.50000	0.17451
Combined (%)	6/49 (12)	13/46 (28)	10[c]/49 (20)	15[d]/48 (31)
p =	0.05737	0.04462*	0.20651	0.02067*

+Number of tumor bearing animals/Number of animals examined, excluding those that died before week 52.

[a]First adenoma observed at week 53, dose 100 mg/kg/day.
[b]First carcinoma observed at week 73, dose 100 mg/kg/day.
[c]One animal in the 100 mg/kg/day dose group had both an adenoma and a carcinoma.
[d]Three animals in the 1000 mg/kg/day dose group had both an adenoma and a carcinoma.

Note: Significance of trend denoted at control.
Significance of pair-wise comparison with control denoted at dose level.
If *, then $p < 0.05$. If **, then $p < 0.01$.

References

Cox, D.R. (1972) Regression Models and Life Tables (with discussion). J. Royal Stat. Soc. Ser. B. 34, 187-220.

Gart, J.J., D. Krewski, P.N. Lee, R.E. Tarone, and J. Wahrendorf (1986) The Design and Analysis of Long-Term Animal Experiments. In: Statistical Methods in Cancer Research, Volume III. IARC Scientific Publications No. 79. Lyon, France: International Agency for Research on Cancer, p. 18.

Peto, R., M. Pike, N. Day, R. Gray, P. Lee, S. Parish, J. Peto, S. Richard, and J. Wahrendorf (1980) Guidelines for Simple, Sensitive, Significant Tests for Carcinogenic Effects in Long-Term Animal Experiments. In: Monographs on the long-term and short-term screening assays for carcinogens: a critical appraisal. IARC Monographs, Supplement 2. Lyon, France: International Agency for Research on Cancer, pp. 311-426.

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Chemical:	**Benzene hexachloride gamma isomer of ---------- % other isomers of ---------- % Lindane**
	PC Code: *008901* 009001
HED File Code:	**13100 Other Tox Documents**
Memo Date:	**2/26/1970**
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