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

OFFICE OF
PREVENTION, PESTICIDES, AND
TOXIC SUBSTANCES

TXR No. 0052326

MEMORANDUM

DATE: January 29, 2004

SUBJECT: **Penoxsulam** Qualitative Risk Assessment Based On A Fisher 344 Rat Dietary Study

P.C. Code 119031

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Background

A combined chronic toxicity/carcinogenicity study in Fisher 344 rats was conducted by Dow Chemical Company, Midland, Michigan for Dow AgroSciences LLC, Indianapolis, Indiana and dated November 14, 2002 (Laboratory Project Study ID 991244, MRID No. 45830901). The study design allocated groups of 50 rats per sex to dose levels of 0, 5, 50, or 250 mg/kg/day of Penoxsulam for 2 years. An additional 10 rats/sex/group were treated at the same dosages and necropsied after one year of treatment.

An external Pathology Working Group (PWG) reviewed the large granular lymphocyte leukemia (LGL) to establish consensus diagnoses (MRID 45830913). The PWG review was conducted at the Dow Chemical Company, Toxicology Research Laboratory, Midland, MI (Project ID EPL Project No. 368-002, dated November 5, 2002). These analyses were performed using the PWG data. There were no significant compound-related tumors in female rats, therefore, only the statistical analyses of the male rats are presented in this document.

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Survival Analyses

The statistical evaluation of mortality indicated a statistically significant increasing trend with increasing doses of penoxsulam in male rats. See Table 1 for male mortality test results.

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

Tumor Analyses

Male rats had a significant increasing trend at $p<0.05$, and there were significant pair-wise comparisons ($p < 0.01$) of all dose groups with the controls, for large granular lymphocyte leukemia (See Table 2).

Table 1. Penoxsulam - Fisher 344 Rat Study

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

Weeks

Dose (mg/kg/day)	1-26	27-52	53[i]	53-78	79-106[f]	Total
0	0/60	0/60	10/60	1/50	11/49	12/50 (24)*
5	0/60	1/60	10/59	0/49	10/49	11/50 (22)
50	0/60	0/60	10/60	1/50	21/49	22/50 (44)*
250	0/60	0/60	10/60	2/50	18/48	20/50 (40)

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

[i]Interim sacrifice at week 53.

[f]Final sacrifice at week 105/106.

( )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. Penoxsulam - Fisher 344 Rat Study

Male Large Granular Lymphocyte Leukemia Tumor Rates[+] and Peto's Prevalence Test Results

Dose (mg/kg/day)

	0	5	50	250
Leukemia (%)	12/49 (24)	30/49 (61)	29/49 (59)	30/49 (61)
p =	0.03567*	0.00010**	0.00014**	0.00038**

+Number of tumor bearing animals/Number of animals examined, excluding those that died before observation of the first tumor.

[a]First leukemia observed at week 78, dose 250 mg/kg/day.

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 $p < 0.01$.

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