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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

TXR No. 0053807

MEMORANDUM

DATE: October 19, 2005

SUBJECT: **Metconazole:** Qualitative Risk Assessment Based On Fischer 344 Rat Carcinogenicity and Chronic Toxicity Combined Dietary Studies

P.C. Code: 125619

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BACKGROUND

The 104-Week Fischer 344 Rat Carcinogenicity Study (MRID 44721611)

A carcinogenicity study in Fischer 344 rats was conducted by Shell Research Limited, Sittingbourne Research Center, Sittingbourne, Kent, England, for BASF Corporation, Research Triangle Park, North Carolina, and dated June 30, 1992 (Laboratory Report No. SBGR.91.192, MRID No. 44721611).

The study design allocated groups of 50 rats per sex to dose levels of 0, 100, 300 or 1000 ppm (0, 4.6, 13.8 or 46.5 mg/kg/day for males; 0, 5.5, 16.6 or 56.2 mg/kg/day for females) of Metconazole for 104 weeks. There were no compound-related tumors observed in male rats so this document only contains analyses of the females.

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The 104-Week Fischer 344 Rat Chronic Toxicity Study (MRID 44721609)

A chronic toxicity study in Fischer 344 rats was conducted by Sittingbourne Research Centre, Sittingbourne, Kent, England, for BASF Corporation, Research Triangle Park, North Carolina, and dated September 16, 1992 (Laboratory Report No. SBGR.91.193, MRID No. 44721609).

The study design allocated groups of 20 rats per sex to dose levels of 10, 100, 300 or 1000 ppm (0, 0.4, 4.3, 13.1 or 43.9 mg/kg/day for males; 0, 0.5, 5.3, 16.0 or 53.8 mg/kg/day for females) of Metconazole for 104 weeks. A group of 40 rats were designated to the control group. Study termination occurred at weeks 107 and 108. Another 20 rats per sex in the control group and 10 rats per sex for the dosed levels were designated for interim sacrifice at week 52.

There were no compound-related tumors observed in rats of either sex of the chronic study, but the females of this study have been combined with the females of the carcinogenicity study to fully assess the extent of the mononuclear cell leukemia.

ANALYSES

Survival Analyses

There were no statistically significant incremental changes in mortality with increasing doses of Metconazole in female rats of either study. See TXR No. 0053709 for mortality analyses of the carcinogenicity study. The DER of the chronic study indicated no survival disparities among the female rats.

Tumor Analyses

At the request of Bill Burnam, chairman of the CARC committee, the carcinogenicity and chronic studies have been combined to fully assess the extent of the mononuclear cell leukemia in female rats. The results of the combination are presented in this document.

Female rats of the combined carcinogenicity and chronic studies had significant differences in the pair-wise comparisons of the 300 and 1000 ppm dose groups with the controls for mononuclear cell leukemia at all sites, both at $p < 0.05$. There was no statistically significant trend. The statistical analyses of the female rats were based upon *ad hoc* Fisher's Exact Test for pair-wise comparisons and the Exact Test for trend (Table 1).

Table 1. Meteonazole - Fischer 344 Rat Carcinogenicity (MRID 44721611)
and Chronic Toxicity (MRID 44721609) Combined Studies

Female Mononuclear Cell Leukemia Rates and *ad hoc* Fisher's Exact Test and Exact Test for Trend Results

	Dose (ppm)				
	0	10[a]	100	300	1000
Mononuclear Cell Leukemia - All Sites (%)	10/89 (11)	2/19 (11)	10/41# (24)	12/40# (30)	16/70 (23)
p =	0.07181	0.66605	0.05026	0.01054*	0.04032*

+Number of tumor bearing animals/Number of animals examined, excluding those that died or were sacrificed before week 53.

[a]The carcinogenicity study had a control and 3 dose groups. The chronic study had a control and 4 dose groups. Only the chronic study had a 10 ppm dose group.

#Only decedents in the 100 and 300 ppm dose groups were examined for all tissues.

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

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