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

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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

DATE: February 18, 1982

SUBJECT: Review of Methemoglobinemia and Sulfhemoglobinemia in Mice, Dimilin, EPA Reg. No. 148-1268 CASWELL #346A

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Methemoglobin and sulfhemoglobin values were obtained from 5 groups of male and female mice treated with diflubenzuron (Dimilin) at 7 and 14 weeks with 80; 400; 2,000; 10,000; and 50,000 ppm respectively. All the animals, regardless of duration of treatment or dose levels were found to be statistically different from contemporaneously treated control rats at the 95% C.L. A no-observable effect level could not be found in this experiment.

However, the examination of the data showed that the coefficient of correlation was excellant over any given dose range in any one sex of animals, at any given period of treatment either at 7 weeks or at the 14 week period. It was decided therefore, that a no-observable effect level would be justified using regression analyses of the data.

The coefficient of correlation over the various time intervals and dose levels were according to the following schedule.

Coefficient of Correlation

Sulf				Met			
7 wk.		14 wk.		7 wk.		14 wk.	
Male	Female	Male	Female	Male	Female	Male	Female
.98992	.93894	.95302	.99843	.99716	.98502	.98502	.96277

The computer print-out from RTP obtained for the derivation of the NOEL is attached.

NOEL BY REGRESSION ANALYSIS

	7 Weeek				14 Week			
	Sulf.		Met.		Sulf.		Met.	
	Male	Female	Male	Female	Male	Female	Male	Female
ppm	17.11	24.75	3.47	1.43	7.48	28.17	3.11	2.68
mg/kg	2.4	3.5	0.5	0.2	1.1	4.0	0.4	0.4

The no-effect level of 1.1 mg/kg was selected from the non-reversible systemic effect of sulfhemoglobin demonstrated in male mice at the 14 week period. A safety factor of 100 is applied to the no-effect level of 1.1 mg/kg resulting in an ADI of .011 mg/kg/day.

It is difficult to establish a no-effect level for methemoglobinemia since methemoglobinemia is both a normal physiological event and is reversible in many people with the exception of young children and those mature people who do not have the transferase enzyme needed to reverse methemoglobin.

The maximum permissible intake for a 60 kg person would be 0.66 mg/day.