

Telomer Research Program



Clariant



Report Title: *In Vivo* Rat Micronucleus Assay

Author(s): Gregory L. Erexson, Ph.D

Contractor: Covance Laboratories, Inc., Vienna, Virginia

Study Dates:

Initiation: October 18, 2001

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Study Objective: To evaluate 8-2 Alcohol for *in vivo* clastogenic activity and/or disruption of the mitotic apparatus by examining bone marrow polychromatic erythrocytes in male CRL:CD®(SD)IGS BR rats for micronuclei.

Materials and Methods: Groups of male rats (5/group) were administered a single oral gavage dose of either 0 (vehicle 0.5% aqueous methyl cellulose), 500, 1000, or 2000 mg 8-2 Alcohol/kg body weight. A positive control group of rats received a single oral dose of 60 mg cyclophosphamide/kg. At both 24 and 48 hours, 5 rats from each group were sacrificed and bone marrow was extracted from the tibia. Slides were prepared and scored for micronuclei and the PCE/NCE (polychromatic erythrocytes) (normochromatic erythrocytes) cell ratio was counted (scored at least the first 500 erythrocytes on each slide). Assay acceptance criteria was met with the criteria for a positive response being the detection of a statistically significant increase in micronucleated PCE's for at least 1 dose level and a statistically significant dose-related response.

Findings: No lethality or signs of clinical toxicity were seen in the rats given in either 500, 1000, or 2000 mg/kg. 8-2 Alcohol did not induce a statistically significant increase in micronucleated PCE's at any of the dose levels tested. The positive control material showed the expected response demonstrating the sensitivity of the test system.

(Data table follows.)

Treatment	Dose	Harvest Time (HR)	% Micronucleated PCE's Mean of 2000 per Animal ±S.E. Males	Ratio PCE:NCE Mean±S.E. Males
Vehicle Control	0.5% MC	24 hr	0.04±0.02	1.26±0.09
		48 hr	0.07±0.01	1.11±0.04
Positive Control	CP 60.0 mg/kg	24 hr	3.10±0.29 ^a	0.78±0.00 ^b
Test Article	500 mg/kg	24 hr	0.04±0.02	1.13±0.05
		48 hr	0.09±0.02	1.06±0.11
	1000 mg/kg	24 hr	0.15±0.07	1.17±0.06
		48 hr	0.09±0.05	0.95±0.08
	2000 mg/kg	24 hr	0.10±0.03	1.10±0.07
		48 hr	0.09±0.02	1.20±0.08

^aSignificantly greater than the corresponding vehicle control, p≤0.01

^bSignificantly lower than the corresponding vehicle control, p≤0.01

Conclusion: 8-2 Alcohol is considered negative in the rat bone marrow micronucleus assay under the conditions of this assay.

Publications / Presentations:

A) Covance Study 22900-0-454 OECD, 1/25/02.

B) Results cited in: Kennedy, G. L., Jung, R., Iwai, H., Shin-Ya, S., Murphy, S., Drouot, N., Finlay, C., Donner, M., Erexson, G., and Stankowski, L., Jr., "Genetic Toxicology of 8-2 Telomer B Alcohol", Toxicol. Sci. 72(S-1):209:2003.