ADME NTP Study S0977 2,2-bis(Bromomethyl)-1,3-propanediol Toxicokinetics

The contractor used the abbreviation BMP for the test article. Sex/Species: male F344 rats. Vehicle: intravenous, ethanol:water:Cremophore EL 1:1:3.

CASRN 3296-90-0

Radiolabeled with carbon-14 located non-specifically on the carbon molecules; [¹⁴C]2,2-bis(Bromomethyl)-1,3-propanediol

Studies Performed:

Single 10 mg/kg intravenous dose with blood sampling at 7.5, 15, 30, 60, 90, 180, 360, 540, 720, 1440, 2160, and 2880 minutes postdose. (n=3)

Mean ± standard deviation values for total [¹⁴C]BMP in whole blood extracts for the concentration-time curves were displayed in figures and are not shown here. No individual animal data for toxicokinetic blood concentrations were available. No evidence of BMP glucuronide in blood was obtained; HPLC analysis showed only a single peak coeluting with [¹⁴C]BMP standard. [¹⁴C]BMP radioactivity values were below the limit of quantification after 48 hours.

Toxicokinetics:

The best fit model for the data was a three-compartment model with first order elimination (WinNonlin, Pharsight).

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Table 1

Kinetic parameters for BMP following IV administration (10 mg/kg, 50 μCi/kg) in male F-344 rats (N=3, mean ± S.D.) based on a best-fit-analyses using a three-compartment model fit (WinNonLin, Pharsight). Kinetic parameters were calculated using [¹⁴C] BMP in blood, as determined by LSC & HPLC-radiometric detection.

Dose	AUC	t _{1/2α}	4	t _{1/2γ}	CL _b	V _{ss}
(µg)	(min*µg/mL)		. ,	(h)	(mL/min)	(mL)
1885.5	33,382	1.5	41.3	36.3	0.1	10.4

AUC: area under the blood concentration-time curve from 0 to infinity. $t_{1/2\alpha}$: half-life of distribution; $t_{1/2\beta}$: initial half life of elimination; $t_{1/2\gamma}$: terminal half life of elimination; CL_b : systemic clearance from blood; V_{ss} : volume of distribution at steady-state.