ADME NTP Study S0829 1-Bromopropane Toxicokinetics

The contractor used the abbreviation 1-BrP for the test article.
Sex/Species: male F344 rats.
Vehicle: intravenous, 0.9% saline and 5% Alkamuls.

CASRN 106-94-5

Radiolabeled with carbon-14 in the C-1 position; 1-Bromopropane, [1-^{14}C]

Studies Performed:

- Single 5 mg/kg intravenous dose with blood sampling 2, 5, 10, 20, 30, 45, 60, 90, 120, 150, 180, and 240 minutes postdose. (n=5)

- Single 20 mg/kg intravenous dose with blood sampling 2, 5, 10, 20, 30, 45, 60, 90, 120, 150, 180, and 240 minutes postdose. (n=5)

Toxicokinetics:

Mean blood 1-BrP concentration-time data were analyzed by model-dependent methods using WinNonlin (Scientific Consulting Inc., Apex, NC). A biexponential function was used to generate pharmacokinetic parameters for each set of data (weighting: $1/y^2$). A two-compartment pharmacokinetic model gave the best fit to the blood 1-BrP concentration-time data. Plasma levels were displayed in figures (not shown) and individual animal data (separate file).

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Table 1

1-BrP Pharmacokinetic Parameters[a] in Male F-344 Rats Derived After Intravenous Bolus Administration of 1-BrP

Parameter	Units	5 mg/kg		20 mg/kg	
		Mean	SE[b]	Mean	SE
A	---	3.75	1.35	12.16	5.31
α	---	14.36	4.53	14.67	5.59
B	---	0.37	0.13	1.51	0.3
β	---	1.76	0.35	0.82	0.09
AUC_0^∞	h*µg/mL	0.47	0.06	2.68	0.26
$T_{1/2\alpha}$	h	0.05	0.02	0.05	0.02
$T_{1/2\beta}$	h	0.39	0.08	0.85	0.09
K10	1/h	8.73	2.34	5.11	1.77
K12	1/h	4.49	2.15	8.03	3.85
K21	1/h	2.89	0.85	2.34	0.61
C_0	µg/mL	4.12	1.39	13.67	5.36
V_c	mL	303	102	366	143
CL	mL/h	2648	325	1869	184
AUMC	h^2*µg/mL	0.14	0.02	2.32	0.27
MRT	h	0.29	0.05	0.87	0.10
V_{ss}	mL	775	187	1619	286

[a] Pharmacokinetic parameters calculated from mean 1-BrP blood concentrations (n=5 rats).

[b] Standard Error of estimated parameter mean.

Abbreviations of Estimated and Secondary parameters:
A, The zero time intercept associated with the Alpha phase;
α, Rate constant associated with the distribution phase;
$T_{1/2\alpha}$, Half-life associated with the macro constant α;
B, The zero time intercept associated with the beta phase;
β, Rate constant associated with the elimination phase;
$T_{1/2\beta}$, Half-life associated with the macro constant β;
AUC_0^∞, Area under the concentration time curve from time zero to infinity;
C_0, The concentration extrapolated at time = 0.
V_c, Volume of the central compartment;
Cl, Systemic clearance;
AUMC, Area under moment curve
MRT, Mean residence time, and
V_{ss}, Volume of the distribution at steady state.