Experiment Number: K13114 | **Toxicokinetics Data Summary** | **Request Date:** 3/12/2021

Route: Intravenous, Oral Gavage | **Compound & Analyte:** 2-(2H-Benzotriazol-2-yl)-4-tert-butylphenol | **Request Time:** 2:30:16

Species/Strain: Rat/Harlan Sprague-Dawley | **CAS Number:** 3147-76-0 | **Lab:** BAT

Male

	Treatment Group (mg/kg)		
	2.25 IV[a] Blood	**30 Gav[b] Blood**	**300 Gav[b] Blood**
C_0min_pred (ng/mL)	3050 ± 450		
Cmax_pred (ng/mL)		1070 ± 230	4640 ± 1100
Tmax_pred (hour)		1.18 ± 0.27	2.72 ± 0.62
Cmax_obs (ng/mL)	2890	1320	8660
Tmax_obs (hour)		0.750	2.00
Alpha_Half-life (hour)	0.196 ± 0.040	0.863 ± 2.41	2.47 ± 2.13
Beta_Half-life (hour)	1.16 ± 0.19	13.6 ± 2.7	16.8 ± 10.6
Gamma_Half-life (hour)	30.5 ± 5.9		
k01 ($hour^{-1}$)		0.923 ± 2.81	0.483 ± 0.499
k01_Half-life (hour)		0.751 ± 2.28	1.44 ± 1.48
k10 ($hour^{-1}$)	1.85 ± 0.24	0.649 ± 1.81	0.247 ± 0.196
k10_Half-life (hour)	0.375 ± 0.048	1.07 ± 2.98	2.81 ± 2.23
k12 ($hour^{-1}$)	0.996 ± 0.383	0.142 ± 0.438	0.0277 ± 0.0436
k21 ($hour^{-1}$)	0.971 ± 0.257	0.0629 ± 0.0154	0.0468 ± 0.0342
k13 ($hour^{-1}$)	0.309 ± 0.052		
k31 ($hour^{-1}$)	0.0266 ± 0.0051		
Cl1 (mL/hr/kg)	1360 ± 80		
Cl2 (mL/hr/kg)	734 ± 234		
Cl3 (mL/hr/kg)	228 ± 36		
Cl1_F (mL/hr/kg)		7240 ± 1450	7590 ± 1730
Cl2_F (mL/hr/kg)		1580 ± 890	853 ± 809
V1 (mL/kg)	737 ± 110		
V2 (mL/kg)	756 ± 148		
V3 (mL/kg)	8560 ± 2200		
V1_F (mL/kg)		11100 ± 32400	30800 ± 29000
V2_F (mL/kg)		25100 ± 11000	18200 ± 9800

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	Treatment Group (mg/kg)		
	2.25 IV[a] Blood	**30 Gav[b] Blood**	**300 Gav[b] Blood**
MRT (hour)	7.37 ± 1.60		
AUC_0-T (ng/mL·hr)	1700	4270	34700
AUC_inf (ng/mL·hr)	1650 ± 100	4140 ± 930	39500 ± 9100

LEGEND

MODELING METHOD & BEST FIT MODEL

[a] WinNonlin three-compartment model with bolus input, first order output, and 1/Yhat^2 weighting (model #18); Cmax_pred based on the model prediction at 0 minutes.

[b] WinNonlin two-compartment model with first order input, first order output, and 1/Yhat^2 weighting (model #13).

ANALYTE

2-(2H-Benzotriazol-2-yl)-4-tert-butylphenol

TK PARAMETERS

C_0min_pred = Fitted plasma concentration at time zero (IV only)
Cmax_obs = Observed maximum plasma concentration
Cmax_pred = Predicted maximum plasma concentration
Tmax_obs = Time at which observed Cmax occurs
Tmax_pred = Time at which predicted Cmax occurs
Alpha_Half-life = Half-life for the alpha phase
Beta_Half- life = Half-life for the beta phase
Gamma Half-life = Half-life for the gamma phase
k01 = Absorption rate constant, ka
k01_Half-life = Half-life of the absorption process to the central compartment
k10 = Elimination rate constant from the central compartment also ke or kelim
k10_Half_life = Half-life for the elimination process from the central compartment
k12 = Distribution rate constant from first to second compartment
k21 = Distribution rate constant from second to first compartment
k13 = Distribution rate constant from first to third compartment
k31 = Distribution rate constant from third to first compartment

TK PARAMETERS (cont'd)

Cl1 = Clearance of central compartment
Cl2 = Clearance of the secondary compartment
Cl3 = Clearance of the tertiary compartment
Cl1_F = Apparent clearance of the central compartment, also Cl_F for gavage groups in non-compartmental model
Cl2_F = Apparent clearance of the secondary compartment
V1 = Volume of distribution of the central compartment, includes Vd and V volume of distribution
V2 = Volume of distribution for the peripheral compartment
V3 = Volume of distribution for the peripheral compartment
V1_F = Apparent volume of distribution for the central compartment includes Vd_F, V_F for oral groups, and Vc_F
V2_F = Apparent volume of distribution for the peripheral compartment
MRT = Mean residence time
AUC_0-T = Area under the plasma concentration versus time curve, AUC, from time ti (initial) to tf (final), AUClast
AUC_inf = Area under the plasma concentration versus time curve, AUC, extrapolated to time equals infinity

TK PARAMETERS PROTOCOL

BLOOD

IV_2.25_Rat_Male

Harlan Sprague Dawley male rats were intravenously administered a single 2.25 mg/kg dose of 2-(2H-benzotriazol-2-yl)-4-tert-butylphenol (tBu-BZT). An automated blood sampling system (Culex) was used for this study. Whole blood samples were taken from n=3 animals/timepoint/per group at pre-dose and 16 timepoints at 0.0333, 0.0833, 0.167, 0.25, 0.333, 0.5, 0.75, 1, 2, 4, 8, 12, 18, 24, 48, and 72 hrs. Parent (free) was analyzed by LC-MS/MS with a lower limit of quantitation (LLOQ) of 1.0 ng/mL. Parameter estimates are reported to three significant figures with standard error (SE). Observed values do not have a reported SE.

BLOOD

Gavage_30_Rat_male, 300 Rat Male

Harlan Sprague Dawley male rats were administered a single gavage dose of 30 or 300 mg/kg 2-(2H-benzotriazol-2-yl)-4-tert-butylphenol (tBu-BZT). An automated blood sampling system (Culex) was used for this study. Whole blood samples were taken from n=3 animals/timepoint/per group at pre-dose and 16 timepoints at 0.0333, 0.0833, 0.167, 0.25, 0.333, 0.5, 0.75, 1, 2, 4, 8, 12, 18, 24, 48, and 72 hrs. Parent (free) was analyzed by LC-MS/MS with a lower limit of quantitation (LLOQ) of 1.0 ng/mL. Parameter estimates are reported to three significant figures with standard error (SE). Observed values do not have a reported SE.