Experiment Number: S0609
Route: Gavage, IV
Species/Strain: Mouse/B6C3F1

Toxicokinetics Data Summary
Test Compound: 3'-Azido-3'-deoxythymidine
CAS Number: 30516-87-1

Date Report Requested: 01/11/2017
Time Report Requested: 12:22:28
Lab: Research Triangle Institute International

Male

	Treatment Groups (mg/kg)						
	15 #	**15 ***	**25 #**	**25 ~**	**25 ***	**25 °**	**50 °**
				Plasma			
C_{max} (ug/mL)	5.91	0.0863	13.0	0.163	0.205	0.224	0.308
T_{max} (hour)	0.0833	0.500	0.333	0.500	0.500	8.00	0.333
Lambda$_z$ (hour^-1)	1.64		2.50				
$t_{1/2}$ (hour)	0.423		0.277				
Cl (mL/min/kg)	62.5		41.7				
V_1 (L/kg)							
$V_{1(F)}$ (L/kg)	2.29		1.00				
MRT (hour)	0.537		0.558				
AUC_{0-t} (ug*hr/mL)		0.0072		0.0136	1.23	0.453	0.343

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Male

	Treatment Groups (mg/kg)								
	50 #	**50 ***	**50 ~**	**90 ***	**90 ~**	**90 °**	**90 #**	**100 °**	**100 ~**
	Plasma								
$C_{max(obs)}$ (ug/mL)	28.9	0.795	0.219	0.868	0.530	0.601	74.9	0.720	0.493
$T_{max(obs)}$ (hour)	0.333	0.333	0.0833	0.167	0.500	0.333	0.333	0.500	0.333
$Lambda_Z$ (hour^-1)	1.41						1.51		
$t_{1/2}$ (hour)	0.491						0.461		
Cl (mL/min/kg)	36.3						26.3		
V_1 (L/kg)									
$V_{1(F)}$ (L/kg)	1.54						1.05		
MRT (hour)	0.606						0.833		
AUC_{0-t} (ug*hr/mL)		2.01	0.120	6.48	0.276	0.620		0.269	1.75

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Male

	Treatment Groups (mg/kg)							
	100 *	**100 #**	**15 IV #**	**15 IV ***	**15 IV ~**	**50 IV #**	**50 IV °**	**50 IV ***
	Plasma							
$C_{max(obs)}$ (ug/mL)	1.01	61.5	37.6	2.28	0.0890	79.5	0.230	3.55
$T_{max(obs)}$ (hour)	0.167	0.0833		2.00	0.500		0.250	0.250
$Lambda_Z$ (hour^-1)		2.10	1.76			2.63		
$t_{1/2}$ (hour)		0.330	0.395			0.263		
Cl (mL/min/kg)		31.3	27.3			32.0		
V_1 (L/kg)			0.934			0.729		
$V_{1(F)}$ (L/kg)		0.895						
MRT (hour)		1.06	0.294			0.453		
AUC_{0-t} (ug*hr/mL)	8.24			16.8	0.0659		0.0813	7.26

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Male

	Treatment Groups (mg/kg)				
	50 IV ~	**100 IV °**	**100 IV #**	**100 IV ***	**100 IV ~**
			Plasma		
$C_{max(obs)}$ (ug/mL)	1.28	1.18	184	7.61	0.674
$T_{max(obs)}$ (hour)	0.250	0.250		6.00	0.750
$Lambda_Z$ (hour^-1)			1.96		
$t_{1/2}$ (hour)			0.353		
Cl (mL/min/kg)			21.0		
V_1 (L/kg)			0.643		
$V_{1(F)}$ (L/kg)					
MRT (hour)			0.767		
AUC_{0-t} (ug*hr/mL)	0.107	0.899		69.1	0.218

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Female

	Treatment Groups (mg/kg)							
	15 #	**25 ~**	**25 ***	**25 #**	**50 ***	**50 ~**	**50 #**	**50 º**
	Plasma							
$C_{max(obs)}$ (ug/mL)	7.86	0.100	1.96	13.6	0.869	0.302	32.5	0.173
$T_{max(obs)}$ (hour)	0.333	0.333	8.00	0.167	1.50	0.167	0.333	0.167
$Lambda_z$ (hour^-1)	1.51			2.02			0.960	
$t_{1/2}$ (hour)	0.459			0.343			0.720	
Cl (mL/min/kg)	43.5			33.3			26.8	
V_1 (L/kg)								
$V_{1(F)}$ (L/kg)	1.73			0.990			1.67	
MRT (hour)	0.585			0.580			0.927	
AUC_{0-t} (ug*hr/mL)		0.0401	10.9		2.07	0.0761		0.0488

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Female

	Treatment Groups (mg/kg)							
	15 IV #	**15 IV ***	**50 IV #**	**50 IV ***	**100 IV °**	**100 IV ***	**100 IV ~**	**100 IV #**
	Plasma							
$C_{max(obs)}$ (ug/mL)	18.5	1.81	32.7	3.56	0.850	4.90	0.445	130
$T_{max(obs)}$ (hour)		8.00		0.250	0.250	8.00	0.750	
$Lambda_Z$ (hour^-1)	2.08		2.16					1.78
$t_{1/2}$ (hour)	0.333		0.321					0.389
Cl (mL/min/kg)	25.8		30.8					22.4
V_1 (L/kg)	0.743		0.855					0.756
$V_{1(F)}$ (L/kg)								
MRT (hour)	0.448		0.567					0.619
AUC_{0-t} (ug*hr/mL)		5.36		6.22	0.593	63.6	0.229	

LEGEND

Data are displayed as mean values

MODELING METHOD & BEST FIT MODEL

WinNonlin (Model 200 and 201, WinNonlin Ver. 1.5A, Scientific Consulting, Inc. now Pharsight Corporation, Apex, NC); Non compartmental analysis

ANALYTE

3'-Azido-3'-deoxythymidine

* 3’-Amino-3’-deoxythymidine

˜ 3’-amino-3’-deoxythymidine glucuronide

° Beta-D-glucuronide

TK PARAMETERS

C_{max} = Observed or Predicted Maximum plasma (or tissue) concentration

T_{max} = Time at which C_{max} predicted or observed occurs

$Lambda_z$ = Non-compartmental analysis (NCA) terminal elimination rate constant, NCA k_e or k_{elim}

$t_{½}$ = $Lambda_z$ half-life, $t_{1/2}$, the terminal elimination half-life based on non-compartmental analysis

Cl = Clearance, includes total clearance

V_1 = Volume of distribution of the central compartment, includes V_d and V_{volume} of distribution, V_z apparent volume of distribution NCA, V_{app} apparent volume of distribution for intravenous studies

$V_{1(F)}$ = Apparent volume of distribution for the central compartment includes $V_{d(F)}$, $V_{(F)}$ for oral groups, and $V_{c(F)}$

MRT = Mean residence time

AUC_{0-t} = Area under the plasma concentration versus time curve, AUC, from time t_i (initial) to t_f (final), AUC_{last}

** END OF REPORT **