

	Male					
	Treatment Groups (mg/kg)					
	10 <sup>a</sup>	30 <sup>a</sup>	100 <sup>a</sup>	400 <sup>a</sup>	2.5 IV <sup>a</sup>	10 IV <sup>a</sup>
	Brain					
C <sub>max(pred)</sub> (ug/mL)						
T <sub>max(pred)</sub> (minute)						
C <sub>max(obs)</sub> (ug/g) *	3.44 ± 1.10	15.3 ± 1.3	57.4 ± 16.3	165 ± 25	2.61 ± 0.55	9.86 ± 0.88
T <sub>max(obs)</sub> (minute)	19	28	96	26	7	7
t <sub>1/2</sub> (minute)	18.6	38.9	33.5	124	16.1	24.3
k <sub>01</sub> (minute^-1)						
t <sub>1/2(k01)</sub> (minute)						
k <sub>10</sub> (minute^-1)						
t <sub>1/2(k10)</sub> (minute)						
k <sub>12</sub> (minute^-1)						
k <sub>21</sub> (minute^-1)						
Cl <sub>1</sub> (mL/min/kg)						
Cl <sub>1(F)</sub> (mL/min/kg)						
V <sub>1</sub> (mL/kg)						
V <sub>2</sub> (mL/kg)						
V <sub>1(F)</sub> (mL/kg)						
AUC <sub>0-t</sub> (ug*min/g)	150	1130	12900	53000	69.7	474
AUC <sub>inf</sub> (ug*min/g)	151	1180	12900	54700	70.6	476

**Experiment Number:** NA  
**Route:** Gavage, IV  
**Species/Strain:** Rat/F344

**Toxicokinetics Data Summary**  
**Test Compound:** 2-Methyltetrahydrofuran  
**CAS Number:** 96-47-9

**Date Report Requested:** 01/09/2017  
**Time Report Requested:** 11:25:04  
**Lab:** Battelle Columbus

Male										
Treatment Groups (mg/kg)										
40 IV <sup>a</sup>		10 <sup>b</sup>			30 <sup>b</sup>		100 <sup>c</sup>		400 <sup>c</sup>	
Brain							Plasma		2.5 IV <sup>d</sup>	
C <sub>max(pred)</sub> (ug/mL)		4.89	±	0.32	21.1	±	1.8	46.8	±	15
T <sub>max(pred)</sub> (minute)		16	±	1.3	33.1	±	3.5			
C <sub>max(obs)</sub> (ug/g) *	35.1 ± 3.4									
T <sub>max(obs)</sub> (minute)	11									
t <sub>1/2</sub> (minute)	44.5									
k <sub>01</sub> (minute <sup>-1</sup> )		0.0945	±	0.0172	0.0516	±	0.0146	0.219	±	1.103
t <sub>1/2(k01)</sub> (minute)		7.34	±	1.34	13.4	±	3.8	3.17	±	1.6
k <sub>10</sub> (minute <sup>-1</sup> )		0.0388	±	0.0025	0.0158	±	0.0031			0.0741 ± 0.0077
t <sub>1/2(k10)</sub> (minute)		17.8	±	1.2	43.8	±	8.5			9.35 ± 0.97
k <sub>12</sub> (minute <sup>-1</sup> )										0.05 ± 0.022
k <sub>21</sub> (minute <sup>-1</sup> )										0.0727 ± 0.0298
Cl <sub>1</sub> (mL/min/kg)										40.7 ± 1.9
Cl <sub>1(F)</sub> (mL/min/kg)		42.7	±	2.8	13.3	±	1			
V <sub>1</sub> (mL/kg)										549 ± 55
V <sub>2</sub> (mL/kg)										378 ± 86
V <sub>1(F)</sub> (mL/kg)		1100	±	130	844	±	176	499	±	39
AUC <sub>0-t</sub> (ug*min/g)	2750							10000		62.5
AUC <sub>inf</sub> (ug*min/g)	2810	234	±	15	2250	±	180	10000		61.4 ± 2.9

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**Lab:** Battelle Columbus

Male				
	Treatment Groups (mg/kg)			
	10 IV <sup>d</sup>		40 IV <sup>e</sup>	
	Plasma			
C <sub>max(pred)</sub> (ug/mL)				
T <sub>max(pred)</sub> (minute)				
C <sub>max(obs)</sub> (ug/g) *				
T <sub>max(obs)</sub> (minute)				
t <sub>1/2</sub> (minute)				
k <sub>01</sub> (minute^-1)				
t <sub>1/2(k01)</sub> (minute)				
k <sub>10</sub> (minute^-1)	0.0676 ±	0.0242		
t <sub>1/2(k10)</sub> (minute)	10.2 ±	3.7		
k <sub>12</sub> (minute^-1)	0.258 ±	0.234	0.0843 ±	0.0851
k <sub>21</sub> (minute^-1)	0.264 ±	0.08	0.0949 ±	0.0672
Cl <sub>1</sub> (mL/min/kg)	22 ±	0.9		
Cl <sub>1(F)</sub> (mL/min/kg)				
V <sub>1</sub> (mL/kg)	325 ±	120	601 ±	166
V <sub>2</sub> (mL/kg)	317 ±	97		ND
V <sub>1(F)</sub> (mL/kg)				
AUC <sub>0-t</sub> (ug*min/g)	475		3830	
AUC <sub>inf</sub> (ug*min/g)	455 ±	19	3830	

**Experiment Number:** NA  
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**Species/Strain:** Rat/F344

**Toxicokinetics Data Summary**  
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**Date Report Requested:** 01/09/2017  
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**Lab:** Battelle Columbus

	Female					
	Treatment Groups (mg/kg)					
	10 <sup>a</sup>	30 <sup>a</sup>	100 <sup>a</sup>	400 <sup>a</sup>	2.5 IV <sup>a</sup>	10 IV <sup>a</sup>
	Brain					
C <sub>max(pred)</sub> (ug/mL)						
T <sub>max(pred)</sub> (minute)						
C <sub>max(obs)</sub> (ug/g) *	3.32 ± 0.52	11.0 ± 4.1	60.3 ± 6.4	209 ± 24	2.05 ± 0.39	8.83 ± 1.83
T <sub>max(obs)</sub> (minute)	12	24	12	10	7	9
t <sub>1/2</sub> (minute)	18.2	23.2	31.3	146	13.5	21.1
k <sub>01</sub> (minute <sup>-1</sup> )						
t <sub>1/2(k01)</sub> (minute)						
k <sub>10</sub> (minute <sup>-1</sup> )						
t <sub>1/2(k10)</sub> (minute)						
k <sub>12</sub> (minute <sup>-1</sup> )						
k <sub>21</sub> (minute <sup>-1</sup> )						
Cl <sub>1</sub> (mL/min/kg)						
Cl <sub>1(F)</sub> (mL/min/kg)						
V <sub>1</sub> (mL/kg)						
V <sub>2</sub> (mL/kg)						
V <sub>1(F)</sub> (mL/kg)						
AUC <sub>0-t</sub> (ug*min/g)	139	792	7320	46400	51	475
AUC <sub>inf</sub> (ug*min/g)	140	800	7330	47200	51.2	476

**Experiment Number:** NA  
**Route:** Gavage, IV  
**Species/Strain:** Rat/F344

**Toxicokinetics Data Summary**  
**Test Compound:** 2-Methyltetrahydrofuran  
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		Female														
		Treatment Groups (mg/kg)														
		40 IV <sup>a</sup>	10 <sup>b</sup>			30 <sup>b</sup>			100 <sup>c</sup>			400 <sup>c</sup>		2.5 IV <sup>d</sup>		
		Brain							Plasma							
C <sub>max(pred)</sub> (ug/mL)			3.52	±	0.38	21.4	±	1.4	51.1	±	4.0	196	±	18		
T <sub>max(pred)</sub> (minute)			11.3	±	2.5	23.5	±	2.0								
C <sub>max(obs)</sub> (ug/g) *	43.4 ± 6.3															
T <sub>max(obs)</sub> (minute)	10															
t <sub>1/2</sub> (minute)	30.5															
k <sub>01</sub> (minute^-1)			0.194	±	0.081	0.071	±	0.0137	0.436	±	0.333	0.752	±	0.912		
t <sub>1/2(k01)</sub> (minute)			3.56	±	1.49	9.76	±	1.88	1.59	±	1.21	0.922	±	1.117		
k <sub>10</sub> (minute^-1)			0.0304	±	0.0068	0.023	±	0.0021							0.0829	± 0.0045
t <sub>1/2(k10)</sub> (minute)			22.8	±	5.1	30.1	±	2.7							8.36	± 0.45
k <sub>12</sub> (minute^-1)															0.0112	± 0.0021
k <sub>21</sub> (minute^-1)															0.0274	± 0.0072
Cl <sub>1</sub> (mL/min/kg)															46.9	± 1.6
Cl <sub>1(F)</sub> (mL/min/kg)			61.2	±	8	18.8	±	1.2								
V <sub>1</sub> (mL/kg)															565	± 40
V <sub>2</sub> (mL/kg)															231	± 40
V <sub>1(F)</sub> (mL/kg)			2010	±	400	816	±	106	280	±	25	301	±	28		
AUC <sub>0-t</sub> (ug*min/g)	2650								8540			69300			53.6	
AUC <sub>inf</sub> (ug*min/g)	2660		164	±	21	1600	±	100	8540			70000			53.3	± 1.8

**Experiment Number:** NA  
**Route:** Gavage, IV  
**Species/Strain:** Rat/F344

**Toxicokinetics Data Summary**  
**Test Compound:** 2-Methyltetrahydrofuran  
**CAS Number:** 96-47-9

**Date Report Requested:** 01/09/2017  
**Time Report Requested:** 11:25:04  
**Lab:** Battelle Columbus

Female				
	Treatment Groups (mg/kg)			
	10 IV <sup>d</sup>		40 IV <sup>e</sup>	
	Plasma			
C <sub>max(pred)</sub> (ug/mL)				
T <sub>max(pred)</sub> (minute)				
C <sub>max(obs)</sub> (ug/g) *				
T <sub>max(obs)</sub> (minute)				
t <sub>1/2</sub> (minute)				
k <sub>01</sub> (minute^-1)				
t <sub>1/2(k01)</sub> (minute)				
k <sub>10</sub> (minute^-1)	0.0873 ±	0.0222		
t <sub>1/2(k10)</sub> (minute)	7.94 ±	2.01		
k <sub>12</sub> (minute^-1)	0.299 ±	0.163	0.0534 ±	0.06
k <sub>21</sub> (minute^-1)	0.256 ±	0.041	0.0783 ±	0.075
Cl <sub>1</sub> (mL/min/kg)	26.1 ±	0.8		
Cl <sub>1(F)</sub> (mL/min/kg)				
V <sub>1</sub> (mL/kg)	299 ±	79	565 ±	137
V <sub>2</sub> (mL/kg)	349 ±	59	ND	
V <sub>1(F)</sub> (mL/kg)				
AUC <sub>0-t</sub> (ug*min/g)	402		3110	
AUC <sub>inf</sub> (ug*min/g)	384 ±	11	3110	

**Experiment Number:** NA

**Route:** Gavage, IV

**Species/Strain:** Rat/F344

## Toxicokinetics Data Summary

**Test Compound:** 2-Methyltetrahydrofuran

**CAS Number:** 96-47-9

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**Lab:** Battelle Columbus

### LEGEND

Data are displayed as mean  $\pm$  SEM

\*Data are displayed as mean  $\pm$  SD

ND = not detected

### MODELING METHOD & BEST FIT MODEL

<sup>a</sup> WinNonlin; Noncompartmental analysis.

<sup>b</sup> WinNonlin; Calculated based on a one-compartment model with first order input and output.

<sup>c</sup> A two-compartment Michaelis-Menten model was written and compiled using WinNonlin code; Two-compartment model with Michaelis-Menten elimination.

<sup>d</sup> WinNonlin; Two-compartment model with first order elimination.

<sup>e</sup> WinNonlin; Two-compartment model with Michaelis-Menten elimination. IV data sets were modeled using WinNonlin library compartmental and Michaelis-Menten (MM) models. In addition, a two-compartment MM model was written and compiled using WinNonlin code for higher IV dosage groups. For the MM model, the WinNonlin output did not include calculations for the AUC. In order to obtain AUC values, the data sets (average concentration versus target time point) were analyzed using NCA. The equations used included:  $K_m = C_0 / \ln [C_0^*/C_0]$  and  $V_{max} = k \times V_d \times K_m$  Where  $K_m$  is the Michaelis-Menten (MM) constant ( $\mu\text{g/mL}$ ),  $C_0$  is the concentration ( $\mu\text{g/mL}$ ) at time 0 and (\*) back-extrapolated concentration at time 0,  $V_{max}$  is the maximum velocity or metabolic rate ( $\mu\text{g/min}$ ),  $k$  is the terminal linear slope (1/min), and  $V_d$  is the volume of distribution (mL).

### ANALYTE

2-Methyltetrahydrofuran

### TK PARAMETERS

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

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

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

$k_{01}$  = Absorption rate constant,  $k_a$

$t_{1/2(k01)}$  = Half-life of the absorption process to the central compartment

$k_{10}$  = Elimination rate constant from the central compartment also  $k_e$  or  $k_{elim}$

$t_{1/2(k10)}$  = Half-life for the elimination process from the central compartment

$k_{12}$  = Distribution rate constant from first to second compartment etc.

$k_{21}$  = Distribution rate constant from second to first compartment etc.

$Cl_1$  = Clearance of central compartment,  $Cl_{app}$  or apparent clearance for intravenous groups

$Cl_{1(F)}$  = Apparent clearance of the central compartment, also  $Cl_{(F)}$  for gavage groups in non-compartmental model

$V_1$  = 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

$V_2$  = Volume of distribution for the peripheral compartment

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

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

$AUC_{inf}$  = Area under the plasma concentration versus time curve, AUC, extrapolated to time equals infinity

**\*\* END OF REPORT \*\***