

**Experiment Number:** C96016  
**Route:** Dosed Water, Dosed Water and Gavage Challenge, Gavage, IV  
**Species/Strain:** Mouse/B6C3F1

**Toxicokinetics Data Summary**  
**Test Compound:** Dichloroacetic Acid  
**CAS Number:** 79-43-6

**Date Report Requested:** 11/09/2016  
**Time Report Requested:** 14:02:17  
**Lab:** Battelle Columbus

Female				
Treatment Groups (mg/kg)				
	74 <sup>a</sup>	100 <sup>b</sup>	148 <sup>c</sup>	200 <sup>d</sup>
Plasma				
C <sub>max(pred)</sub> (ug/mL)	19.5 ± 2.9	8.96 ± 1.16	103.0 ± 13.0	59.6 ± 6.5
T <sub>max(pred)</sub> (minute)	9.62 ± 1.18	7.36 ± 0.69	17.3 ± 0.8	8.53 ± 0.72
k <sub>01</sub> (min <sup>-1</sup> )	0.104 ± 0.013	0.136 ± 0.013	0.0579 ± 0.0026	0.117 ± 0.01
t <sub>1/2(k01)</sub> (minute)	6.67 ± 0.82	5.10 ± 0.48	12.0 ± 0.5	5.91 ± 0.50
k <sub>10</sub> (min <sup>-1</sup> )	0.104 ± 0.013	0.136 ± 0.013	0.0579 ± 0.0026	0.117 ± 0.01
t <sub>1/2(k10)</sub> (minute)	6.67 ± 0.82	5.10 ± 0.48	12.0 ± 0.5	5.91 ± 0.50
Cl (mL/min/kg)				
Cl <sub>1</sub> (mL/min/kg)	145.0 ± 23.0	558.0 ± 70.0	30.6 ± 3.3	145.0 ± 16.0
V <sub>1</sub> (mL/kg)				
V <sub>1(F)</sub> (mL/kg)	1400.0 ± 210.0	4110.0 ± 530.0	529.0 ± 65.0	1240.0 ± 130.0
MRT (minute)				
AUC <sub>0-t</sub> (ug/mL*min)	436.0	268.0	4440.0	1360.0
AUC <sub>inf</sub> (ug/mL*min)	510.0 ± 80.0	179.0 ± 23.0	4840.0 ± 516.0	1380.0 ± 160.0

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**Female**

	<b>Treatment Groups (mg/kg)</b>			
	<b>400<sup>d</sup></b>		<b>100 IV<sup>e</sup></b>	
	<b>Plasma</b>			
$C_{max(pred)}$ (ug/mL)	162.0	± 12.0	309.0	± 26
$T_{max(pred)}$ (minute)	16.0	± 1.0		
$k_{01}$ (min <sup>-1</sup> )	0.0626	± 0.0041		
$t_{1/2(k01)}$ (minute)	11.1	± 0.7		
$k_{10}$ (min <sup>-1</sup> )	0.0626	± 0.0041	0.145	± 0.012
$t_{1/2(k10)}$ (minute)	11.1	± 0.7	4.79	± 0.39
Cl (mL/min/kg)			46.9	± 2.9
$Cl_1$ (mL/min/kg)	56.9	± 5.2		
$V_1$ (mL/kg)			323.0	± 27
$V_{1(F)}$ (mL/kg)	908.0	± 67.0		
MRT (minute)			6.90	± 0.57
$AUC_{0-t}$ (ug/mL*min)	6670.0		1900.0	
$AUC_{inf}$ (ug/mL*min)	7030.0	± 640.0	2130	± 130

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## LEGEND

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Data are displayed as mean  $\pm$  SEM

### MODELING METHOD & BEST FIT MODEL

- <sup>a</sup> WinNonlin, Pharsight Corporation, Mountain View, CA; one-compartment model with equal first order absorption and elimination and 1/Yhat weighting
- <sup>b</sup> WinNonlin, Pharsight Corporation, Mountain View, CA; one-compartment model with equal first order absorption and elimination with 1/Y weighting
- <sup>c</sup> WinNonlin, Pharsight Corporation, Mountain View, CA; one-compartment model with equal first order absorption and elimination and 1/Yhat<sup>2</sup> weighting
- <sup>d</sup> WinNonlin, Pharsight Corporation, Mountain View, CA; one-compartment model with equal first order absorption and elimination with 1/Yhat weighting
- <sup>e</sup> WinNonlin, Pharsight Corporation, Mountain View, CA; one-compartment model with bolus input, first order output, and 1/Yhat weighting

### ANALYTE

Dichloroacetic acid

### TK PARAMETERS

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

$T_{\max(\text{pred})}$  = Time at which  $C_{\max}$  predicted or observed occurs

$k_{01}$  = 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  $k_{\text{elim}}$

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

Cl = Clearance, includes total clearance

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

$V_1$  = Volume of distribution of the central compartment, includes  $V_d$  and  $V_{\text{volume}}$  of distribution,  $V_z$  apparent volume of distribution NCA,  $V_{\text{app}}$  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),  $AUC_{\text{last}}$

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

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