

Experiment Number: K01807

Route: Gavage

Species/Strain: Rats/Sprague-Dawley

Toxicokinetics Data Summary

Compound: 2,3,7,8- Tetrachlorodibenzo-p-dioxin

Analyte: 2,3,7,8- Tetrachlorodibenzo-p-dioxin

CAS Number: 1746-01-6

Request Date: 12/27/2021

Request Time: 2:40:16

Lab: RTI

Female

Treatment Group A (ng/kg)

100_2.5 mL/kg

100_2.5 mL/kg

100_2.5 mL/kg

100_2.5 mL/kg

100_2.5 mL/kg

Lung^{a,b}

Liver^{a,c}

Plasma^{a,d}

Adipose Mesenteric^a

Adipose Perirenal^a

Cmax_pred (pg/mL)	.	943	34.7	483	384
Tmax_pred (day)	.	1	.	20	2
Lambda_z (day ⁻¹)		0.0024		0.0168	0.0144
Half-life (day)		542		40.3	48.6
AUC_0-T (pg-day/mL)	.	14600	0.361	19200	21000

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Treatment Group B (ng/kg)

100_5.0 mL/kg

100_5.0 mL/kg

100_5.0 mL/kg

100_5.0 mL/kg

100_5.0 mL/kg

Lung^{a,e}

Liver^{a,f}

Plasma^{a,g}

Adipose Mesenteric^a

Adipose Perirenal^a

Cmax_pred (pg/mL)	101	1350	210	397	434
Tmax_pred (day)	70	1	2	20	20
Lambda_z (day ⁻¹)				0.0096	0.0072
Half-life (day)				70.1	109
AUC_0-T (pg-day/mL)	1510	13500	816	27500	29600

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Treatment Group C (ng/kg)

50_2.5 mL/kg

50_2.5 mL/kg

50_2.5 mL/kg

50_2.5 mL/kg

50_2.5 mL/kg

Lung^{a,e}

Liver^{a,h}

Plasma^{a,i}

Adipose Mesenteric^a

Adipose Perirenal^a

Cmax_pred (pg/mL)	233	494	.	105	267
Tmax_pred (day)	40	1	.	40	2
Lambda_z (day ⁻¹)		0.0408		0.0144	0.0336
Half-life (day)		17.3		51.4	20.4
AUC_0-T (pg-day/mL)	2330	8600	.	5300	5820

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LEGEND

MODELING SOFTWARE

WinNonlin Ver. 1.5A

MODELING METHOD & BEST FIT MODEL

^aWinNonlin Ver. 1.5A, Pharsight Corporation, Apex, NC, Noncompartmental analysis-Model 200

EXCEPTIONS

^bTCDD non-detectable or below LOQ in 11 of 11 samples. Cmax, Tmax, and AUClast not detected, Lambda_z and Half-life not applicable

^cTCDD non-detectable in 7 of 11 samples

^dTCDD was not detectable or below LOQ for all but one sample out of 65 samples. Tmax not detected, Lambda_z and Half-life not applicable

^eTCDD non-detectable or below LOQ in 10 of 11 samples. Lambda_z and Half-life not applicable

^fTCDD non-detectable in 7 of 11 samples. AUC was calculated manually using the trapezoidal rule since modeling was unsuccessful through WinNonlin (algorithm unable to converge). Lambda_z and Half-life not applicable

^gTCDD was not detectable in 56 of 65 samples. Lambda_z and Half-life not applicable

^hTCDD non-detectable in 6 of 10 samples

ⁱTCDD was not detectable in all 65 samples. Cmax, Tmax and AUClast not detected, Lambda_z and Half-life not applicable

ANALYTE

2,3,7,8- Tetrachlorodibenzo-p-dioxin

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TK PARAMETERS

Cmax = Observed or Predicted Maximum plasma (or tissue) concentration

Tmax = Time at which Cmax predicted or observed occurs

Lambda_z = Non-compartmental analysis (NCA) terminal elimination rate constant, NCA ke or kelim

Half-life = Lambda z Half life, t 1/2, the terminal elimination half-life based on non-compartmental analysis

AUC_0-T = Area under the plasma concentration versus time curve, AUC, from time ti (initial) to tf (final), AUClast

TK PARAMETERS PROTOCOL

ANALYSIS METHOD

TCDD doses were in units of ng/kg, which was converted to pg/kg units. Hence, the units for pharmacokinetic parameter estimates obtained from WinNonlin are pg, mL, and hours. Any plasma and tissue concentrations that were not detectable or were less than the limit of quantitation were set to zero for these pharmacokinetic analyses.

All Treatment Groups

Animals were administered a single oral dose of either 100 ng TCDD/kg in corn oil at 2.5 mL/kg in Study A and 5.0 mL/kg in Study B or 50 ng TCDD/kg in corn oil at 2.5 mL/kg in Study C. All concentration-time data were analyzed using time in hours that later was converted to days for reporting purposes and concentration in pg/mL which is equivalent to pg/g, assuming the density of tissues to be 1 g/mL.