Experiment Number: K10076
Route: IV, Gavage
Species/Strain: Rats/Harlan Sprague Dawley

Toxicokinetics Data Summary
Compound: Sodium Perfluorooctane Sulfonate
Analyte: Perfluorooctane Sulfonate
CAS Number: 1763-23-1

Request Date: 7/11/2023
Request Time: 10:03:16
Lab: Battelle Columbus

Male

	Treatment Group (mg/kg)			
	2 Single Dose IV Plasma[c]	**2 Single Dose Gavage Plasma[d]**	**20 Single Dose Gavage Plasma[d]**	**2 Repeated Dose Gavage Plasma[d]**
Cmax_pred (ng/mL)	4800 ± 360	6620 ± 900	106000 ± 13000	55100 ± 6600
Tmax_pred (hour)		14.3 ± 2.7	16.4 ± 2.7	0.942 ± 0.149
Cmax_obs (ng/mL)		7190	97700	35500
Tmax_obs (hour)		12.0	12.0	6.00
Alpha Half-life (min)	111 ± 65	73.8 ± 58.1	95.7 ± 68.8	7.87 ± 3.25
Beta Half-life (min)	952 ± 106	972 ± 133	860 ± 101	801 ± 47
k01 ($hour^{-1}$)		0.284 ± 0.074	0.256 ± 0.060	4.94 ± 1.20
k01 Half-life (min)		2.44 ± 0.63	2.70 ± 0.63	0.140 ± 0.034
K10 ($hour^{-1}$)	0.00131 ± 0.00012	0.00145 ± 0.00027	0.00152 ± 0.00026	0.00199 ± 0.00029
k10 Half-life (hour)	528 ± 50	478 ± 90	457 ± 77	349 ± 50
k12 ($hour^{-1}$)	0.00220 ± 0.00161	0.00404 ± 0.00394	0.00269 ± 0.00256	0.0486 ± 0.0233
k21 ($hour^{-1}$)	0.00347 ± 0.00211	0.00463 ± 0.00355	0.00385 ± 0.00269	0.0383 ± 0.0146
Cl (mL/hr/kg)	0.546 ± 0.031			
Cl1_F (mL/hr/kg)		0.406 ± 0.031	0.267 ± 0.019	0.0688 ± 0.0035
V1 (mL/kg)	417 ± 31			
V2 (mL/kg)	264 ± 71			
V1_F (mL/kg)		280 ± 48	176 ± 27	34.6 ± 4.8
V2_F (mL/kg)		244 ± 81	123 ± 42	43.9 ± 7.7
MRT (hour)	1250 ± 100			
AUC_0-T (ng/mL*hr)	3450000	4130000	68600000	26500000
AUCinf_pred (ng/mL*hr)	3660000 ± 210000	4930000 ± 370000	74900000 ± 5300000	29100000 ± 1500000
F (percent)		135	205	

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Female

	Treatment Group (mg/kg)			
	2 Single Dose IV Plasma[c]	**2 Single Dose Gavage Plasma[d]**	**20 Single Dose Gavage Plasma[d]**	**2 Repeated Dose Gavage Plasma[d]**
Cmax_pred (ng/mL)	6720 ± 980	7960 ± 900	136000 ± 17000	68200 ± 9500
Tmax_pred (hour)		12.2 ± 5.2	13.7 ± 3.3	0.924 ± 0.165
Cmax_obs (ng/mL)		7350	121000	41700
Tmax_obs (hour)		24.0	12.0	12.0
Alpha Half-life (hour)	6.33 ± 8.22	19.1 ± 49.3	53.0 ± 72.5	6.32 ± 3.65
Beta Half-life (hour)	786 ± 70	977 ± 83	865 ± 95	863 ± 60
k01 ($hour^{-1}$)		0.292 ± 0.128	0.291 ± 0.078	4.96 ± 1.40
k01 Half-life (min)		2.38 ± 1.04	2.38 ± 0.63	0.140 ± 0.039
K10 ($hour^{-1}$)	0.00126 ± 0.00020	0.00102 ± 0.00040	0.00137 ± 0.00028	0.00161 ± 0.00028
k10 Half-life (hour)	552 ± 88	682 ± 265	506 ± 104	432 ± 74
k12 ($hour^{-1}$)	0.0322 ± 0.0453	0.0107 ± 0.0369	0.00485 ± 0.00802	0.0540 ± 0.0364
k21 ($hour^{-1}$)	0.0770 ± 0.100	0.0254 ± 0.0573	0.00765 ± 0.00995	0.0548 ± 0.0294
Cl (mL/hr/kg)	0.373 ± 0.027			
Cl1_F (mL/hr/kg)		0.226 ± 0.013	0.186 ± 0.013	0.0448 ± 0.0025
V1 (mL/kg)	297 ± 43			
V2 (mL/kg)	124 ± 62			
V1_F (mL/kg)		222 ± 84	136 ± 25	27.9 ± 4.7
V2_F (mL/kg)		93.4 ± 93.0	86.3 ± 37.3	27.5 ± 6.5
MRT (hour)	1130 ± 100			
AUC_0-T (ng/mL*hr)	4790000	8330000	95900000	39700000
AUCinf_pred (ng/mL*hr)	5360000 ± 390000	8870000 ± 510000	107000000 ± 8000000	44600000 ± 2500000
F (percent)		165	200	

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Male

	Treatment Group (mg/kg)		
	2 Single Dose Gavage	**20 Single Dose Gavage**	**2 Repeated Dose Gavage**
	Brain[a]	**Brain[b]**	Brain[b]
Cmax_obs (ng/g)	ND	10300	4000
Tmax_obs (hour)	ND	24.0	24.0
Half-life (hour)	ND	537	669

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Female

	Treatment Group (mg/kg)		
	2 Single Dose Gavage	20 Single Dose Gavage	2 Repeated Dose Gavage
	Brain[a]	Brain[b]	Brain[b]
Cmax_obs (ng/g)	ND	11400	4270
Tmax_obs (hour)	ND	24.0	6.00
Half-life (hour)	ND	1670	800

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Male

	Treatment Group (mg/kg)		
	2 Single Dose Gavage	**20 Single Dose Gavage**	**2 Repeated Dose Gavage**
	Kidney[b]	**Kidney[b]**	**Kidney[b]**
Cmax_obs (ng/g)	5510	73900	30600
Tmax_obs (hour)	24.0	6.00	6.00
Half-life (hour)	651	824	1040

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Female

	Treatment Group (mg/kg)		
	2 Single Dose Gavage Kidney[b]	20 Single Dose Gavage Kidney[b]	2 Repeated Dose Gavage Kidney[b]
Cmax_obs (ng/g)	10900	132000	66300
Tmax_obs (hour)	24.0	6.00	6.00
Half-life (hour)	1280	1120	1490

Experiment Number: K10076
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Male

	Treatment Group (mg/kg)		
	2 Single Dose Gavage	**20 Single Dose Gavage**	**2 Repeated Dose Gavage**
	Liver[b]	**Liver[b]**	**Liver[b]**
Cmax_obs (ng/g)	28000	168000	106000
Tmax_obs (hour)	24.0	6.00	6.00
Half-life (hour)	1760	1110	1270

Experiment Number: K10076
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Toxicokinetics Data Summary
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CAS Number: 1763-23-1

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Female

	Treatment Group (mg/kg)		
	2 Single Dose Gavage	**20 Single Dose Gavage**	**2 Repeated Dose Gavage**
	Liver[b]	**Liver[b]**	**Liver[b]**
Cmax_obs (ng/g)	23800	151000	101000
Tmax_obs (hour)	6.00	24.00	6.00
Half-life (hour)	1050	1270	1310

LEGEND

MODELING SOFTWARE

WinNonlin, Version 5.0.1

MODELING METHOD & BEST FIT MODEL

[a] WinNonlin, Version 5.0.1, Unable to determine lambda z due to only one measurable time point.
[b] WinNonlin, Version 5.0.1, non-compartment model with first order input, first order output, and uniform weighting
[c] WinNonlin, Version 5.0.1, two-compartment model with bolus input, first order output, and l/Yhat2 weighting
[d] WinNonlin, Version 5.0.1, two-compartment model with first order input, first order output, and 1/Yhat2 weighting

ANALYTE

Perfluorooctane Sulfonate

TK PARAMETERS

Cmax = Observed or Predicted Maximum plasma (or tissue) concentration
Tmax = Time at which Cmax predicted or observed occurs
Half-Life = Lambda z Half life, t 1/2, the terminal elimination half-life based on non-compartmental analysis
Alpha Half-life = Half-life for the alpha phase
Beta Half-life = Half-life for the beta 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 of the absorption process to the central compartment
k12 = Distribution rate constant from first to second compartment
k21 = Distribution rate constant from second to first compartment

TK PARAMETERS (cont'd)

Cl = Clearance, includes total clearance
CL1_F = Apparent clearance of the central compartment, also Cl_F for gavage groups in non-compartmental model
V1 = Volume of distribution of the central compartment, includes Vd and V volume of distribution, Vz apparent volume of distribution NCA, Vapp apparent volume of distribution for intravenous studies
V2 = 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
AUCinf_pred = Area under the plasma concentration versus time curve, AUC, extrapolated to time equals infinity
F = Bioavailability, absolute bioavailability

TK PARAMETERS PROTOCOL

ANALYSIS METHOD

Rat blood samples of approximately 0.7 mL were collected using the retro-orbital method. Animals were anesthetized with CO2-O2 prior to bleeding. Each rat was bled at no more than two separate time points. Blood samples were collected at 12 time points post-administration (three blood samples per time point). Perfluorooctane sulfonate (PFOS) plasma and tissue PFOS concentrations were measured using liquid chromatography with mass spectroscopy (LC-MS/MS). The target LOQ for PFOS (IV and gavage) in plasma was 25 ng/mL and for PFOS in liver, kidney, and brain 5 ng tissue.

TK PARAMETERS PROTOCOL (cont'd)

TK_INTRAVENOUS PLASMA

2 mg/kg Male and Female

Animals were weighed the morning of dosing to calculate the correct dosing volume. Animals were administered a single intravenous dose delivered through an implanted jugular catheter.

TK_GAVAGE PLASMA

2 mg/kg Single Dose Male and Female

Animals were weighed the morning of dosing to calculate the correct dosing volume. Animals were given a single gavage administration. 2 mg/kg dose mean weight include rats assigned to both the single and repeated administration group, a total of 46 animals.

20 mg/kg Single Dose Male and Female

Animals were weighed the morning of dosing to calculate the correct dosing volume. Animals were given a single gavage administration.

2 mg/kg Repeated Dose Male and Female

Animals were weighed the morning of dosing to calculate the correct dosing volume. Animals were given repeated gavage administrations (5 consecutive days) with samples collected on Study Day 5 post-dosing. 2 mg/kg dose mean weight include rats assigned to both the single and repeated administration group, a total of 46 animals.

TK PARAMETERS PROTOCOL (cont'd)

ANALYSIS METHOD

Following blood collection, each animal was terminated with CO2, and the liver, kidneys, and brain were collected. Tissue samples (liver, kidney, brain) were collected from rats in all gavage dosage groups and from single and repeated dose rats at 5 time points (3 samples per time point). Perfluorooctane sulfonate (PFOS) plasma and tissue PFOS concentrations were measured using liquid chromatography with mass spectroscopy (LC-MS/MS). The target LOQ for PFOS (IV and gavage) in plasma was 25 ng/mL and for PFOS in liver, kidney, and brain 5 ng tissue.

TK_GAVAGE PLASMA

2 mg/kg Single Dose Male and Female

Animals were weighed the morning of dosing to calculate the correct dosing volume. Animals were given a single gavage administration. 2 mg/kg dose mean weight include rats assigned to both the single and repeated administration group, a total of 46 animals.

20 mg/kg Single Dose Male and Female

Animals were weighed the morning of dosing to calculate the correct dosing volume. Animals were given a single gavage administration.

2 mg/kg Repeated Dose Male and Female

Animals were weighed the morning of dosing to calculate the correct dosing volume. Animals were given repeated gavage administrations (5 consecutive days) with samples collected on Study Day 5 post-dosing. 2 mg/kg dose mean weight include rats assigned to both the single and repeated administration group, a total of 46 animals.