Experiment Number: S0623
Route: Gavage
Species/Strain: Rats/Harlan Sprague Dawley

Toxicokinetics Data Summary
Compound: 2,3,4,7,8-Pentachlorodibenzofuran
Analyte: 2,3,4,7,8-Pentachlorodibenzofuran
CAS Number: 57117-31-4

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

Female

Treatment Group (ng/kg)	
6 Gavage Whole Blood[a,e]	200 Gavage Whole Blood[a,e]

NO DATA RECORDED

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Female

Treatment Group (ng/kg)

	6 Gavage Lung[a,f]	200 Gavage Lung[b,f]
NO DATA RECORDED		
Cmax_obs (pg/g)		77
Tmax_obs (hour)		2

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Female

	Treatment Group (mg/kg)	
	6 Gavage Fat[a,g]	**200 Gavage Fat[c,h]**
NO DATA RECORDED		
Cmax_obs (pg/g)		412 ± 99
Tmax_obs (day)		32
k10 (day^{-1})		0.0046
K10 Half-life (day)		152
AUC_0-T (day*pg/g)		68500
AUCinf_Pred (day*pg/g)		88500

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Female

	Treatment Group (ng/kg)	
	6 Gavage Liver[d,i]	**200 Gavage Liver[c,j]**
Cmax_obs (pg/g)	182 ± 37	5958 ± 1570
Tmax_obs (day)	5	1
k10 (day^{-1})	0.0046	0.0059
K10 Half-life (day)	151	118
AUC_0-T (day*pg/g)	22900	674000
AUCinf_pred (day*pg/g)	38800	746000

LEGEND

MODELING SOFTWARE

WinNonlin, Version 4.0

MODELING METHOD & BEST FIT MODEL

[a]Not Applicable

[b]Not applicable, only Cmax and Tmax determined. Cmax n=2

[c]Data sets were analyzed by non-compartmental analysis using WinNonlin (Version 4.0 Pharsight Corp., Mountain View, CA), Non-compartmental analysis was performed using individual animal PeCDF concentrations obtained at each time point for a given tissue and dosage level. The interval concentration time points that provided the best R2 value (goodness of fit statistic) from the linear regression analysis were used to define the terminal linear phase of the concentration time profile. Model 200 (extravascular dosing), from the WinNonlin library, was used to calculate the reported toxicokinetic parameters. For AUC_0-T, T=365 days

[d]Data sets were analyzed by non-compartmental analysis using WinNonlin (Version 4.0 Pharsight Corp., Mountain View, CA), Non-compartmental analysis was performed using individual animal PeCDF concentrations obtained at each time point for a given tissue and dosage level. The interval concentration time points that provided the best R2 value (goodness of fit statistic) from the linear regression analysis were used to define the terminal linear phase of the concentration time profile. Model 200 (extravascular dosing), from the WinNonlin library, was used to calculate the reported toxicokinetic parameters. For AUC_0-T, T=212 days

EXCEPTIONS

[e]Blood concentrations were below the limit of quantitation and could not be analyzed by compartmental analysis

[f]The low and transient lung PeCDF concentrations (for both dosages) did not allow non-compartmental analysis to be performed.

[g]Low PeCDF concentrations in the fat (low dosage) prevented non-compartmental analysis from being performed for these data sets.

[h]Final sampling time, T, is 365 days. Some parameters are based on concentrations at time points ranging from 32-365 days.

[i]The first order rate constant, k, associated with the terminal (log-linear) phase of the profile was generated using the Day 5 to 212 terminal linear phase. AUC_0-T is based on time points from 0 to 212 days.

[j]Final sampling time, T, is 365 days. Parameters are based on time points ranging from 1-365 days.

ANALYTE

2,3,4,7,8-Pentachlorodibenzofuran

TK PARAMETERS

Cmax_obs = Observed or Predicted Maximum plasma (or tissue) concentration
Tmax_obs = Time at which Cmax predicted or observed occurs
k10 = Elimination rate constant from the central compartment also ke or kelim
k10 Half-life = Half-life for the elimination process from the central compartment
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

TK PARAMETERS PROTOCOL

ANALYSIS METHOD

Concentrations of 2,3,4,7,8-Pentachlorodibenzofuran (PeCDF) were assayed, using validated gas chromatography-high resolution mass spectrometry (GC/HR/MS) methods, in blood, lung, fat, and liver collected at post-administration sampling times ranging from 0.5 hours to 365 days. Limit of Quantitation, LOQ, is less than 30 pg/mL blood. PeCDF was not measurable in the blood samples collected from the 200 ng/kg dosage group. Consequently, blood samples from the 6 ng/kg group collected at time points greater than 1 day were not analyzed.

TK PARAMETERS PROTOCOL (cont'd)

TK_GAVAGE WHOLE BLOOD

6 ng/kg, 200 ng/kg Female

Rats were given a single gavage dose per phase. Approximately 3 to 5 mL of whole blood was collected by cardiac puncture. Five rats/dose level were bled at each time point. Post-dose time points were 0.5, 1, 1.5, 2, 3, 8, 16, and 24 hours for the early study phase. Body weight range for all 88 animals in the early group pool was 214.3 to 341.2 g. Animals were received on 10-15-1998 and dosed on 11-19-1998 at 22 weeks of age. Post-dose time points were days 5, 12, 32, 61, 92, 120, 166, 212, 250, 281, 309, 341, and 365 for the late study phase. Body weight range for all 144 animals in the late group pool was 175.0 to 344.4 g. Late phase animals were received on 11-5-1998 and dosed on 12-7-1998 at 20 weeks of age. At each dose level, there were 44 early phase animals and 72 late phase animals. City tap water and NTP diet (irradiated pellets) were available ad libitum.

ANALYSIS METHOD

Concentrations of 2,3,4,7,8-Pentachlorodibenzofuran (PeCDF) were assayed, using validated gas chromatography-high resolution mass spectrometry (GC/HR/MS) methods, in blood, lung, fat, and liver collected at post-administration sampling times ranging from 0.5 hours to 365 days. Limit of Quantitation, LOQ, is less than 60 pg/g lung. PeCDF was not measurable in the 6 ng/kg dosage group samples.

TK PARAMETERS PROTOCOL (cont'd)

TK_GAVAGE LUNG

6 ng/kg Female

Rats were given a single gavage dose per phase. Approximate lung weights were 1.2 to 2.7 g. Five rats per time point per dose level. Post-dose time points were 0.5, 1, 1.5, 2, 3, 8, 16, and 24 hours for the early study phase. Body weight range for all 88 animals in the early group pool was 214.3 to 341.2 g. Animals were received on 10-15-1998 and dosed on 11-19-1998 at 22 weeks of age. Post-dose time points were days 5, 12, 32, 61, 92, 120, 166, 212, 250, 281, 309, 341, and 366 for the late study phase. Body weight range for all 144 animals in the late group pool was 175.0 to 344.4 g. Late phase animals were received on 11-5-1998 and dosed on 12-7-1998 at 20 weeks of age. At each dose level, there were 44 early phase animals and 72 late phase animals. City tap water and NTP diet (irradiated pellets) were available ad libitum.

ANALYSIS METHOD

Concentrations of 2,3,4,7,8-Pentachlorodibenzofuran (PeCDF) were assayed, using validated gas chromatography-high resolution mass spectrometry (GC/HR/MS) methods, in blood, lung, fat, and liver collected at post-administration sampling times ranging from 0.5 hours to 365 days. Limit of Quantitation, LOQ, is less than 60 pg/g lung. At 200 ng/kg, measurable lung PeCDF concentrations were observed in a few animals but only for several hours after dosing. During the first 8 hours, the Cmax and Tmax values were 77 pg/g (n=2) and 2 hours.

TK PARAMETERS PROTOCOL (cont'd)

TK_GAVAGE LUNG

200 ng/kg Female

Rats were given a single gavage dose per phase. Approximate lung weights were 1.2 to 2.7 g. Five rats per time point per dose level. Post-dose time points were 0.5, 1, 1.5, 2, 3, 8, 16, and 24 hours for the early study phase. Body weight range for all 88 animals in the early group pool was 214.3 to 341.2 g. Animals were received on 10-15-1998 and dosed on 11-19-1998 at 22 weeks of age. Post-dose time points were days 5, 12, 32, 61, 92, 120, 166, 212, 250, 281, 309, 341, and 366 for the late study phase. Body weight range for all 144 animals in the late group pool was 175.0 to 344.4 g. Late phase animals were received on 11-5-1998 and dosed on 12-7-1998 at 20 weeks of age. At each dose level, there were 44 early phase animals and 72 late phase animals. City tap water and NTP diet (irradiated pellets) were available ad libitum.

ANALYSIS METHOD

Concentrations of 2,3,4,7,8-Pentachlorodibenzofuran (PeCDF) were assayed, using validated gas chromatography-high resolution mass spectrometry (GC/HR/MS) methods, in blood, lung, fat, and liver collected at post-administration sampling times ranging from 0.5 hours to 365 days. Limit of Quantitation, LOQ, is less than 37.5 pg/g mesenteric fat. For the fat, there were only a few samples with measurable concentrations from the 6 ng/kg group.

TK PARAMETERS PROTOCOL (cont'd)

TK_GAVAGE FAT

6 ng/kg, 200 ng/kg Female

Rats were given a single gavage dose per phase. Approximate mesenteric fat weights were 0.4 to 7.1 g. Five rats per time point per dose level. Post-dose time points were 0.5, 1, 1.5, 2, 3, 8, 16, and 24 hours for the early study phase. Body weight range for all 88 animals in the early group pool was 214.3 to 341.2 g. Animals were received on 10-15-1998 and dosed on 11-19-1998 at 22 weeks of age. Post-dose time points were days 5, 12, 32, 61, 92, 120, 166, 212, 250, 281, 309, 341, and 366 for the late study phase. Body weight range for all 144 animals in the late group pool was 175.0 to 344.4 g. Late phase animals were received on 11-5-1998 and dosed on 12-7-1998 at 20 weeks of age. At each dose level, there were 44 early phase animals and 72 late phase animals. City tap water and NTP diet (irradiated pellets) were available ad libitum.

ANALYSIS METHOD

Concentrations of 2,3,4,7,8-Pentachlorodibenzofuran (PeCDF) were assayed, using validated gas chromatography-high resolution mass spectrometry (GC/HR/MS) methods, in blood, lung, fat, and liver collected at post-administration sampling times ranging from 0.5 hours to 365 days. Limit of Quantitation, LOQ, is less than 50 pg/g liver. For the liver, measurable liver PeCDF concentrations were first observed at 6 ng/kg 3 hours after dosing. After the peak on Day 1, the liver PeCDF concentrations steadily declined up through Day 212.

TK PARAMETERS PROTOCOL (cont'd)

TK_GAVAGE LIVER

6 ng/kg Female

Rats were given a single gavage dose per phase. Liver weights ranged from 6.110-13.798 g but were generally between 7-10 g. Five rats per time point per dose level. Post-dose time points were 0.5, 1, 1.5, 2, 3, 8, 16, and 24 hours for the early study phase. Body weight range for all 88 animals in the early group pool was 214.3 to 341.2 g. Animals were received on 10-15-1998 and dosed on 11-19-1998 at 22 weeks of age. Post-dose time points were days 5, 12, 32, 61, 92, 120, 166, 212, 250, 281, 309, 341, and 366 for the late study phase. Body weight range for all 144 animals in the late group pool was 175.0 to 344.4 g. Late phase animals were received on 11-5-1998 and dosed on 12-7-1998 at 20 weeks of age. At each dose level, there were 44 early phase animals and 72 late phase animals. City tap water and NTP diet (irradiated pellets) were available ad libitum.

ANALYSIS METHOD

Concentrations of 2,3,4,7,8-Pentachlorodibenzofuran (PeCDF) were assayed, using validated gas chromatography-high resolution mass spectrometry (GC/HR/MS) methods, in blood, lung, fat, and liver collected at post-administration sampling times ranging from 0.5 hours to 365 days. Limit of Quantitation, LOQ, is less than 50 pg/g liver. At 200 ng/kg, measurable liver PeCDF concentrations were first observed at 1 hour after dosing. After the peak period on Day 1, the liver PeCDF concentrations steadily declined up through Day 365

TK PARAMETERS PROTOCOL (cont'd)

TK_GAVAGE LIVER

200 ng/kg Female

Rats were given a single gavage dose per phase. Liver weights ranged from 6.110-13.798 g but were generally between 7-10 g. Five rats per time point per dose level. Post-dose time points were 0.5, 1, 1.5, 2, 3, 8, 16, and 24 hours for the early study phase. Body weight range for all 88 animals in the early group pool was 214.3 to 341.2 g. Animals were received on 10-15-1998 and dosed on 11-19-1998 at 22 weeks of age. Post-dose time points were days 5, 12, 32, 61, 92, 120, 166, 212, 250, 281, 309, 341, and 366 for the late study phase. Body weight range for all 144 animals in the late group pool was 175.0 to 344.4 g. Late phase animals were received on 11-5-1998 and dosed on 12-7-1998 at 20 weeks of age. At each dose level, there were 44 early phase animals and 72 late phase animals. City tap water and NTP diet (irradiated pellets) were available ad libitum