Experiment Number: S0559-3 (K00571)
Route: Inhalation
Species/Strain: Rats/Fischer 344

Toxicokinetics Data Summary
Compound: Carbon disulfide/ **Analyte:** Free Carbon disulfide
CAS Number: 75-15-0

Request Date: 7/11/2023
Request Time: 10:03:16
Lab: RTI Midwest Research Institute

Female

	Treatment Group (ppm)	
	500 Inhalation Blood[a,b]	**800 Inhalation Blood[a,b]**
Cmax (ug/g)	6.6	10.8
Alpha Half-life (minute)	2.7	2.0
Beta Half-life (minute)	77.4	66.4
k10 ($minute^{-1}$)	0.16	0.18
k10 Half-life (minute)	4.4	3.9
k12 ($minute^{-1}$)	0.094	0.16
k21 ($minute^{-1}$)	0.015	0.020
Cl (mL/min)	0.39	0.38
V1 (mL)	2.5	2.1
Vss (mL)	18.4	18.8
MRT (minute)	47.3	49.5
AUCinf_pred (ug*min/mL)	1280	2110

LEGEND

MODELING SOFTWARE

PCNONLIN

MODELING METHOD & BEST FIT MODEL

[a] nonlinear regression analysis using PCNONLIN, Statistics Consultants, Inc., Lexington, KY, linear two-compartment model.

EXCEPTION

[b] V1 represent Vc, Volume of distribution of the central compartment

ANALYTE

Free Carbon disulfide

TK PARAMETERS

Cmax = Observed or Predicted Maximum plasma (or tissue) concentration
Alpha Half-Life = Half-life for the alpha phase
Beta Half-Life = Half-life for the beta phase
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
k12 = Distribution rate constant from first to second compartment
k21 = Distribution rate constant from second to first compartment
Cl = Clearance, includes total clearance
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
Vss = Volume of distribution at steady state
MRT = Mean Residence Time
AUCinf_pred = Area under the plasma concentration versus time curve, AUC, extrapolated to time equals infinity

TK PARAMETERS PROTOCOL

ANALYSIS METHOD

Blood specimens were analyzed for free carbon disulfide with a validated method by analyzing the headspace over the samples using gas chromatography with flame photometric detection with sulfur mode filter using methyl sulfide as the internal standard. The limit of quantitation (LOQ) was 1 or 2 ug/mL, dependent on the data obtained from the standards on each day of analysis. The data from groups 3 and 4 were combined. The data was modeled using both steady state and declining concentration data (i.e., model for intravenous infusion or inhalation profiles) The parameters were determined using nonlinear regression analysis (PCNONLIN, Statistics Consultants, Inc., Lexington, KY). A linear two-compartment model was found to be the best fit for the data.

TK_INHALATION BLOOD

500 mg/kg, 800 mg/kg

Two sets of 6 cannulated rats were exposed once to carbon disulfide at each concentration for 180 minutes in nose-only exposure tubes. Blood samples were collected from one set of rats (Group 3) at 4, 8, 15, 30, 60, and 180 minutes at the start of exposure and 4 (184), 8 (188), and 15 (195) minutes after the termination of exposure to determine the rapid uptake and elimination time constants. Blood was collected from the second set of rats (Group 4) 60 and 180 minutes at the start of the exposure and 30 (210), 60 (240), 90 (270), 120 (300), and 240 (420) minutes after the termination of the exposure to determine the terminal elimination time constant. The data from all 12 animals was combined using the average concentration for each time point for toxicokinetic analysis. Animals were dosed and blood samples were collected at one laboratory and the blood samples were shipped to a second laboratory for analysis.