Intended for

Denka Performance Elastomer LLC, Request for Correction

Exhibit A

Date

July 15, 2021

SUPPLEMENTAL MATERIALS A
SUPPLEMENTAL TABLES

Table S-1: Physiological Parameters for PBPK Model										
Parameter	**Abbreviation**	**Units**	**Mice**		**Source**	**Rats**		**Source**	**Humans**	**Source**
			Male	**Female**		**Male**	**Female**			
Body Weight	BW	kg	0.04	0.04	NTP (1998) time and survival weighted average BW control animals	0.407	0.256	NTP (1998) time and survival weighted average BW control animals	70	USEPA 1988
Alveolar Ventilation	QPC	$L/h/kg^{0.75}$	29.1	29.1	Brown et al. 1997 (Table 31)	22.4	22.4	Brown et al. 1997 (Table 31)	24.0	Clewell et al. 2001 (Table 1)
Cardiac Output	QCC	$L/h/kg^{0.75}$	20.1	20.1	Marino et al. 2006 (QPC/QCC = 1.45)	18.7	18.7	Brown et al. 1997 (Table 22)	16.5	Clewell et al. 2001 (Table 1)
FRACTIONAL BLOOD FLOWS TO TISSUES										
Flow to Liver as fraction Cardiac Output	QLC	unitless	0.161	0.161	Brown et al. 1997 (Table 23)	0.183	0.183	Brown et al. 1997 (Table 23)	0.227	Brown et al. 1997 (Table 23)
Flow to Fat as fraction Cardiac Output	QFC	unitless	0.07	0.07	Brown et al. 1997 (Table 23; Same as rat value)	0.07	0.07	Brown et al. 1997 (Table 23)	0.052	Brown et al. 1997 (Table 23)
Flow to Slow as fraction Cardiac Output	QSC	unitless	0.159	0.159	Brown et al. 1997 (Table 23); Same as that reported for muscle	0.278	0.278	Brown et al. 1997 (Table 23); Same as that reported for muscle	0.191	Brown et al. 1997 (Table 23); Same as that reported for muscle
Flow to Kidney as fraction Cardiac Output	QKC	unitless	0.09	0.09	Brown et al. 1997 (Table 23)	0.14	0.14	Brown et al. 1997 (Table 23)	0.175	Brown et al. 1997 (Table 23)
FRACTIONAL VOLUMES OF TISSUES										
Volume Liver as fraction Body Weight	VLC	unitless	0.0549	0.0549	Brown et al. 1997 (Table 4)	0.0366	0.0366	Brown et al. 1997 (Table 5)	0.0257	Brown et al. 1997 (Table 7)

Table S-1: Physiological Parameters for PBPK Model										
Parameter	**Abbreviation**	**Units**	**Mice**		**Source**	**Rats**		**Source**	**Humans**	**Source**
			Male	**Female**		**Male**	**Female**			
Volume Lung as fraction Body Weight	VLUC	unitless	0.0073	0.0073	Brown et al. 1997 (Table 4)	0.005	0.005	Brown et al. 1997 (Table 5)	0.0076	Brown et al. 1997 (Table 7)
Volume Fat as fraction Body Weight	VFC	unitless	0.1	0.1	Brown et al. 1997 (Table 10)	0.1	0.1	Brown et al. 1997 (Table 13)	0.27	Brown et al. 1997 (Table14); Average of total male and female
Volume Rapid Perfused as fraction Body Weight	VRC	unitless	0.08098	0.08098	Brown et al. 1997 (Table 4); Sum of adrenals, brain, stomach, small intestine, large intestine, heart, lungs, pancreas, spleen and thyroid	0.04644	0.04644	Brown et al. 1997 (Table 5); Sum of adrenals, brain, stomach, small intestine, large intestine, heart, lungs, pancreas, spleen and thyroid	0.0533	Brown et al. 1997 (Table 7); Sum of adrenals, brain, stomach, small intestine, large intestine, heart, lungs, pancreas, spleen and thyroid
Volume Slow Perfused as fraction Body Weight	VSC	unitless	0.384	0.384	Brown et al. 1997 (Table 4); Same as that reported for muscle	0.4	0.4	Brown et al. 1997 (Table 5); Same as that reported for muscle	0.4	Brown et al. 1997 (Table 7); Same as that reported for muscle
Volume Kidney as fraction Body Weight	VKC	unitless	0.0167	0.0167	Brown et al. 1997 (Table 4)	0.0073	0.0073	Brown et al. 1997 (Table 5)	0.0044	Brown et al. 1997 (Table 7)

Table S-2: Partition Coefficients for PBPK Model			
	Mice	**Rats**	**Humans**
Blood:Air	7.83	7.35	4.54
Lung:Blood	2.38	1.85	2.94
Liver:Blood	1.26	1.58	2.37
Fat:Blood	17.35	16.99	28.65
Muscle:Blood [a]	0.59	0.60	1.00
Kidney:Blood [b]	1.76	2.29	2.67

[a] used for slowly perfused tissues

[b] used for rapidly perfused tissues

Table S-3: *In Vitro* Metabolism Parameters			
Sex & Species	**Parameter**	**Source**	
		Yang et al. 2012 MCMC Mean[a]	**This Analysis Mean (95% Confidence Interval)**
Female mouse	Vmax, liver (μmol/h/mg protein)	0.13 (0.11 – 0.15)	0.105 (0.087 - 0.127)
	Vmax, lung (μmol/h/mg protein)	0.03 (0.010 – 0.050)	0.022 (0.015 – 0.031)
	Vmax, kidney (μmol/h/mg protein) [b]	0.004 (-0.016 – 0.024)	ND
	Km, liver (μmol/L)	0.88 (0.606 – 1.154)	0.448 (0.302 – 0.652)
	Km, lung (μmol/L)	2.82 (-0.140 – 5.780)	2.369 (1.555 – 3.549)
	Km, kidney (μmol/L) [b]	176.11 (-1632.71 – 1984.94)	ND
Male mouse	Vmax, liver (μmol/h/mg protein) [c]	0.26 (0.240 – 0.280)	0.212 (0.161 – 0.257)
	Vmax, lung (μmol/h/mg protein) [c]	0.14 (0.120 – 0.160)	0.085 (0.069 – 0.105)
	Vmax, kidney (μmol/h/mg protein)	0.01 (0.008 – 0.012)	0.012 (0.0088 – 0.015)
	Km, liver (μmol/L) [c]	1.34 (1.183 – 1.497)	0.689 (0.472 – 0.903)
	Km, lung (μmol/L) [c]	2.22 (1.946 – 2.494)	1.194 (0.943 – 1.523)
	Km, kidney (μmol/L)	0.77 (0.594 – 0.946)	0.647 (0.469 – 0.902)
Female rat	Vmax, liver (μmol/h/mg protein)	0.09 (0.070 – 0.110)	0.069 (0.056 – 0.085)
	Vmax, lung (μmol/h/mg protein) [b]	NC	0.00408 (0.00152 – 0.00618)
	Vmax, kidney (μmol/h/mg protein)	0.003 (0.0024 – 0.0036)	0.0018 (0.0013 – 0.0026)
	Km, liver (μmol/L)	0.56 (0.501 – 0.619)	0.718 (0.544 – 0.933)
	Km, lung (μmol/L) [b]	NC	2.369 (fixed to female mouse Km)
	Km, kidney (μmol/L)	0.60 (0.443 – 0.757)	0.449 (0.298 – 0.687)
Male rat	Vmax, liver (μmol/h/mg protein) [c]	0.10 (0.094 – 0.106)	0.072 (0.066 – 0.078)
	Vmax, lung (μmol/h/mg protein) [b]	NC	ND
	Vmax, kidney (μmol/h/mg protein)	0.003 (0.0024 – 0.0036)	0.0019 (0.0014 – 0.0026)
	Km, liver (μmol/L) [c]	0.56 (0.501 – 0.619)	0.417 (0.367 – 0.477)
	Km, lung (μmol/L) [b]	NC	ND
	Km, kidney (μmol/L)	0.76 (0.544 – 0.976)	0.619 (0.437 – 0.885)
Humans	Vmax, liver (μmol/h/mg protein) [c]	0.05 (0.048 – 0.052)	0.055 (0.052 – 0.059)
	Vmax, lung (μmol/h/mg protein) [b]	NC	ND
	Vmax, kidney (μmol/h/mg protein) [b]	NM	NM
	Km, liver (μmol/L) [c]	0.45 (0.430 – 0.470)	0.349 (0.312 – 0.394)
	Km, lung (μmol/L) [b]	NC	ND
	Km, kidney (μmol/L) [b]	NM	NM

[a]95% CI calculated as mean +/- SD*1.96 reported in Yang et al. 2012

[b]ND: not determinable; NM: not measured; NC: not comparable

[c]The initial amount of chloroprene was estimated for each concentration as the time-course data were constructed from multiple vials

Table S-4: Metabolism Parameters for PBPK Model			
Sex & Species	**Parameter**	**Source**	
		Yang et al. 2012	**This Analysis (Table S-3)**
Female Mouse	VmaxC, liver (mg/h/kg**3/4)	8.88	7.99
	VmaxC, lung (mg/h/kg**3/4)	0.11	0.12
	VmaxC, kidney (mg/h/kg**3/4) [a]	0.03	ND
	Km, liver (mg /L)	0.08	0.040
	Km, lung (mg /L)	0.25	0.21
	KM, kidney (mg /L) [a]	9.59	ND
Male Mouse	VmaxC, liver (mg/h/kg**3/4) [b]	18.54	16.09
	VmaxC, lung (mg/h/kg**3/4) [b]	0.6	0.49
	VmaxC, kidney (mg/h/kg**3/4)	0.078	0.14
	Km, liver (mg /L) [b]	0.12	0.061
	Km, lung (mg /L) [b]	0.2	0.11
	KM, kidney (mg /L)	0.068	0.057
Female Rat	VmaxC, liver (mg/h/kg**3/4)	9.37	6.36
	VmaxC, lung (mg/h/kg**3/4) [a]	NC	0.03
	VmaxC, kidney (mg/h/kg**3/4)	0.018	0.015
	Km, liver (mg /L)	0.09	0.064
	Km, lung (mg /L) [a]	NC	0.21
	KM, kidney (mg /L)	0.053	0.040
Male Rat	VmaxC, liver (mg/h/kg**3/4) [b]	9.48	7.42
	VmaxC, lung (mg/h/kg**3/4) [a]	NC	ND
	VmaxC, kidney (mg/h/kg**3/4)	0.018	0.018
	Km, liver (mg /L) [b]	0.05	0.037
	Km, lung (mg /L) [a]	NC	ND
	KM, kidney (mg /L)	0.067	0.055
Humans	VmaxC, liver (mg/h/kg**3/4) [b]	20.4	14.51
	VmaxC, lung (mg/h/kg**3/4) [a]	NC	0.0031
	VmaxC, kidney (mg/h/kg**3/4) [a]	NM	NM
	Km, liver (mg /L) [b]	0.04	0.031
	Km, lung (mg /L) [a]	NC	0.031
	KM, kidney (mg /L) [a]	NM	NM

[a] ND: not determinable; NM: not measured

[b] The initial amount of chloroprene was estimated for each concentration as the time-course data were constructed from multiple vials

Table S-5: Plethysmography Data			
Pulmonary Function Data Protocol 07039 Summary			**Exposure #1**
Exposure	**Frequency (BPM)**	**Tidal Volume (ml)**	**Minute Ventilation (ml/min)**
0ppm	Average	Average	Average
Animal 1	193.5	0.247	48.4
Animal 2	168.2	0.284	47.2
Animal 3	251.9	0.212	51.6
Animal 4	201.7	0.311	61.6
Average	203.8	0.264	52.2
Stdev	35.1	0.043	6.5
Pulmonary Function Data Protocol 07039 Summary			**Exposure #2**
Exposure	**Frequency (BPM)**	**Tidal Volume (ml)**	**Minute Ventilation (ml/min)**
13 ppm	Average	Average	Average
Animal 20	221.9	0.261	57.6
Animal 21	221.0	0.264	57.6
Animal 22	140.9	0.224	32.0
Animal 23	131.2	0.218	28.9
Average	178.7	0.242	44.0
Stdev	49.4	0.024	15.7
Pulmonary Function Data Protocol 07039 Summary			**Exposure #3**
Exposure	**Frequency (BPM)**	**Tidal Volume (ml)**	**Minute Ventilation (ml/min)**
32 ppm	Average	Average	Average
Animal 54	253.3	0.269	66.1
Animal 55	225.0	0.269	59.4
Animal 56	249.8	0.282	69.5
Animal 57	235.2	0.293	67.9
Average	240.8	0.278	65.7
Stdev	13.1	0.012	4.4
Pulmonary Function Data Protocol 07039 Summary			**Exposure #4**
Exposure	**Frequency (BPM)**	**Tidal Volume (ml)**	**Minute Ventilation (ml/min)**
90 ppm	Average	Average	Average
Animal 88	216.3	0.276	59.4
Animal 89	178.4	0.242	43.2
Animal 90	217.9	0.277	59.8
Animal 91	166.2	0.278	45.8
Average	194.7	0.268	52.0
Stdev	26.4	0.017	8.8

Table S-6: Arterial Blood Concentrations			
13 ppm Exposure			
Time point	**Average [CD]**	**Std Dev. CD**	**RSD%**
Control	0	0	0%
0.5 hours	1.03	0.18	17%
3 hours	1.93	0.80	41%
6 hours	1.58	0.35	22%
5 min post exposure	0.66	0.07	101%
10 min post exposure	0.70	0.11	157%
15 min post exposure	0	0	0%
32 ppm Exposure			
Time point	**Average [CD]**	**Std Dev. CD**	**RSD%**
Control	0	0	0%
0.5 hours	1.68	0.70	42%
3 hours	2.90	1.15	40%
6 hours	2.44	1.24	51%
5 min post exposure	0.61	0.22	35%
10 min post exposure	0.18	0.09	48%
15 min post exposure	0.30	0.23	78%
90 ppm Exposure			
Time point	**Average [CD]**	**Std Dev. CD**	**RSD%**
Control	0	0	0%
0.5 hours	6.41	1.83	29%
3 hours	7.33	3.52	48%
6 hours	8.00	1.02	13%
5 min post exposure	1.71	0.78	46%
10 min post exposure	0.92	0.33	35%
15 min post exposure	0.68	0.15	23%

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