Time course of congener uptake and elimination in rats after short-term inhalation exposure to an airborne polychlorinated biphenyl (PCB) mixture

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Table of Content

Chemicals

Extraction and clean-up procedure

Volatilization model

Quality assurance / quality control

Table S1. Method detection limits (MDL) for all PCB congeners.

Table S2. Recovery rate of spiked surrogate standards during the PCB extraction process from

rat liver, lung, blood, adipose tissue and brain after exposure to Aroclor 1242 vapor mixture.

Table S3. Recovery rate of spiked ongoing precision and recovery standards during the PCB

extraction process from rat blood and tissue after exposure to Aroclor 1242 vapor mixture.

Congener uptake and toxicological response in rats after 10-day nose-only exposure

Table S4. Lipid-adjusted mass of prevailing PCB congeners found in rat tissues.

Table S5. Total cell counts and differential cell counts, levels of total protein and LDH activityBAL fluid from rats subacutely exposed to Aroclor 1242 vapor.

Table S6. Concentration of cytokines in BAL fluid from rats subacutely exposed to Aroclor1242 vapor.

Figure S1. Effect of PCBs on body weight gain in rats during 10 d subacute inhalation exposure to Aroclor 1242 vapor.

Biological half lives

Table S7 Biological half lives of detected congeners in rat liver, lung, blood, adipose tissue and brain after acute exposure to PCB vapor mixture from Aroclor 1242.

Time course of individual PCB congener levels in rat tissue

Figure S2 Comparison of time course of concentration change for PCBs 8, 15, 31, 20+28, 52 and 66 after nose-only inhalation to Aroclor 1242 vapor mixture

Figure S3-S30 Time course of concentration change in liver, lung, blood, adipose tissue and brain after acute nose-only inhalation to Aroclor 1242 vapor mixture.

Literature Cited

Chemicals. IUPAC identities, numbered PCB 1 (monochlorobiphenyl) through PCB 209 (decachlorobiphenyl) are used in this document for congener identification (1). Florisil (60-100 mesh), dimethylsulfoxide (anhydrous, 99.9%), sodium sulfite, sulfuric acid (concentrated) and pesticide grade solvents were purchased from Fisher Sci. (Pittsburgh, PA, US). Tetrabutylammonium hydrogen sulfate was purchased from JT Baker (Phillipsburg, NJ, US). Diatomaceous earth was obtained from Dionex (Sunnyvale, CA, US). 3,5-dichlorobiphenyl (PCB 14) and 2,2',3,4,4',5,6,6'-octachlorobiphenyl (PCB 204) were purchased from Cambridge Isotope Laboratories, Inc. (Andover, MA). Deuterium labeled 2,3,5,6-tetrachlorobiphenyl (d-PCB 65) was purchased from CDN isotopes (Quebec, Canada). Ongoing precision and recovery (OPR) standard was purchased as a ready mixture (WHO / NIST/ NOAA congener list) from AccuStandard (New Haven, CT). PCB 3 was synthesized in the laboratory (with a purity of >99%, based on the relative peak) and added to the AccuStandard mixture to represent lower chlorinated PCBs. After dilution it contained 410 ng/mL of PCB 3 and 380 ng/mL each of the following in isooctane: PCBs 8, 18, 28, 44, 52, 66, 77, 81, 101, 105, 114, 118, 123, 126, 128, 137, 153, 156, 157, 167, 169, 170, 180, 187, 189, 195, 206, and 209. For the OPR spike, 250 µL was added for each set of samples.

Extraction and clean-up procedure. The extraction of PCBs was performed by pressurized liquid extraction (PLE) as described elsewhere (*2*, *3*). Briefly, after pre-extraction of PLE cells containing Florisil and diatomaceous earth, tissue samples were thoroughly homogenized into diatomaceous earth and divided to two halves for PCB analysis (Fraction A) and for lipid extraction (Fraction B). Fraction A was placed on top of Florisil in PLE cells and spiked with surrogate standards. The cells were then extracted with hexane-acetone (1:1 v/v) at 120 °C, 1500 psi and one static cycle of 5 min. After concentrating the extract to 1 mL, sulfur impurities were removed by mixing 2-propanol and tetrabutylammonium sulfite, and adding nanopure water afterwards. The organic layer was then mixed with concentrated sulfuric acid and transferred to vials after overnight standing. Fraction B was extracted using chloroform-methoanol (2:1 v/v) at 120 °C and 1500 psi. The total lipid content was determined gravimetrically after evaporation of solvents to dryness.

Volatilization model. A model was established to predict the theoreteical concentration and distribution profile of the vapor mixture generated from volatilization. The solution of Aroclor 1242 used for generation of airborne PCBs was analyzed. The mass fraction of the solution was used as an input to the volatilization model. The atmospheric concentration of each individual congener was assumed to be in equilibrium with the concentration in the solution. Vapor pressures for each congener were obtained from previously reported equations (*5*, *6*). Partial pressure for each congener was calculated based on Raoult's Law:

$$P_i = X_i \times V_{P_i}$$

Where

 P_i = Partial pressure, atm; X_i = Molar fraction of the congener in the solution; V_{P_L} = Vapor pressure of the congener.

The atmospheric concentration was calculated based on the Ideal Gas Law:

$$C_{i} = \frac{Mass(g)}{V(L)} = \frac{P_{i}(atm) \times M.W.(\frac{g}{mole})}{R(\frac{L \cdot atm}{K \cdot moles}) \times T(K)}$$

Where C_i = Estimated atmospheric concentration for the congener; M.W. = Molecular weight of the congener; R = Ideal gas constant; T = Temperature. The total amount of PCBs that the animals were exposed to is:

$$\sum PCB \left(\frac{mg}{m^3}\right) = \frac{\sum_{i=1}^{209} C_i \left(\frac{mg}{m^3}\right) \times Q_{PCB}\left(\frac{L}{min}\right)}{Q_{total}\left(\frac{L}{min}\right)}$$

Where

 $Q_{PCB} = The flow rate passed over the solution; Q_{total} =$

The flow rate passed through the animal exposrue chamber.

The mass percentage of each congener in the vapor mixture was calculated to determine the profile distribution:

$$Mass Percentage_{i} = \frac{C_{air}(\frac{mg}{m^{3}})}{\sum_{i=1}^{209} C_{i} \ (\frac{mg}{m^{3}})}$$

Quality assurance / quality control measures. The quality of the analytical method was assessed by the method blank samples, the recovery of ongoing precision and recovery standard, and measurements of standard reference materials. Every sample was spiked with surrogates and each PCB mass was corrected for recovery. The method detection limit (MDL) was calculated from blank samples analyzed in parallel to all tissue and blood samples according to EPA formula:

$$MDL = t_{n-1} \times SD + \bar{x}$$

where \bar{x} = the mean of replicates of blank measures, t_{n-1} is Student's t-value for (n-1) degrees of freedom at 99% confidence level, and SD is standard deviation of the replicates. Standard Reference Material 1944, New York, New Jersey Waterway sediment (SRM 1944, National Institutes of Standards and Testing) was analyzed and recently reported (4), with an acceptable quantification results with respect to the certified values (mean difference between the measured and certified values was $15 \pm 15\%$).

PCB	MDL	РСВ	MDL	PCB	MDL	PCB	MDL
1		51	0.41	106	0.74	162	
2		52	0.34	107/124		164	
3		54	0.10	108		165	
4	0.23	55	0.38	110/115	0.46	167	0.38
5	0.20	56	0.37	111	0.08	169	0.13
6	0.13	57	0.38	112	0.36	170	0.05
7		58	0.56	114	0.31	171/173	0.08
8	0.14	59		118	0.17	172	0.13
9		60		120	0.13	174	
10		61/70/74/76	0.71	121		175	
11	0.04	62/75	0.09	122	0.28	176	
12/13	0.06	63	2.58	123	0.65	177	
15		64	0.15	126	0.13	178	
16	0.41	66	0.81	127		179	0.13
17	1.83	67		129/138/163	0.08	180/193	0.18
18/30	2.27	68	0.31	130		181	0.08
19		72	0.53	131	0.67	182	
20/28	0.41	73	0.31	132	0.63	183	0.03
21/33	0.41	77	0.48	133	0.21	184	
22	0.88	78	0.17	134/143	0.37	185	0.03
23		79	0.51	135/151		186	
24	0.14	80		136	0.28	187	0.16
25		81	0.29	137		188	
26/29	0.18	82	0.30	139/140		189	0.13
27	0.06	83	0.59	141		190	
31	1.14	84	0.08	142	0.78	191	
32	0.54	85/116/117	0.38	144		192	
34		86/87/97/109/119/125	0.21	145		194	
35	0.04	88/91	0.14	146		195	
36	0.34	89		147/149	0.70	196	
37	0.51	90/101/113	0.97	148		197	0.53
38		92		150	0.03	198/199	0.17
39		93/100		152	0.05	200	
40/41/71	0.17	94		153/168	0.31	201	
42	0.89	95	0.56	154	0.40	202	0.66
43	0.78	96	0.09	155	0.05	203	
45	0.50	98/102	0.29	156/157	0.18	205	
46	0.18	99	0.36	158		206	0.14
48	0.20	103		159		207	0.08
49/69	0.52	104		160	0.10	208	
50/53		105	0.23	161		209	0.13

Table S1. Method detection limits (MDL) for all PCB congeners determined from blank samples analyzed in parallel with tissue and blood samples. Values are expressed in ng.^a

 aAll samples were injected from a final volume of 100 $\mu L.$ -- indicates that MDL ≤ 0.02 ng.

Table S2. Recovery rate of spiked surrogate standards during PCB extraction process from rat liver, lung, blood, adipose tissue and brain after exposure to Aroclor 1242 vapor mixture. Values are expressed as mean \pm standard deviation. Surrogates are injected into every sample and each PCB mass is corrected for recovery.

	Liver	Lung	Blood	Adipose	Brain
PCB 14 ^a	$77 \pm 24\%$	$66 \pm 30\%$	$86\pm25\%$		
d-PCB 65 ^a	$86 \pm 34\%$	$82 \pm 37\%$	$87 \pm 17\%$		
PCB 14 ^b	$30 \pm 8\%$	$20\pm7\%$	$31 \pm 6\%$	$21 \pm 13\%$	$40 \pm 10\%$
d-PCB 65 ^b	$41 \pm 8\%$	$29 \pm 9\%$	$60 \pm 8\%$	$38 \pm 21\%$	$53 \pm 10\%$

^aTen-day subacute exposure to Aroclor 1242 vapor mixture, n=22 (number of samples).

^bTwo-hour acute exposure to Aroclor 1242 vapor mixture, n=27 (number of samples).

Table S3. Recovery rate of spiked ongoing precision and recovery standards during PCB extraction process from rat blood and tissue after exposure to Aroclor 1242 vapor mixture. Values are corrected for surrogate recovery, expressed as mean recovery rate and standard deviation (SD).

Congener	Average ^a	SD^{a}	Average ^b	SD^b
3	46.15%	17.45%	72.24%	21.30%
8	95.96%	2.57%	91.06%	18.84%
18	81.86%	38.69%	106.85%	21.15%
28	96.79%	28.04%	103.00%	14.38%
44	80.23%	15.43%	82.52%	18.10%
52	88.09%	8.42%	103.18%	8.54%
66	85.63%	0.33%	104.24%	10.68%
77	73.52%	10.83%	103.14%	20.51%
81	77.60%	7.81%	105.17%	14.13%
101	71.62%	2.81%	108.87%	12.62%
105	68.18%	7.96%	107.21%	20.02%
114	70.63%	7.37%	102.96%	16.00%
118	69.75%	7.49%	103.28%	16.53%
123	69.02%	6.94%	104.91%	17.70%
126	59.28%	9.98%	116.99%	51.59%
128	66.93%	14.20%	106.61%	20.27%
137	68.96%	15.60%	107.93%	23.92%
153	70.44%	13.25%	109.57%	20.72%
156+157	63.83%	19.98%	106.66%	28.66%
167	69.72%	19.95%	108.86%	49.68%
169	69.34%	20.77%	114.36%	38.02%
170	70.91%	21.00%	102.32%	24.37%
180	70.50%	24.46%	103.49%	29.96%
187	71.10%	18.06%	108.97%	22.35%
189	86.85%	34.48%	110.76%	39.62%
195	85.43%	32.27%	99.97%	42.30%
206	93.09%	36.68%	114.27%	49.15%
209	94.35%	38.02%	112.69%	50.99%

^aTen-day subacute exposure to Aroclor 1242 vapor mixture, n=2 (number of sample sets).

^bTwo-hour acute exposure to Aroclor 1242 vapor mixture, n=6 (number of sample sets).

Tissue		Liver		Lung		Blood	
Congener		[ng/g lipid weight]	% of total	[ng/g lipid weight]	% of total	[ng/g lipid weight]	% of total
1	Mono	5.1	0.08	5.5	0.08	0.03	0.15
2		3.6	0.05	1.4	0.02		
3		2.3	0.03	1.4	0.02	0.01	0.03
4	Di	25.8	0.39	54.2	0.81	0.03	0.20
8		44.7	0.67	117.3	1.75	0.10	0.57
15		12.0	0.18	12.3	0.18	0.03	0.14
16	Tri	10.7	0.16	37.2	0.55	0.03	0.15
17		20.3	0.30	29.0	0.43	0.02	0.10
20/28*		1387.7	20.77	2383.1	35.50	4.1	22.88
21/33*		49.2	0.74	89.4	1.33	0.06	0.34
31		68.4	1.02	112.5	1.68	0.16	0.88
32		15.7	0.24	28.2	0.42	0.03	0.15
49*/69	Tetra	1160.9	17.37	146.1	2.18	2.1	11.24
52		158.1	2.37	158.6	2.36	0.5	2.87
60		280.8	4.20	359.8	5.36	0.8	4.72
61/70*/74*/76		403.4	6.04	542.5	8.08	1.4	7.81
64		48.3	0.72	85.1	1.27	0.17	0.93
66		703.0	10.52	865.8	12.90	2.4	13.61
77		14.3	0.21			0.01	0.05
82	Penta	10.3	0.15			0.06	0.33
83*/99*/112		965.4	14.45	545.0	8.12	2.4	13.31
85*/116/117		235.9	3.53	82.6	1.23	0.3	1.53
86/87*/97*/109/119/125		56.6	0.85	45.6	0.68	0.2	0.98
90/101*/113		165.0	2.47	120.8	1.80	0.40	2.22
95		105.4	1.58	79.2	1.18	0.16	0.91
105		119.8	1.79	104.6	1.56	0.5	2.73
110*/115		49.4	0.74	45.5	0.67	0.4	2.36
118		190.4	2.85	240.5	3.58	0.8	3.74
129/138*/163	Hexa	29.5	0.44	11.8	0.18	0.07	0.41
147/169		27.3	0.41	25.2	0.38	0.05	0.30
153*/168		25.0	0.37	27.4	0.41	0.04	0.21
Total PCBs		6681.3	100.00	6714.2	100.00	18.0	100.00

Table S4. Lipid-adjusted mass of prevailing PCB congeners found in rat tissues. Values are expressed as ng/g lipid weight and mass percentage of total PCB amount for each congener. Data shown are the mean of N=7 rats from the 10-day Aroclor 1242 vapor exposed group. Bold indicates PCB mass percentage over 2% in any tissue.

*Major congeners of the coeluting congener set in Aroclor 1242.

Table S5. Total cell counts and differential cell counts, levels of total protein and LDH activity BAL fluid from rats subacutely exposed to Aroclor 1242 vapor. Values are expressed as mean \pm SE. None of these outcomes measures was significantly different between sham and exposed rats.

	Total	Differentia	$1 \text{ Cells} (10^3 \text{ pe})$	Total	וח ו		
Exposure Group	Cells (10^3 per mL)	Macrophages	Neutrophils	Lymphocytes	protein	activity	
F	BAL)			_jpo.j.co	(µg/mL)	(U/L)	
PCB	45.54 ±	44.92 ± 7.19	0.40 ± 0.20	0.21 ± 0.09	66.6 ± 5.2	66 ± 6	
Sham	42.61 ± 6.31	41.71 ± 6.33	0.24 ± 0.07	0.63 ± 0.20	70.6 ± 5.5	62 ± 7	

Table S6. Concentration [pg/mL (mean \pm SE)] of cytokines in BAL fluid from rats subacutely exposed to Aroclor 1242 vapor. Values are expressed as mean \pm SE. LLOD = lower limit of detection. None of these outcomes measures was significantly different between sham and exposed rats.

	GM- CSF	IFN-γ	IL-1α	IL-1β	IL-2	IL-4	IL-6	IL-10	IL-12	TNF-α
PCB	1.61 ±	$1.30 \pm$	$9.93 \pm$	$5.53 \pm$	$101.55 \pm$	$8.40 \pm$	$2.72 \pm$	$75.83 \pm$	$2.90 \pm$	$0.35 \pm$
	0.00	0.08	0.00	0.96	26.36	0.28	0.00	0.00	0.00	0.00
Sham	$1.61 \pm$	$1.38 \pm$	$9.93 \pm$	$4.26 \pm$	$80.20 \pm$	$8.93 \pm$	$2.67 \pm$	$86.48 \pm$	$2.50 \pm$	$0.35 \pm$
	0.00	0.00	0.00	0.59	21.39	0.23	0.03	10.65	0.25	0.00
LLOD	1.61	1.38	9.93	5.36	36.10	11.31	2.72	75.83	2.90	0.35

Table S7. Biological half lives of detected congeners in rat liver, lung, blood, adipose tissue and
brain after acutely exposed to PCB vaor mixture from Aroclor 1242. Values are expressed in hr.
Negative values are presented as indications that the material was accumulating instead of being
eliminated.

PCB	Congener No.	Liver	Lung	Blood	Adipose	Brain
di	6	1.75	5.00	3.96	64.06	1.35
	8	3.61	5.56	9.47	37.08	1.61
	15	3.07	6.36	5.52	-18.04	2.28
tri	16	2.51	9.01	19.32	26.59	20.71
	17	5.48	8.30	18.14	-3396.16	2.00
	18*/30	4.35	6.28	12.37	29.88	10.84
	20/28*	7.34	9.34	11.53	-20.84	9.18
	21/33*	3.01	3.54	8.41	16.52	3.19
	22	1.03	1.71	22.96	9.23	1.37
	24	2.05	9.41	3.58	-13.29	-5.90
	25	2.41	1.79	2.15	14.69	
	26*/29	4.07	5.18	3.79	63.09	1.97
	31	4.00	4.46	8.40	23.05	3.19
	32	4.18	4.24	22.47	838.19	3.68
	37	4.83	2.83	2.81	-26.48	4.53
tetra	49*/69	24.83	28.00	-33.65	-15.73	17.75
	52	6.21	7.53	16.33	-31.23	46.00
	59	2.92	2.07	7.36	82.93	35.23
	60	8.34	9.00	9.63	-6.62	12.37
	61/70*/74*/76	4.17	-12.70	11.48	-17.87	6.89
	64	4.30	9.39	9.49	-115.71	2.96
	66	6.18	12.93	13.56	-12.01	4.24
	77	5.76	12.93	3.33	6.44	1.83
penta	83	24.53	22.95	11.41	-9.18	-5.63
	99	15.01	55.99	22.50	-9.36	-11.29
	105	4.82	4.06	5.17	-13.75	-179.83
	112	-95.46	83.65	29.44	-6.66	-7.10
	118	3.93	28.98	12.15	-11.18	3.90

*Major congeners of the coeluting congener set in Aroclor 1242.



Figure S1. Effect of PCBs on body weight gain in rats during 10 d subacute inhalation exposure to Aroclor 1242 vapor. Repeated-measures analysis of variance (ANOVA) showed a significantly diminished weight gain in PCB-exposed rats (p = 0.006).



Time post exposure (hr)

Figure S2 Time course of concentration change in liver, lung, blood, adipose tissue and brain for PCB 8 (A), PCB 15 (B), PCB 31 (C), PCB 20+28 (D), PCB 52 (E) and PCB 66 (F) after nose-only inhalation. Graphs were arranged according to chlorine numbers: A-B, di-chlorinated; C-D, tri-chlorinated; E-F, tetra-chlorinated. The six congeners were selected to reflect the impact of structural dissimilarity on the time course.



Figure S3. Time course of concentration change in liver, lung and adipose tissue for PCB 6 after nose-only inhalation. * The average level of the samples was below the method detection limit of the respective congener.



Figure S4. Time course of concentration change in liver, lung, adipose tissue and brain for PCB 8 after nose-only inhalation. * The average level of the samples was below the method detection limit of the respective congener.



Figure S5. Time course of concentration change in liver, lung, blood, adipose tissue and brain for PCB 15 after nose-only inhalation. [#]Average congener level of treatment group is less than twice of that in blood samples of sham/sentinels.



Figure S6. Time course of concentration change in liver, lung, adipose tissue and brain for PCB 16 after nose-only inhalation. * The average level of the samples was below the method detection limit of the respective congener.



Figure S7. Time course of concentration change in liver, lung, adipose tissue and brain for PCB 17 after nose-only inhalation. * The average level of the samples was below the method detection limit of the respective congener.



Figure S8. Time course of concentration change in liver, lung, adipose tissue and brain for PCB 18+30 after nose-only inhalation. * The average level of the samples was below the method detection limit of the respective congener.



Figure S9. Time course of concentration change in liver, lung, adipose tissue and brain for PCB 20+28 after nose-only inhalation.



Figure S10. Time course of concentration change in liver, lung, blood, adipose tissue and brain for PCB 21+33 after nose-only inhalation. * The average level of the samples was below the method detection limit of the respective congener. [#]Average congener level of treatment group is less than twice of that in blood samples of sham/sentinels.



Figure S11. Time course of concentration change in liver, lung and adipose tissue for PCB 22 after nose-only inhalation. Dotted lines represent the possible trend of decreasing when the concentrations are no longer detectable at 12 hr post exposure. * The average level of the samples was below the method detection limit of the respective congener.



Figure S12. Time course of concentration change in liver, lung, adipose tissue and brain for PCB 24 after nose-only inhalation. * The average level of the samples was below the method detection limit of the respective congener.



Figure S13. Time course of concentration change in liver, lung, and adipose tissue for PCB 25 after nose-only inhalation.



Figure S14. Time course of concentration change in liver, lung, blood, adipose tissue and brain for PCB 26+29 after nose-only inhalation. * The average level of the samples was below the method detection limit of the respective congener. [#]Average congener level of treatment group is less than twice of that in blood samples of sham/sentinels.



Figure S15. Time course of concentration change in liver, lung, blood, adipose tissue and brain for PCB 31 after nose-only inhalation. * The average level of the samples was below the method detection limit of the respective congener. [#]Average congener level of treatment group was below 2 fold of that in blood samples of sham/sentinels.



Figure S16. Time course of concentration change in liver, lung, adipose tissue and brain for PCB 32 after nose-only inhalation. * The average level of the samples was below the method detection limit of the respective congener.



Figure S17. Time course of concentration change in liver, lung, blood, adipose tissue and brain for PCB 37 after nose-only inhalation. * The average level of the samples was below the method detection limit of the respective congener.



Figure S18. Time course of concentration change in liver, lung, blood, adipose tissue and brain for PCB 49+69 after nose-only inhalation. * The average level of the samples was below the method detection limit of the respective congener.



Figure S19. Time course of concentration change in liver, lung, adipose tissue and brain for PCB 52 after nose-only inhalation.



Figure S20. Time course of concentration change in liver, lung, adipose tissue and brain for PCB 59 after nose-only inhalation.



Figure S21. Time course of concentration change in liver, lung, blood, adipose tissue and brain for PCB 60 after nose-only inhalation. Dotted lines represent the possible trend of change when the concentrations are not detectable at 3 hr post exposure. [#]Average congener level of treatment group is less than twice of that in blood samples of sham/sentinels.



Figure S22. Time course of concentration change in liver, lung, adipose tissue and brain for PCB 61+70+74+76 after nose-only inhalation. *The average level of the samples was below the method detection limit of the respective congener.



Figure S23. Time course of concentration change in liver, lung, adipose tissue and brain for PCB 64 after nose-only inhalation. ^{*}The average level of the samples was below the method detection limit of the respective congener.



Figure S24. Time course of concentration change in liver, lung, blood, adipose tissue and brain for PCB 66 after nose-only inhalation. ^{*}The average level of the samples was below the method detection limit of the respective congener.



Figure S25. Time course of concentration change in liver, lung and adipose tissue for PCB 77 after nose-only inhalation. *The average level of the samples was below the method detection limit of the respective congener.



Figure S26. Time course of concentration change in liver, lung, adipose tissue and brain for PCB 83 after nose-only inhalation. ^{*}The average level of the samples was below the method detection limit of the respective congener.



Figure S27. Time course of concentration change in liver, lung, adipose tissue and brain for PCB 99 after nose-only inhalation. *The average level of the samples was below the method detection limit of the respective congener.



Figure S28. Time course of concentration change in liver, lung, blood and adipose tissue for PCB 105 after nose-only inhalation. *The average level of the samples was below the method detection limit of the respective congener. [#]Average congener level of treatment group is less than twice of that in blood samples of sham/sentinels.



Figure S29. Time course of concentration change in liver, lung, blood, adipose tissue and brain for PCB 112 after nose-only inhalation. ^{*}The average level of the samples was below the method detection limit of the respective congener.



Figure S30. Time course of concentration change in liver, lung, adipose tissue and brain for PCB 118 after nose-only inhalation. *The average level of the samples was below the method detection limit of the respective congener.

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