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**Increase of Polychlorinated Dibenzo-*p*-dioxins and Dibenzofurans and
Dioxin-like Polychlorinated Biphenyls in Human Milk from China in 2007 - 2011**

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12

13 **Abstract**

14 A national survey was conducted to determine polychlorinated dibenzo-p-dioxins and
15 dibenofurans (PCDD/Fs) and dioxin-like polychlorinated biphenyls (dl-PCBs) in human milk
16 samples collected from 16 provinces to assess current exposure and temporal trends in China. The
17 arithmetic mean concentration of total TEQ (PCDD/Fs and dl-PCBs) is 6.7 pg TEQ g⁻¹ lipid with
18 a range of 2.9 – 15.4 pg TEQ g⁻¹ lipid in 2011. Levels have been compared to data obtained during
19 a previous national study conducted in 2007. The mean of PCDD/Fs has increased about 32.6%
20 and 99.9% for total TEQ concentration (3.7 pg TEQ g⁻¹ in 2007 vs 4.9 pg TEQ g⁻¹ in 2011) and
21 mass concentration (66.7 pg g⁻¹ lipid in 2007 vs 133.3 pg g⁻¹ lipid in 2011) during the period of
22 2007-2011, respectively. Continuous surveillance on PCDD/Fs and dl-PCBs in human milk is
23 critical to evaluate the human health effect and environment impact in China.

24 **Keywords:** PCDD/Fs, dl-PCBs, human milk, trends

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26 **1. Introduction**

27 Polychlorinated dibenzo-*p*-dioxins and dibenzofurans (PCDD/Fs) and dioxin-like
28 polychlorinated biphenyls (dl-PCBs) are ubiquitous and recognized as persistent organic
29 pollutants. Due to their stability and lipophilic properties, PCDD/Fs and dl-PCBs can be stored in
30 fat tissues and bioaccumulate through food chain (WHO, 1998). Approximately 90% of the intake
31 of these pollutants stems from food, especially from animal origin foods (WHO, 1998; Liem et al.,
32 2000). Some experimental studies and epidemiology studies have implied neurodevelopmental
33 toxicity, immunotoxicity, reproductive effects and endocrine disturbing effects of PCDD/Fs and
34 dl-PCBs (Guo et al., 2000; Weisglas-Kuperus et al., 2000; Yonemoto, 2000; Demers et al., 2002;
35 Pavuk et al., 2003; Scippo et al., 2008). POPs in various matrices including human samples has
36 therefore become a matter of great concern, and international efforts like Stockholm Convention
37 have been made to reduce/eliminate these contaminants worldwide.

38 Human milk monitoring recommended by WHO/UNEP is an important and convenient
39 non-invasive method for assessing the body burden on the mother and the exposure of the infant,
40 and is now a part of the Stockholm Convention (Stockholm Convention; WHO, 2007). In China,
41 the Convention was ratified in 2004, and the first national survey of POPs in human milk was
42 carried out in 2007 as the background determination (Li et al., 2009). As a part of the Convention
43 performance evaluation, the 2nd national human milk monitoring was carried out in 2011, and 1
44 760 milk samples were collected. In the current study, PCDD/Fs and dl-PCBs in these milk
45 samples were measured to update the human exposure and investigate the temporal trend from
46 2007 to 2011, as well as the impact of some contamination sources on the pattern of PCDD/Fs in

47 human milk.

48 **2. Material and methods**

49 **2.1 Human milk samples collection**

50 The criteria for the selection of volunteering mothers and collection of human milk samples
51 followed the 'Guideline for Developing a National Protocol' of the Fourth WHO-Coordinated
52 Survey of Human milk for Persistent Organic Pollutants in Cooperation with UNEP (WHO, 2007).
53 All participants were told the objective of this study and signed the participant information and
54 consent form. Donors were all primiparas, willing to provide a minimum of 100 mL milk.

55 A multistage random cluster sampling method was applied to select sampling sites. First, all
56 provinces were classified into northern area and southern area according to geographical attribute
57 and resident dietary pattern. Then, 16 provinces were randomly sampled, including Heilongjiang,
58 Liaoning, Jilin, Hebei, Ningxia, Shaanxi, Neimenggu, Qinghai, Henan, Shanghai, Hubei, Jiangxi,
59 Fujian, Guangdong, Guangxi, Sichuan. The population of the provinces involved in this study
60 accounts for about 55% of the total population of China. In each province, one urban site and two
61 rural sites were selected for sampling. 50 donors were selected in each urban area, and 30 donors
62 in each rural area. Finally, a total of 1 760 human milk samples were obtained in 2011. These
63 samples were divided into 32 pools based on mother's residence. For each province, the urban
64 individual human milk samples were pooled into one composite sample, and rural samples were
65 pooled into another composite sample. All samples were stored at -20 °C until analyzed.

66 The questionnaire was applied to record the mothers' information included their health status,
67 smoking history, dietary habits, residence, and work histories. The age of volunteering mothers
68 was 25.3±3.9 years (mean ± standard deviation), and none of the mothers smoked and suffered

from occupational exposure.

2.2 Standard solutions and chemical reagents

Calibration standard solutions, ¹³C-labeled surrogate standards and injection standards specified in US EPA methods 1613 and 1668a were purchased from Wellington Laboratories (Guelph, Canada). All solvents were ultra resi-analyzed grade (J.T.Baker, Center Valley, PA, USA). Silica gel was purchased from Merck KGaA (Darmstadt, Germany).

2.3 Analytical methods

The analysis of PCDD/Fs and dl-PCBs were described elsewhere (Zhang et al., 2015), with slightly modification. Briefly, about 50 mL milk sample was freeze-dried. Then, after spiking ¹³C-labeled internal standards, samples were extracted by an ASE 350 (Thermo Scientific, Sunnyvale, CA, USA) using n-hexane / dichloromethane mixture (1:1, v/v) as solvent. Gravimetric lipid determination was performed after solvent evaporation. The bulk lipid was removed by shaking with acid-modified silica-gel and further cleanup was achieved using a Power Prep instrument (Fluid Management Systems, Waltham, MA, USA) with multiple commercial silica-gel columns, alumina columns and carbon columns. Two fractions containing PCDD/Fs and dl-PCBs were collected and concentrated to approximately 20 µL, respectively. After adding ¹³C-labeled injection standard, the final extract was analyzed by a high-resolution gas chromatograph – high resolution mass spectrometer (HRGC-HRMS) on a Trace 1300 Gas Chromatography (Thermo Scientific, Milan, Italy) equipped with a DB-5MS capillary column (60 m × 0.25 mm i.d. × 0.25 µm) and coupled to a DFS High Resolution Mass Spectrometer (Thermo Scientific, Bremen, Germany). The mass resolution was set at >10,000 for the measurement.

2.4 QA/QC

One test of procedural blank was carried out for every eight samples. Any 2,3,7,8-substituted CDD/Fs should not be detectable in the procedural blank sample. For PCBs, the concentration must be lower than 1/3 of that in human milk samples. If not, the samples of the same batch should be re-analyzed. The recoveries of internal standards were all in the range of 45–110%. The method detection limit was 0.01pg g⁻¹ lipid, 0.2-0.5 pg g⁻¹ lipid, and 0.02-0.05 pg g⁻¹ lipid for TCDD/Fs, OCDD/Fs, and other PCDD/F congeners, respectively, and 0.4 pg g⁻¹ lipid, 0.5-1.0 pg g⁻¹ lipid for non-ortho PCBs and mono-ortho PCB, respectively. The laboratory performance was validated by successfully participating in the Interlaboratory Comparison on Dioxins organized by Norwegian Institute of Public Health in 2012–2014. Z-scores for total TEQ of PCDD/Fs and dl-PCBs were in the range of -0.60 to 0.54. We also participated in the Second Round of UNEP-coordinated Global Interlaboratory Assessment 2013. PCDD/Fs and dl-PCBs in the human milk sample were tested, and the Z-score for total TEQ of PCDD/Fs and dl-PCBs was 0.15.

2.5 Statistical analysis

The normality of data of PCDD/Fs and dl-PCBs were tested by Shapiro-Wilk, and the data with non-normal distribution were natural logarithmic transformed. Paired t-test was applied to determine the difference of PCDD/Fs and dl-PCBs in human milk in 2011 and 2007, as well as urban/rural difference. Spearman rank correlation analysis was used to investigate the correlation between the concentrations of PCDD/Fs and dl-PCBs and dietary intake. The differences of the profile of PCDD/ and dl-PCB congeners were investigated by Principal Component Analysis. Values below detection limits were replaced by '0' for the statistical analyses. All statistical analyses were performed with the SPSS version 19.0. The *p* value is two-tailed, and α was set at a significance level of 0.05.

3. Results

With the exception of 1,2,3,7,8,9-HxCDF, 1,2,3,4,7,8,9-HpCDF, and OCDF, the other 26 PCDD/F and dl-PCB congeners are detected in almost all pooled milk samples. The concentrations of PCDD/Fs and dl-PCBs in pooled human milk samples from China in 2011 are shown in Table 1. By mass concentration, the PCDD/Fs concentrations with a mean of 131.5 pg g⁻¹ lipid are notably lower than the dl-PCBs concentration with a mean of 2652.5 pg g⁻¹ lipid ($p<0.01$). OCDD is the most predominant congener in all samples with the mean percentage contribution of 71.3% to total PCDD/Fs, followed by 1,2,3,4,6,7,8-HpCDD (6.2%), 2,3,4,7,8-PeCDF (5.5%), and 1,2,3,6,7,8-HxCDD (2.9%). For PCBs, PCB-118, PCB-156 and PCB-105 are the most predominant congeners, accounting for 52.5%, 16.8%, and 15.5% of the total dl-PCBs, respectively. By TEQ concentration, the total TEQ of PCDD/Fs and dl-PCBs is 6.7 ± 2.8 pg TEQ g⁻¹ lipid (mean ± standard deviation) within the range of 2.9 pg TEQ g⁻¹ lipid to 15.4 pg TEQ g⁻¹ lipid (WHO-TEF 1998). The highest PCDD/Fs and dl-PCBs in human milk are from Shanghai. And the levels of total TEQ in human milk from Neimenggu and Qinghai are notably lower than that from the other provinces. The average total-TEQ concentration in urban milk samples (7.0 pg TEQ g⁻¹ lipid) is slightly higher than that in rural milk (6.5 pg TEQ g⁻¹ lipid), but no statistical difference is found ($p>0.05$). 2,3,4,7,8-PeCDF makes the highest contribution to the total TEQ of PCDD/Fs plus dl-PCBs, accounting for 32.1%, followed by PCB-126 (17.0%), 1,2,3,7,8-PeCDD (16.8%), and 2,3,7,8-TCDD (8.1%). In all samples, the contribution of PCDD/Fs with a mean of 73.7% is much higher than that of dl-PCBs ($p<0.01$). A significant correlation between PCDD/Fs-TEQ and PCBs-TEQ is found ($r=0.767$, $p<0.01$). More detailed information of PCDD/Fs and dl-PCBs concentrations is listed in Supplementary Table 1.

By comparison with the 1st human milk survey in China in 2007(Li et al., 2009), there is significant difference in total TEQ and $\sum$ PCDD/Fs-TEQ (paired t-test, $p<0.05$). And the mean of total TEQ and $\sum$ PCDD/Fs-TEQ increased of 24.1% (5.4 pg TEQ g⁻¹ in 2007 vs 6.7 pg TEQ g⁻¹ in 2011) and 32.6% (3.7 pg TEQ g⁻¹ in 2007 vs 4.9 pg TEQ g⁻¹ in 2011) during the period of 2007-2011, respectively. Although the average concentration of $\sum$ dl-PCBs-TEQ shows a slightly increase of about 7.5% from 2007 to 2011, no statistical difference was found. By mass concentration, the change of PCDD/F and dl-PCB congeners is shown in Fig.1. For PCDD/Fs, with the exception of OCDF and 1,2,3,4,7,8-HxCDF, there is an increase in the concentration of the other 15 congeners including the most toxic congener, 2,3,7,8-TCDD (paired t-test, $p<0.05$). The mean of $\sum$ PCDD/Fs shows a notable increase of 106% from 63.9 pg g⁻¹ lipid in 2007 to 131.6 pg g⁻¹ lipid in 2011. For dl-PCBs, the mean concentration of PCB-77 and PCB-81 decreases of 17.8% and 42.6%, respectively. The significant elevation is found for PCB-114 (29.4%), PCB-156 (18.4%), PCB-157 (27.8%), PCB-167(20.1%), and PCB-189(64.8%) ($p<0.05$). But, for the concentration of $\sum$ dl-PCBs, there is no statistical difference during the period of 2007-2011 ($p>0.05$).

3. Discussion

3.1 Levels comparison

In present study, the maximum of total TEQ of PCDD/Fs and dl-PCBs in human milk was more than 5 times of the minimum, indicating large difference of human body burden of PCDD/Fs and dl-PCBs among regions of China. Generally, increasing emission of PCDD/Fs and dl-PCBs from industrialization as well as abundant foods of animal origin in the recipes related with high human exposure to PCDD/Fs and dl-PCBs (Çok et al., 2009; Ulaszewska et al., 2011). Some

regions such as Shanghai, and Guangdong from which high level of PCDD/Fs and dl-PCBs were detected in human milk samples have developed economy and high level of industrialization in China, and more animal origin foods, especially fish, are consumed by the resident of these regions. In contrast, low levels of PCDD/Fs and dl-PCBs were determined in human milk from the agricultural and animal husbandry regions such as Qinghai and Neimenggu. In addition, the emission of PCDD/Fs and dl-PCBs in China has been assessed in a previous study (Zheng et al., 2008b). The geographical distribution of human body burden in the present study was in line with that of the emission inventory.

Some previous studies have shown higher PCDD/Fs and dl-PCBs in human milk from urban area due to high urbanization or industrialization (Çok et al., 2009; Li et al., 2009; Ulaszewska et al., 2011). In present study, total-TEQ of urban samples were more than 1.3 – 2.1 times of that in rural samples from half provinces, including Heilongjiang, Hebei, Shaanxi, Ningxia, Hubei, Jiangxi, and Shanghai. However, rural samples from Jilin, Henan, Fujian, Guangxi, and Qinghai were approximately 16%-100% higher than that from urban areas. A study in New Zealand also showed high PCDD/Fs and dl-PCBs in rural areas compared to urban areas probably result from local agricultural industry (Mannetje et al., 2013).

As an ideal matrix, human milk has been applied for the determination of dioxin like compounds in numerous studies (Ulaszewska et al., 2011; Croes et al., 2012; Pratt et al., 2012; Fång et al., 2013; Mannetje et al., 2013; Wong et al., 2013). A summary of results from recent studies was listed in Table 2. In addition, the latest WHO/UNEP coordinated global surveys of human milk for persistent organic pollutants, including PCDD/Fs and dl-PCBs, was conducted in 2008-2011(UNEP, 2013). Unfortunately, detailed data of PCDD/Fs and dl-PCBs cannot be

obtained from the UNEP report (2013). Nevertheless, the range of total TEQ concentration in human milk from China resembled that from these studies.

3.2 Dietary intake and human body burden

For non-occupational people, more than 90% of total exposure to PCDD/Fs and dl-PCBs attributes to dietary intake, especially foods of animal origin (Liem et al., 2000). In China, total diet studies (TDS) has been performed to evaluate the long-term dietary exposure of residents (Zhang et al., 2013; Zhang et al., 2015). There is a strong association between total TEQ levels in human milk and dietary exposure calculated in TDS 2011 ($r=0.657$, $p<0.01$), indicating essential role of dietary in human exposure.

Some studies have showed the change of pattern of PCDD/Fs and dl-PCBs through the food chain (HuweandSmith, 2005; McLachlan, 1997; PirardandDe Pauw, 2005). Fig. 2 illustrates the difference of the pattern of PCDD/Fs and dl-PCBs in human milk and dietary intake from TDS 2011. The contribution of OCDD, OCDF, and HpCDFs to total PCDD/Fs in human milk was lower than that in dietary exposure, and the percentage contribution of some lower chlorinated chemicals such as PeCDD/Fs and HxCDD/Fs was higher in human milk. Higher chlorinated PCDD/F congeners showed a relatively high excretion, indicating poorer absorption or bioaccumulation (HuweandSmith, 2005; PirardandDe Pauw, 2005). In addition, carryover ratios of PCDD/Fs from feed to cow have been calculated in a previous study (McLachlan, 1997). In the current study, PCDD/F congeners with high carryover ratio showed increasing percentage contribution in human milk samples, and decreasing contribution for congeners with low carryover ratio.

For dl-PCBs, it has been recognized that PCB congeners with adjacent unsustituted *meta* and

para position, and some of those with adjacent unsustituted *ortho* and *meta* position are the more readily metabolized in human (Alcock et al., 1998). In the present study, a notably decline of PCB-77 from dietary intake to human body burden was similar with the observation from a recent study where higher PCB-77 was found in various food, but lower PCB-77 in human milk and serum samples(Shen et al., 2012). Increasing percentage contribution of PCB-114, 118, 156, 157, and 167 in human milk samples might result from the high bioaccumulation or high lipophilicity of higher chlorinated biphenyls (Xing et al., 2009).

3.3 The influence of contamination source on the pattern in human milk

The emission of PCDD/Fs and dl-PCBs in China has been evaluated in a previous study, and combustion process in metal smelting industry, thermoelectricity power generation, and municipal waste incineration were major sources of PCDD/Fs and dl-PCBs contamination in China (Zheng et al., 2008b). In addition, the usage of Na-PCP as well as E-Waste incineration was thought to be also not neglectable pollution source in China (Zheng et al., 2008a; Zheng et al., 2008b; Zhu et al., 2008). The Pattern of PCDD/Fs in human milk from typical E-Waste recycling area (Chan et al., 2007) and schistosomiasis region with Na-PCP spray (Schecter et al., 1994) has been investigated in some studies, respectively. Fig. 3 shows the score plots of the principal component analysis (PCA) to represent the difference among human milk samples from the current study and those from typical pollution regions. The plots of endemic areas of schistosomiasis, including Hubei (No.7), Sichuan (No.8), Guangxi (No.9), Jiangxi (No.11), Fujian (No.12), Guangdong (No.15), where Na-PCP had been largely used to kill the sail of genus *oncomelania* (Zheng et al., 2012), were closed to that of the typical Na-PCP sprayed area (Schecter et al., 1994). This indicates the contribution of Na-PCP application to human exposure in these areas, notwithstanding cease

application of Na-PCP to control schistosomiasis in last ten years in China (Wang et al., 2014). However, the plots of some non-endemic areas including Henan (No.4), Shaanxi (No.6) and Qinghai (No.14) were also closed to the plot of the typical Na-PCP sprayed area, suggesting the Na-PCP pollution in these areas. Besides killing the snail, Na-PCP had been liberally used as wood preservative, herbicide, pesticide, and fungicide among China (Wang et al., 2014). Furthermore, the congener profiles in all human milk samples in the present study are clearly different from that from Taizhou, a typical area of E-waste recycling (Chan et al., 2007), indicating neglectable relation of the E-waste dismantling to human exposure to PCDD/Fs in selected regions of China in the current study.

3.4 Time trend

Comparative data on the concentrations of PCDD/Fs and dl-PCBs in breast milk from different regions of the world have been obtained from five rounds of breast milk surveys by the WHO/UNEP during the period of 1987-2011, indicating a consistent decline in the TEQ concentrations of PCDD/Fs and dl-PCBs due to global efforts and strict regulation on dioxin emission worldwide (UNEP, 2013). In addition, other studies also found a time-related decrease in PCDD/Fs and dl-PCBs in human milk from European countries (Lignell et al., 2009; Guerranti et al., 2011; Fång et al., 2013), Canada (Ryan and Rawn, 2014), and New Zealand (Mannetje et al., 2013) over the last decades. However, conversely, there was a significant increase of concentrations of PCDD/Fs and some PCB congeners in human milk during the period of 2007-2011, which might probably result from the elevation of dioxin pollution in China. There was limited information of temporal trend on dioxin emission in China from publications. Limited

studies have indicated the elevation of PCDD/Fs in sediment from the lower reaches of the Yangtze River basin from 1995-2010 (Nie et al., 2013) and increasing PCDD/Fs emission from municipal waste incineration in China during the period of 2003-2010 (Tian et al., 2012), respectively. However, there was a recent study reported the notable decline of PCDD/Fs and dl-PCBs contamination levels in rice hull from hot spot areas like Guiyu, a typical E-waste recycling area of China, probably due to the effort to control the dioxin pollution from China authority (Fu et al., 2012). Nevertheless, it is worthy to conduct further studies to investigate the source of increasing emission, and the regulation should be strengthened to protect human health and environment. Furthermore, it is necessary to investigate the potential health risk from both the adult and nursing infants in China.

4. Conclusion

A national survey of PCDD/Fs and dl-PCBs in human breast milk has been conducted in China. The range of PCDD/Fs and dl-PCBs in human milk resembled that from recent studies in other countries. By comparison with our previous study, there was a significant increase in PCDD/Fs and some dl-PCB congeners in human milk during the period of 2007-2011, probably due to the increasing dioxin pollution in China. Thus, further studies should be done to investigate the health effect and environmental impact of the increasing dioxin and strengthen the regulation of emission in China.

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382 Table legends:

383 Table 1 Concentrations of PCDD/Fs and dl-PCBs in human milk samples from various regions of
384 China in 2011 (ND=0)

385 Table 2 The summary of PCDD/Fs and dl-PCBs concentrations in human milk from recent studies

398 **Figure captions**

399 Fig 1 The comparison of concentrations of PCDD/Fs and dl-PCBs in human milk from China in
400 2007 and 2011 (For accurate comparison, the data in milk sample from Neimenggu,
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404 Fig.3 PCA score plots for breast milk samples. The number represents the sampling site (1,
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387 Table 1

388 Concentrations of PCDD/Fs and dl-PCBs in human milk samples from various regions of China in 2011 (ND=0)^a

Regions	lipid content ^b	PCDD/Fs		DL-PCBs		PCDD/Fs+ DL-PCBs
		$\sum$ PCDD/Fs (pg/g lipid)	WHO _{PCDD/Fs} -TEQ (pg TEQ/g lipid)	$\sum$ DL-PCBs (pg/g lipid)	WHO _{DL-PCBs} -TEQ (pg TEQ/g lipid)	WHO _{PCDD/Fs+DL-PCBs} -TEQ (pg TEQ/g lipid)
Urban area of Hebei	4.8	70.3	5.8	3417.9	1.9	7.7 (6.4)
Rural area of Hebei	3.8	59.9	4.6	3778.5	1.2	5.8 (4.4)
Urban area of Heilongjiang	5.0	36.2	3.7	2711.4	1.6	5.3 (4.3)
Rural area of Heilongjiang	4.0	35.3	3.1	1654.6	1.0	4.2 (3.4)
Urban area of Liaoning	5.7	37.3	4.2	2592.6	2.0	6.2 (5.1)
Rural area of Liaoning	4.0	31.9	4.1	2969	2.3	6.4 (5.5)
Urban area of Henan	4.1	50.1	2.5	1738.4	0.7	3.2 (2.4)
Rural area of Henan	3.4	61.9	4.0	2251.2	1.2	5.2 (4.1)
Urban area of Ningxia	3.9	52.0	4.5	1060.9	0.6	5.2 (4.5)
Rural area of Ningxia	3.5	37.0	3.4	780.2	0.4	3.7 (2.9)
Urban area of Shaanxi	3.2	125.3	6.0	2887.6	1.4	7.5 (6.0)
Rural area of Shanxi	4.1	91.9	2.9	661.0	0.6	3.6 (2.9)
Urban area of Hubei	3.3	355.2	5.5	2617.1	2.0	7.5 (6.4)
Rural area of Hubei	4.7	209.8	5.0	2692.3	0.8	5.8 (4.6)
Urban area of Sichuan	3.0	488.8	4.9	2440.9	1.9	6.7 (6.0)
Rural area of Sichuan	4.9	142.4	4.4	2191.5	1.6	6.1 (5.2)
Urban area of Guangxi	4.1	120.7	4.3	3137.6	1.6	5.9 (5.0)
Rural area of Guangxi	4.4	400.5	5.0	2466.3	1.8	6.9 (6.1)
Urban area of Shanghai	3.1	97.6	10.3	8450.4	5.1	15.4 (12.8)
Rural area of Shanghai	3.7	83.0	8.6	5653.1	3.2	11.8 (10.0)

Urban area of Jiangxi	6.3	267.2	6.7	2546.0	2.5	9.3 (8.0)
Rural area of Jiangxi	3.8	135.9	5.1	2502.3	2.3	7.4 (6.2)
Urban area of Fujian	4.7	89.1	4.6	3325.8	2.3	6.9 (5.7)
Rural area of Fujian	4.4	79.4	5.0	4432.6	2.9	8.0 (6.8)
Urban area of Neimenggu	4.5	24.8	2.1	1041.4	0.8	3.0 (2.5)
Rural area of Neimenggu	3.9	31.0	2.3	1397.6	1.0	3.3 (2.8)
Urban area of Qinghai	4.0	68.6	2.2	748.7	0.7	2.9 (2.5)
Rural area of Qingha	2.6	160.4	4.7	1271.3	1.2	5.8 (5.0)
Urban area of Guangdong	4.5	289.2	8.0	3205.9	2.6	10.7 (9.0)
Rural area of Guangdong	6.0	318.0	7.1	2756.8	2.5	9.5 (8.4)
Urban area of Jilin	2.7	92.7	4.8	2094.6	1.7	6.5 (5.5)
Rural area of Jilin	2.3	64.2	8.7	3405.5	2.6	11.2 (9.3)

389 ^a TEF 1998(Van den Berg et al., 1998) was applied to calculated the TEQ; The TEQ concentration calculated by TEF 2005 (Van den Berg et al., 2006)was shown in
390 parentheses; ND : not detected.
391 ^b the weight of lipid (g) per 100 mL human milk.

392

393 Table 2

394 The summary of PCDD/Fs and dl-PCBs concentrations in human milk from recent studies^a

Country/region	Period of sampling	General information	PCDD/Fs plus dl-PCBs ^b (pg TEQ/g lipid)	Reference
Sweden	2008-2011	8 pooled sample from 79 individual human milk samples WHO-TEF1998, ND=1/2LOQ	Mean: 7.2 Range: 5.6 – 8.9	Fång et al., 2013
Italy	2008-2009	59 individual human milk samples WHO-TEF2005, ND=1/2LOD	Mean: 9.85	Ulaszewska et al., 2011
Belgium	2009-2010	One pooled sample from 84 individual samples WHO-TEF1998, ND=LOQ	14.3	Croes et al., 2012
Ireland	2010	11 pooled samples from 109 individual samples WHO1998, ND=LOQ	Mean:10.15 Range: 7.49 – 13.72	Pratt et al., 2012
New Zealand	2007-2010	39 individual samples, WHO-TEF2005, ND=1/2 LDO	Mean: 4.83	Mannetje et al., 2013
Hong Kong, China	2009	4 pooled samples from 137 individual samples WHO-TEF1998	Mean: 11.27 Range: 9.84 – 13.38	Wong et al., 2013
China	2011	32 pooled samples from 1760 individual samples WHO-TEF1998, ND=0	Mean: 6.7 Range: 2.9 – 15.4	This study

395 ^a The sampling year was later than 2007.396 ^b The mean concentration was calculated from the published data.

397

Figure captions

Fig 1 The comparison of concentrations of PCDD/Fs and dl-PCBs in human milk from China in 2007 and 2011 (For accurate comparison, the data in milk sample from Neimenggu, Qinghai, Jilin, and Guangdong were excluded in 2011)

Fig.2 The average percentage contribution of PCDD/F and dl-PCB congeners in human milk samples and dietary intake

Fig.3 PCA score plots for breast milk samples. The number represents the sampling site (1, Hebei; 2, Heilongjiang; 3, Liaoning; 4, Henan; 5, Ningxia; 6, Shaanxi; 7, Hubei; 8, Sichuan; 9, Guangxi; 10, Shanghai; 11, Jiangxi; 12, Fujian; 13, Neimenggu; 14, Qinghai; 15, Guangdong; 16, Jilin). NaCP represents the typical breast milk from areas with Na-PCP spayed in China (Schecter et al., 1994), and E-waste represents the breast milk from Taizhou, China (Chan et al., 2007).

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