The Exposure to chemical compounds in the Japanese People

- Survey of the Exposure to chemical compounds in Human (2011 ～) -

2017

Environmental Risk Assessment Office,
Environmental Health Department,
Ministry of the Environment, Japan

Introduction

The Environmental Risk Assessment Office, Environmental Health Department, Ministry of the Environment, Japan (MOE) has conducted a survey titled "Survey of the Exposure to Dioxins and other chemical compounds in Humans" to evaluate exposure and accumulation levels of dioxins and other chemical compounds in Japanese in FY 2011, and "Survey of the Exposure to chemical compounds in Humans" since FY 2012.

The Environmental Risk Assessment Office has compiled 6 years of survey results conducted during FY 2011–2016.

Summary of "Survey of the Exposure to chemical compounds in Humans"

Survey objectives

- Assess accumulated levels of dioxins and other chemical compounds in Japanese.
- Evaluate chronological changes in the accumulation levels of dioxins in participants who participated in the previous servey titled "Survey on the accumulation of dioxins and other chemical compounds in humans" (FY 2002–2010) (hereinafter referred to as "previous servey").
- Conduct a biomonitoring survey of Persistent Organic Pollutants (POPs) in biological samples requested by the Stockholm Convention.

Scope and methods of the survey

- Select three areas from the survey area of the previous survey in each year.
- Recruit about 80 residents who meet criteria (40–59 year-old and longtime resident) in each survey area.
- Measure dioxins and other chemical compounds in the blood and urine of the participants.
- Collect food samples over a three-day period from 15 participants in each year and measure concentrations of chemical compounds to calculate intakes.
- Conduct a survey on lifestyle based on the questionnaire.

Results from the dioxins survey

- Blood concentration: the average of 490 participants was 11 pg-TEQ/g-fat, with a range of 0.39–56 pg-TEQ/g-fat. Decrease of dioxin levels was observed in 83 out of 87 participants who participated in the previous survey.
- Intakes: the average of 90 participants was 0.49 pg-TEQ/kg body weight/day with a range of 0.035–2.4 pg-TEQ/kg body weight/day. No one exceeded the Japanese tolerable daily intake (TDI) of 4 pg-TEQ/kg body weight/day.

Results from the organic fluorine compounds survey

- Blood concentration: the PFOS average of 406 participants was 4.1 ng/ml with a range of 0.29-17 ng/mL, and the PFOA average of those was 2.2 ng/mL with a range of 0.27-13 ng/mL. These results were within the range of surveys conducted from FY 2008 to 2010.
- Intake: the PFOS average of 15 participants was 0.57 ng/kg body weight/day with a range of N.D. to 1.7 ng/kg body weight/day, and the PFOA average of those was 0.69 ng/kg body weight/day with a range of N.D.to 2.9 ng/kg body weigh/day.

Results from the metals survey

- Blood concentration: total mercury, lead, cadmium, total arsenic, copper, selenium, zinc, and manganese were measured. The median value of total mercury of 490 participants was 8.3 ng/mL, with a range of 1.3-41 ng/mL.
- Urine concentration: cadmium and arsenic compounds were measured. The median value of cadmium of 420 participants was 0.74 μg/gCr, with a range of 0.11-4.7 μg/gCr.
- Intake: total mercury, methyl mercury, lead, cadmium, total arsenic, copper, selenium, zinc, manganese were measured for 90 participants. The median value of methyl mercury was 0.053 μg/kg body weigt/day, with a range of N.D. to 0.34 μg/kg body weight/day. One participant exceeded the methyl mercury Japanese TDI of 2.0 μ g/ kg body weight/ week (subjected to pregnant or possibly pregnant women)while the participant was not applied to the condition. The median value of cadmium was 0.23 μg/kg body weigt/day, with a range of 0.059-0.57μg/kg body weigt/day. No participants exceeded the Japanese cadmium TDI of 7 μg/kg body weight/week.

Results from other chemical compounds (including pesticides and plasticizers)

- Blood concentration of pesticides and plasticizers of 75 participants and urine concentration of 420 participants were measured.

Results from the POPs survey

- Blood concentrations of 86 participants and intake of 15 participants were measured (conducted only in FY 2011).

Table of Contents

1. Overview of "Survey of the Exposure to chemical compounds in Humans"

The Environmental Risk Assessment Office, Environmental Health Department, Ministry of the Environment, Japan, carried out a survey titled "Survey on the accumulation of dioxins and other chemical compounds in humans" during FY 2002–2010 (hereinafter referred to as "previous servey"). In this survey, blood dioxin concentrations were measured in 2,264 participants living in typical environment in Japan. Food samples provided by 625 participants were measured and the intake from food was calculated (see Supplementary Information at endnote).

For conducting following-up survey, three areas were selected from the previous survey in each year for"Survey of the Exposure to chemical compounds in Humans" in FY 2011 and "Survey of the Exposure to chemical compounds in Humans" since FY 2012. Blood and urine were collected from the participants, and the accumulation of dioxins and other chemical compounds were measured.

Furthermore, a food study (duplicate portions study) was conducted targeting a subset of participants. The concentrations of chemical compounds in the food were measured, and the intakes were calculated.

Thereafter, blood of 490 participantsand urine of 491 participants from 18 survey areas were measured and the intakes of chemical compounds were estimated for 90 participants.

"Survey of the Exposure to chemical compounds in Human"

Organization responsible for the survey	Environmental Risk Assessment Office, Environmental Health Department, Ministry of the Environment, Japan
Survey period	FY 2011 and thereafter
Survey regions	Three regions per year
Survey specimens	Blood (to ascertain the accumulation of chemical compounds in the body), urine (to ascertain the excreted amounts of rapidly-metabolized chemical compounds), and food (to ascertain the amount of intake of chemical compounds).
Number of participants	491 people (FY 2011, 86 people; FY 2012, 84 people; FY 2013, 83 people; FY 2014, 81 people; FY 2015, 77people; FY 2016, 80 people; and 90 people participated in the food study).

2. Survey methods

2-1 Target regions and participants

In "Survey on the accumulation of dioxins and other chemical compounds in humans" conducted during FY2002–2010, Japan was divided into five regions, of which one prefecture was selected for each fiscal year. In a prefecture, three areas each classified as urban, agricultural, or fishery area were selected. From FY 2011, three regions were selected from regions of participated in previous studies. The local administrative authorities recruited the study participants from local residents, including those who have participated in previous studies, fulfilling the following criteria.

Target participants criteria

- Age: 40–59
- A resident of the survey region for 10 years or more
- Rarely absent from the survey region for work or other reasons
- Ability to provide blood samples with no restrictions (e.g., no anemia)

2-2 Methods

● Blood (all participants)

Blood was collected from survey participants by a nurse in the presence of a physician. Generally, fasting blood samples were taken.

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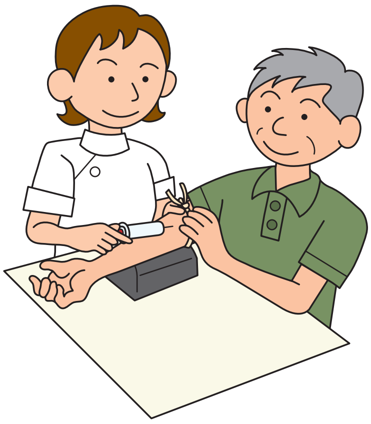


Analytes

Analytes	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
・Chlorinated dioxins	○	○	○	○	○	○
・Brominated dioxins		○				
・Organic fluorine compounds	○		○	○	○	○
・Metals	○	○	○	○	○	○
・Hydroxylated polychlorinated biphenyls (PCB)		○	○	○	○	○
・POPs	○					
・General health examination items: blood count, hepatic function, renal function, and glucose metabolism	○	○	○	○	○	○
・Health effect indexes: thyroidal function, allergic function, and fatty acids	○	○	○	○	○	○

● Urine (sampled from all participants; analysis for a subset of the participants)

Urine was collected in a container on the same day of blood sampling.

Analytes

Analytes	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
・Pesticides and their matabolites (organophosphate, pyrethroid etc.)	○	○	○	○	○	○
・Plasticizers, phthalate metabolites, and bisphenol A	○	○	○	○	○	○
・Metals (cadmium and arsenic)	○	○	○	○	○	○
・Other chemical substances (PAH, cotinine, and caffeine)		○	○	○	○	○
・General health examination items: specific gravity, glucose, and protein	○	○	○	○	○	○

● Food (conducted on a subset of the participants)

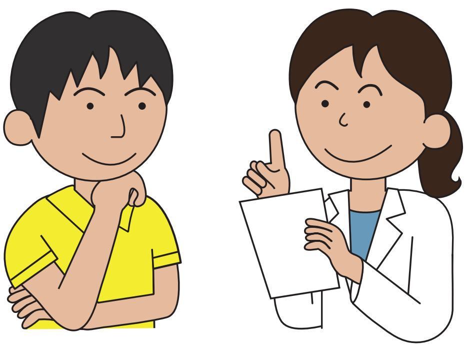
The food study was conducted over three days during the survey period. A "duplicate portions study" was conducted whereby duplicates of the participants' meals were stored in containers and collected afterwards. Nutritionists checked the food items and weight. The meals were then homogenized, the chemical compounds were measured, and the intake of each chemical compound (kg body weight per day) was estimated.

Analytes

Analyzed chemicals	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016
• Chlorinated dioxins	○	○	○	○	○	○
• Organic fluorine compounds	○					
• Metals	○	○	○	○	○	○
• POPs	○					

● Lifestyle survey (questionnaire)

A public health nurse or a nutritionist investigated the lifestyles of survey participants through individual interviews, referring to the questionnaire that was answered in advance.



Items of the questionnaire

- Personal medical history, residential history, occupational history, smoking habit, dietary history, lifestyle, and birth history

3. Results and Discussion

3-1 Dioxins survey

3-1-1 Blood (chlorinated dioxins)

● Results summary

The blood dioxin concentrations are shown in Table 1. The average concentration of the 490 survey participants was 11 pg-TEQ/g-fat. The range of the concentration was 0.39–56 pg-TEQ/g-fat.

☐ Table 1. Statistics for blood dioxin concentrations

(unit: pg-TEQ/g-fat)

	FY 2011 (n=86)	FY 2012 (n=84)	FY 2013 (n=83)	FY 2014 (n=81)	FY 2015 (n=76)	FY 2016 (n=80)	Total (n=490)
PCDDs+PCDFs +Co-PCBs							
Average	17	10	9.9	9.8	9.7	10	11
Standard deviation	10	6.9	6.6	5.9	7.0	6.3	7.9
Median	14	9.0	8.9	8.3	8.4	9.1	9.4
Range	0.83 ～ 56	0.42 ～ 40	0.40 ～ 33	1.1 ～ 34	0.39 ～ 49	0.92 ～ 29	0.39 ～ 56

(According to WHO 2006 TEFs)

● Comparison with previous survey results

Table 2 summarizes the comparison of the present results with the results from the “Survey on the accumulation of dioxins and other chemical compounds in humans (FY 2002 to FY 2010),” conducted on 2,264 participants. Although it was difficult to compare in a simplified manner because the average age and number of participants differed between the surveys, the blood dioxin concentrations obtained in the present survey were generally within the range of concentrations obtained in the previous surveys.

☐ Table 2. Comparison with previous survey results

(unit: pg-TEQ/g-fat)

Survey name	Survey on the Accumulation of Dioxins and other chemical compounds	This survey
Survey year	FY 2002 to FY 2010	FY2011 to FY2016
Participants	People living in the general envionment	People living in the general envionment
Number of participants	2,264	490
Age		
Average (years)	44.5	49.9
Range	15 ～ 76	24 ～ 77
PCDDs+PCDFs +Co-PCBs		
Average	19	11
Standard deviation	14	7.9
Median	16	9.4
Range	0.10 ～ 130	0.39 ～ 56

(According to WHO 2006 TEFs)

● Comparison of results for the same participants

87 people participated in both the present and previous surveys, and a comparison of the results are shown in Table 3. The dioxin concentrations in the blood decreased in most of the participants.

☐ Table 3. Comparison of blood dioxin concentrations in the same participants

(unit: pg-TEQ/g-fat)

Survey name	Past survey (n=87)	This survey (n=87)
Survey year	FY 2002 to FY2007	FY 2011 to FY 2016
PCDDs+PCDFs +Co-PCBs		
Average	21	12
Standard deviation	16	9.3
Median	17	9.7
Range	0.96 ～ 95	1.2 ～ 56

(According to WHO 2006 TEFs)

3-1-2 Food (chlorinated dioxins)

● Results summary

Table 4 summarizes the dioxin intake from food. The average intake was 0.49 pg-TEQ/kg bw/day with a range of 0.035–2.4 pg-TEQ/kg bw/day. Conceivable routes of intake include food, ambient air, and soil, but the intake from food is estimated to account for the largest portion (see the p33). In Japan, the tolerable daily intake (TDI) for dioxins is 4 pg-TEQ/kg bw/day as stipulated by the Law Concerning Special Measures against Dioxins. The TDI indicates the maximum ingestion of a given chemical substance per kg of body weight/day, and humans do not show adverse health effects even when the chemical is ingested below this level over a long period. No participants in the survey exceeded this TDI value.

☐ Table 4. Statistics for intake of intake from food

(unit: pg-TEQ/kg bw/day)

	FY 2011 (n=15)	FY 2012 (n=15)	FY 2013 (n=15)	FY 2014 (n=15)	FY 2015 (n=15)	FY 2016 (n=15)	Total (n=90)
PCDDs+PCDFs +Co-PCBs							
Average	0.65	0.72	0.32	0.43	0.37	0.44	0.49
Standard deviation	0.71	0.55	0.41	0.35	0.27	0.41	0.48
Median	0.39	0.57	0.23	0.34	0.25	0.33	0.33
Range	0.035～2.4	0.071～2.3	0.046～1.6	0.086～1.3	0.13～1.1	0.069～1.6	0.035～2.4

(According to WHO 2006 TEFs)

● Comparison with previous survey results

Table 5 summarizes the comparison with the results of "Survey on the Accumulation of Dioxins and other chemical compounds (FY 2002 to FY 2010)" conducted on 625 participants. The results from this survey were generally within the range of concentrations obtained in the previous surveys.

☐ Table 5. Comparison with previous survey results

(unit: pg-TEQ/kg bw/day)

Survey name	Survey on the Accumulation of Dioxins and other chemical compounds	This survey
Survey year	FY 2002 to FY 2010	FY 2011 to FY 2016
Participants	People living in the general envionment	People living in the general envionment
Number of participants	625	90
PCDDs+PCDFs +Co-PCBs		
Average	0.82	0.49
Standard deviation	0.86	0.48
Median	0.56	0.33
Range	0.031 ～ 6.2	0.035 ～ 2.4

(According to WHO 2006 TEFs)

3-1-3 Blood (brominated dioxins)

● Results summary

Table 6 summarizes the brominated dioxin concentrations in the blood for FY 2012 survey, which were below the detection limit for all 84 participants.

☐ Table 6. Statistics for brominated dioxins in the blood

(unit: pg/g-fat)

	FY 2012 (n=84)
PBDDs+PBDFs	
Average	All N.D.
Standard deviation	
Median	
Range	

3-2 Organic fluorine compounds survey

3-2-1 Blood

● Results summary

The results for organic fluorine compound concentrations in the blood are shown in Table 7.

☐ Table 7. Statistics for organic fluorine compound concentrations in the blood

(unit: ng/mL)

	FY 2011 (n=86)	FY 2013 (n=83)	FY 2014 (n=81)	FY 2015 (n=76)	FY 2016 (n=80)	Total (PFOS・PFOA：n=406, and others:n=320)
PFOS						
Average	5.8	5.1	3.0	2.9	3.5	4.1
Standard deviation	3.1	2.9	1.6	2.2	1.8	2.7
Median	4.8	4.5	2.7	2.1	3.3	3.5
Range	1.5 ～ 17	1.3 ～ 16	0.29 ～ 11	0.44 ～ 11	0.63 ～ 11	0.29 ～ 17
PFOA						
Average	2.2	3.2	1.8	2.3	1.5	2.2
Standard deviation	1.4	2.4	1.1	2.1	0.63	1.8
Median	1.8	2.5	1.6	1.6	1.4	1.8
Range	0.66 ～ 9.6	0.27 ～ 13	0.43 ～ 8.4	0.27 ～ 12	0.36 ～ 3.4	0.27 ～ 13
PFHxA						
Median	–	All N.D.	All N.D.	All N.D.	All N.D.	All N.D.
Range	–					
PFHpA						
Median	–	N.D.	N.D.	N.D.	N.D.	N.D.
Range	–	N.D. ～ 1.2	N.D. ～ 0.39	N.D. ～ 0.29	N.D. ～ 0.13	N.D. ～ 1.2
PFHxS						
Median	–	0.54	0.42	0.22	0.32	0.35
Range	–	N.D. ～ 1.8	N.D. ～ 1.1	N.D. ～ 0.80	0.071～0.76	N.D. ～ 1.8
PFTeDA						
Median	–	N.D.	N.D.	N.D.	N.D.	N.D.
Range	–	N.D. ～ 0.33	N.D. ～ 0.41	N.D. ～ 0.30	N.D. ～ 0.17	N.D. ～ 0.41
PFNA						
Median	–	2.0	1.3	1.1	1.2	1.3
Range	–	0.60 ～ 7.7	0.35 ～ 5.9	0.30 ～ 5.2	0.41 ～ 4.3	0.30 ～ 7.7
PFDA						
Median	–	0.58	0.55	0.39	0.48	0.51
Range	–	0.23 ～ 2.0	0.092 ～ 2.7	0.12 ～ 1.6	N.D. ～ 1.3	N.D. ～ 2.7
PFUdA						
Median	–	1.4	1.1	1.1	1.1	1.2
Range	–	0.30 ～ 4.6	0.29 ～ 6.4	0.13 ～ 5.1	0.21 ～ 4.2	0.13 ～ 6.4
PFDS						
Median	–	N.D.	All N.D.	All N.D.	All N.D.	N.D.
Range	–	N.D. ～ 0.065				N.D. ～ 0.065
PFDoA						
Median	–	0.18	0.16	0.11	0.11	0.14
Range	–	N.D. ～ 0.66	N.D. ～ 0.89	N.D. ～ 0.65	N.D. ～ 0.49	N.D. ～ 0.89
PFTrDA						
Median	–	0.38	0.45	0.36	0.34	0.38
Range	–	N.D. ～ 1.3	N.D. ～ 2.7	N.D. ～ 2.5	N.D. ～ 1.1	N.D. ～ 2.7

● Comparison with previous survey results

Table 8 summarizes the comparison of the present results with the results from "Survey on the Accumulation of Dioxins and other chemical compounds in Humans" conducted from FY 2008 to FY 2010 on 609 participants. Although it was difficult to compare in a simplified manner because the average age and the number of participants differed between the surveys, the results of present survey were generally within the range of results obtained in the previous surveys.

□ Table 8. Comparison with previous survey results

(unit: ng/mL)

Survey name	Survey on the Accumulation of Dioxins and other chemical compounds	This survey
Survey year	FY 2008 to FY 2010	FY 2011, 2013 to FY 2016
Participants	People living in the general envionment	People living in the general envionment
Number of participants	609	406
PFOS		
Average	7.8	4.1
Standard deviation	9.2	2.7
Median	5.8	3.5
Range	0.73 ～ 150	0.29 ～ 17
PFOA		
Average	3.0	2.2
Standard deviation	2.9	1.8
Median	2.1	1.8
Range	0.37 ～ 25	0.27 ～ 13

3-2-2 Food

The intake of organic fluorine compounds from food for 15 participants is shown in Table 9. The average PFOS concentration was 0.57 ng/kg body weight/day with a range of N.D. to 1.7 ng/kg body weight/day. The TDI has not been established for fluorine compounds in Japan.

□ Table 9. Statistics for the intake of organic fluorine compounds from food

(unit: ng/kg bw/day)

	FY 2011 (n=15)
PFOS	
Average	0.57
Standard deviation	0.51
Median	0.53
Range	N.D. ～ 1.7
PFOA	
Average	0.69
Standard deviation	0.70
Median	0.62
Range	N.D. ～ 2.9

3-3 Metals survey

3-3-1 Blood

● Results summary

The concentrations of metals (total mercury, lead, cadmium, total arsenic, copper, selenium, zinc, and manganese) in the blood were measured (Table 10).

☐ Table 10. Statistics for blood metal concentrations

(unit: ng/mL)

Metals	FY 2011 (n=86)	FY 2012 (n=84)	FY 2013 (n=83)	FY 2014 (n=81)	FY 2015 (n=76)	FY 2016 (n=80)	Total (total mercury: n=490 manganese: n=320, and others: n=404)
Total mercury							
Median	9.1	9.0	7.3	7.2	7.9	8.4	8.3
Range	2.4～29	1.7～41	2.1～33	1.5～22	1.5～38	1.3～40	1.3～41
Lead							
Median	—	12	10	13	11	12	11
Range	—	5.0～28	4.8～31	5.2～37	4.3～25	6.0～54	4.3～54
Cadmium							
Median	—	1.1	1.1	0.97	1.2	1.0	1.0
Range	—	0.25～3.5	0.40～2.7	0.37～4.4	0.38～6.2	0.27～2.8	0.25～6.2
Total arsenic							
Median	—	5.2	4.1	5.7	7.8	5.4	5.4
Range	—	1.4～35	1.2～19	1.0～110	0.70～39	1.5～22	0.70～110
Copper							
Median	—	800	870	890	830	810	840
Range	—	590～1,100	640～1,400	590～1,400	650～1,500	550～1,300	550～1,500
Selenium							
Median	—	180	180	200	200	200	190
Range	—	110～480	130～390	160～260	150～340	140～290	110～480
Zinc							
Median	—	6,300	6,500	6,400	6,500	5,800	6,300
Range	—	4,700～7,800	4,700～7,800	4,500～8,400	3,800～8,600	3,700～7,000	3,700～8,600
Manganese							
Median	—	—	13	14	12	13	13
Range	—	—	7.4～25	7.0～53	5.8～27	7.8～29	5.8～53

3-3-2 Urine

● Results summary

The concentrations in urine of cadmium and arsenic species [As(V), As(III), monomethylarsonic acid, dimethylarsinic acid, and arsenobetaine] were measured (Table 11).

□ Table 11. Statistics for urine metal concentrations

(unit: μg/g Cr)

Metals		Statistics	FY 2011 (n=15)	FY 2012 (n=84)	FY 2013 (n=83)	FY 2014 (n=81)	FY 2015 (n=77)	FY 2016 (n=80)	Total (n=420)
Cadmium		Median	0.97	0.89	0.64	0.81	0.69	0.70	0.74
		Range	0.25～3.9	0.20～3.1	0.11～3.1	0.16～2.8	0.12～4.7	0.12～2.9	0.11～4.7
Arsenic	As(V)	Median	0.30	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
		Range	N.D.～2.5	N.D.～2.9	N.D.～2.2	N.D.～1.6	N.D.～1.7	N.D.～1.5	N.D.～2.9
	As(III)	Median	1.5	1.7	1.5	1.1	1.4	1.4	1.4
		Range	N.D.～6.2	N.D.～6.6	N.D.～6.9	N.D.～4.7	N.D.～5.5	N.D.～15	N.D.～15
	MMA (monomethylarsonic acid)	Median	2.0	2.1	2.1	1.5	1.4	1.6	1.8
		Range	0.89～5.1	0.38～8.5	N.D.～13	N.D.～6.2	N.D.～4.9	N.D.～6.5	N.D.～13
	DMA (dimethylarsinic acid)	Median	42	33	30	27	26	27	29
		Range	12～170	6.7～110	8.5～100	6.2～150	9.4～140	8.3～120	6.2～170
	AB (arsenobetaine)	Median	73	40	31	54	59	44	44
		Range	15～300	2.8～640	2.1～390	6.1～2,300	4.5～1,600	5.5～540	2.1～2,300

3-3-3 Food

● Results summary

Metals (total mercury, methyl mercury, lead, cadmium, total arsenic, copper, selenium, zinc, and manganese) were measured in the food (Table 12). In Japan, among the metals measured in this survey, the TDIs have been established methyl mercury and cadmium. The TDIs for methyl mercury and cadmium are 2.0 μg/kg body weight/week (subjected to pregnant or possibly pregnant women) and 7.0 μg/kg body weight/week, respectively. One participant exceeded the methyl mercury TDI of 2.0 μ g/kg body weight/week, but the participant did not correspond to a condition of " pregnant or possibly pregnant women".

☐ Table 12. Statistics for the intake of metals from food

(unit：μg/kg bw/day)

Metals	FY 2011 (n=15)	FY 2012 (n=15)	FY 2013 (n=15)	FY 2014 (n=15)	FY 2015 (n=15)	FY 2016 (n=15)	Total (total mercury・methyl mercury・lead・cadmium: n=90 manganese: n=60,and others:n=75)
Total mercury							
Median	0.063	0.079	0.039	0.061	0.051	0.048	0.054
Range	N.D.～0.16	0.025～0.30	0.013～0.16	N.D.～0.16	N.D.～0.30	N.D.～0.34	N.D.～0.34
Methyl mercury							
Median	0.063	0.078	0.034	0.056	0.051	0.043	0.053
Range	N.D.～0.14	0.022～0.29	N.D.～0.15	N.D.～0.15	N.D.～0.29	N.D.～0.34	N.D.～0.34
Lead							
Median	0.094	0.11	0.083	0.064	0.048	0.069	0.074
Range	0.024～0.17	0.031～0.28	0.036～0.22	0.032～0.17	N.D.～0.13	0.021～0.17	N.D.～0.28
Cadmium							
Median	0.24	0.25	0.23	0.21	0.19	0.19	0.23
Range	0.059～0.39	0.11～0.57	0.11～0.56	0.13～0.47	0.12～0.42	0.071～0.42	0.059～0.57
Total arsenic							
Median	－	2.8	1.8	2.8	2.0	1.7	2.0
Range	－	1.0～14	0.76～5.8	0.71～10	0.54～3.7	0.40～5.1	0.40～14
Copper							
Median	－	16	19	16	13	12	16
Range	－	8.2～26	12～23	8.2～24	8.6～38	7.1～21	7.1～38
Selenium							
Median	－	1.3	1.2	1.2	1.2	0.97	1.2
Range	－	0.90～1.8	0.64～2.5	0.74～1.9	0.56～1.5	0.55～1.8	0.55～2.5
Zinc							
Median	－	140	130	120	90	100	120
Range	－	80～170	99～190	65～160	73～220	55～190	55～220
Manganese							
Median	－	－	66	52	50	50	54
Range	－	－	38～110	34～72	28～140	27～74	27～140

3-4 Other chemical compounds (including pesticides and plasticizers)

3-4-1 Blood

The results for hydroxylated PCB concentrations in blood are shown in Table 13.

□ Table 13. Statistics for hydroxylated PCB concentrations in blood

(unit：pg/g)

Chemical compounds		Statistics	FY 2012 (n=15)	FY 2013 (n=15)	FY 2014 (n=15)	FY 2015 (n=15)	FY 2016 (n=15)	Total (n=75)
Hydoroxyleted PCB	5Cl-HO-PCBs	Median	24	21	29	35	22	25
		Range	1.2～69	7.6～120	9.2～110	11～110	8.3～77	1.2～120
	6Cl-HO-PCBs	Median	27	30	34	26	36	30
		Range	1.6～120	12～200	11～110	13～170	11～88	1.6～200
	7Cl-HO-PCBs	Median	23	22	40	23	28	27
		Range	4.0～94	9.0～130	9.6～73	9.6～200	8.0～76	4.0～200

3-4-2 Urine

The results of other chemical compounds (including pesticides and plasticizers) in urine are shown in Tables 14-1 to 14-4.

□ Table 14-1. Statistics of pesticides, plasticizers, and others in urine (1)

(unit：μg/g Cr)

Classification	Chemical compounds		Statistics	FY 2011 (n=15)	FY 2012 (n=84)	FY 2013 (n=83)	FY 2014 (n=81)	FY 2015 (n=77)	FY 2016 (n=80)	Total (n=420)
Plasticizers	Phthalate mono-esters	MBP	Median	20	17	20	14	12	19	16
			Range	11～670	6.6～540	5.5～5,200	3.7～48	3.9～57	4.2～320	3.7～5,200
		MEHP	Median	4.2	2.9	3.2	1.9	2.6	2.0	2.6
			Range	0.98～8.1	0.61～21	0.54～22	0.23～13	0.40～21	0.39～12	0.23～22
		MEHHP	Median	15	9.9	11	7.4	5.4	7.4	8.3
			Range	5.7～44	2.7～59	2.8～58	1.8～42	1.2～28	2.5～81	1.2～81
		MEOHP	Median	9.6	6.3	7.1	4.7	4.3	4.9	5.4
			Range	4.6～18	1.6～31	1.1～35	1.0～35	0.55～21	0.37～17	0.37～35
		MBzP	Median	0.59	0.68	0.60	0.44	0.42	0.47	0.53
			Range	0.25～10	N.D.～38	N.D.～7.0	N.D.～15	N.D.～4.3	N.D.～200	N.D.～200
	Bisphenol A		Median	0.76	0.44	0.26	0.26	0.29	0.20	0.29
			Range	0.23～1.4	N.D.～31	N.D.～8.2	N.D.～2.5	N.D.～3.2	N.D.～2.1	N.D.～31

□ Table 14-2. Statistics of pesticides, plasticizers, and others in urine (2)

(unit：μg/g Cr)

Classification	Chemical compounds		Statistics	FY 2011 (n=15)	FY 2012 (n=30)	FY 2013 (n=30)	FY 2014 (n=30)	FY 2015 (n=77, only Ethylenethiourea n=15)	FY 2016 (n=80, only Ethylenethiourea n=15)	Total (n=262, only Ethylenethiourea n=135)
Pesticide metabolites	Organic phosphorus metabolites	DMP	Median	5.6	2.4	3.3	2.9	2.5	2.0	2.5
			Range	1.8～14	0.60～11	N.D.～140	N.D.～15	N.D.～30	N.D.～24	N.D.～140
		DEP	Median	5.8	5.6	2.1	2.0	2.7	3.4	3.2
			Range	N.D.～32	N.D.～520	N.D.～14	N.D.～13	N.D.～150	N.D.～480	N.D.～520
		DMTP	Median	12	7.7	3.5	5.1	2.8	2.3	3.6
			Range	N.D.～62	N.D.～82	N.D.～110	N.D.～61	N.D.～77	N.D.～110	N.D.～110
		DETP	Median	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
			Range	N.D.～2.7	N.D.～8.3	N.D.～4.6	N.D.～5.1	N.D.～16	N.D.～19	N.D.～19
	Pyrethroid pesticide metabolites	PBA	Median	0.22	0.22	N.D.	0.42	0.27	0.47	0.33
			Range	N.D.～3.4	N.D.～1.6	N.D.～3.3	N.D.～2.0	N.D.～8.7	N.D.～21	N.D.～21
		DCCA	Median	N.D.	N.D.	All N.D.	N.D.	N.D.	N.D.	N.D.
			Range	N.D.～13	N.D.～3.1		N.D.～2.5	N.D.～21	N.D.～26	N.D.～26
	Carbamate pesticide metabolite	Ethylenethiourea	Median	N.D.	N.D.	All N.D.	All N.D.	All N.D.	All N.D.	N.D.
			Range	N.D.～0.23	N.D.～0.50					N.D.～0.50
others	Triclosan		Median	1.3	1.3	1.1	1.2	1.7	0.74	0.97
			Range	0.27～79	0.15～120	0.15～380	0.17～130	0.12～270	0.090～83	0.090～380

□ Table 14-3. Statistics of pesticides, plasticizers, and others in urine (3)

(unit：μg/g Cr)

Classification	Chemical compounds		Statistics	FY 2012 (n=30)	FY 2013 (n=15)	FY 2014 (n=15)	FY 2015 (n=15, only Imidachloprid metabolite n=77)	FY 2016 (n=15, only Imidachloprid metabolite n=80)	Total (n=90, only Imidachloprid metabolite n=217)
Pesticides・Pesticide metabolites	Acephate		Median	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
			Range	N.D.～0.30	N.D.～1.9	N.D.～0.61	N.D.～11	N.D.～4.8	N.D.～11
	Methamidophos		Median	N.D.	All N.D.	All N.D.	N.D.	N.D.	N.D.
			Range	N.D.～0.058			N.D.～0.19	N.D.～0.11	N.D.～0.19
	Imidachloprid metabolite	6-Chloronicotinic acid	Median	N.D.	All N.D.	All N.D.	N.D.	N.D.	N.D.
			Range	N.D.～1.8			N.D.～0.74	N.D.～0.39	N.D.～1.8
	Fenitrothion metabolite	3-Methyl-4-nitrophenol	Median	N.D.	0.30	N.D.	N.D.	0.20	N.D.
			Range	N.D.～2.8	N.D.～2.7	N.D.～3.6	N.D.～4.2	N.D.～30	N.D.～30
	p-Nitropheol		Median	0.67	0.97	0.44	0.42	0.52	0.61
			Range	0.23～4.6	0.49～2.4	N.D.～2.6	N.D.～2.9	0.28～44	N.D.～44

☐ Table 14-4. Statistics of pesticides, plasticizers, and others in urine (4)

(unit：μg/g cr)

Classification		Chemical compounds	Statistics	FY 2012 (n=30)	FY 2013 (n=15)	FY 2014 (n=15)	FY 2015 (n=15)	FY 2016 (n=15)	Total (n=90, only 8-OHdG n=30)
Others		Deet	Median	All N.D.	All N.D.	All N.D.	N.D.	N.D.	N.D.
			Range				N.D.～0.087	N.D.～0.12	N.D.～0.12
	Parabens	Methylparaben	Median	55	95	120	91	23	72
			Range	1.3～870	1.4～2,500	3.5～1,100	5.9～630	1.3～810	1.3～2,500
		Ethylparaben	Median	2.5	3.4	2.7	7.6	2.2	3.8
			Range	N.D.～120	N.D.～410	N.D.～290	N.D.～100	N.D.～12	N.D.～410
		Propylparaben	Median	1.0	2.0	1.1	N.D.	N.D.	0.62
			Range	N.D.～71	N.D.～77	N.D.～41	N.D.～110	N.D.～6.8	N.D.～110
		Butylparaben	Median	N.D.	N.D.	0.61	N.D.	N.D.	N.D.
			Range	N.D.～25	N.D.～64	N.D.～87	N.D.～7.0	N.D.～3.9	N.D.～87
		Benzylparaben	Median	All N.D.	All N.D.	All N.D.	All N.D.	All N.D.	All N.D.
			Range						
		Iodine	Median	310	290	300	340	200	300
			Range	110～3,000	75～9,100	73～3,400	110～8,800	70～6,600	70～9,100
		Perchloric acid	Median	3.5	4.7	3.1	3.8	1.1	3.3
			Range	1.2～10	N.D.～67	N.D.～12	N.D.～29	N.D.～7.4	N.D.～67
	PAH metabolites	1-Hydoroxypyrene	Median	0.19	0.071	0.098	0.075	N.D.	0.080
			Range	0.045～0.76	N.D.～0.54	0.022～4.7	N.D.～0.33	N.D.～0.064	N.D.～4.7
		1&9-Hydroxyphenanthrene	Median	0.15	0.085	0.060	0.080	N.D.	0.086
			Range	0.038～0.60	0.029～0.21	N.D.～0.69	N.D.～0.35	N.D.～0.067	N.D.～0.69
		2-Hydroxyphenanthrene	Median	0.14	0.066	N.D.	0.12	0.014	0.073
			Range	0.031～0.39	N.D.～0.19	N.D.～0.46	0.062～0.26	N.D.～0.10	N.D.～0.46
		3-Hydroxyphenanthrene	Median	0.24	0.079	0.057	0.20	0.038	0.14
			Range	0.077～0.65	N.D.～0.37	N.D.～0.57	0.093～0.49	N.D.～0.24	N.D.～0.65
		4-Hydroxyphenanthrene	Median	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
			Range	N.D.～0.20	N.D.～0.043	N.D.～0.12	N.D.～0.065	N.D.～0.045	N.D.～0.20
		Cotinine	Median	0.92	N.D.	0.11	N.D.	0.76	0.34
			Range	0.060～1,600	N.D.～2.0	N.D.～1,400	N.D.～3,000	N.D.～3,600	N.D.～3,600
		8-OHdG	Median	—	—	—	5.0	3.9	4.1
			Range				1.2～7.7	2.0～9.8	1.2～9.8
		Caffeine	Median	1,100	3,200	1,900	1,600	1,900	1,900
			Range	0.36～9,100	100～22,000	360～14,000	230～16,000	2.7～5,900	0.36～22,000
		Benzophenone-3	Median	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
			Range	N.D.～120	N.D.～190	N.D.～2.0	N.D.～120	N.D.～140	N.D.～190
	Phytoestrogens	Genistein	Median	1,700	880	940	800	1,700	1,300
			Range	360～5,700	190～3,800	74～4,700	89～7,600	230～23,000	74～23,000
		Daidzein	Median	2,700	1,600	1,500	1,100	2,300	1,600
			Range	240～7,800	97～19,000	200～17,000	27～9,100	320～27,000	27～27,000
		Equol	Median	690	170	12	510	100	180
			Range	6.1～28,000	N.D.～11,000	4.1～3,100	N.D.～14,000	4.7～16,000	N.D.～28,000

3-5 POPs survey

3-5-1 Blood and food

The results for POPs concentrations in blood and the intake of POPs from food in the FY 2011 survey are shown in Tables 15-1 and 15-2.

☐Table 15-1. Statistics for blood POPs concentrations and the intake of POPs from food (1)

Chemical compounds		Statistics	Blood concentration FY 2011(n=86)	Intake from food FY 2011(n=15)
		Unit	pg/g-fat	pg/kg bw/day
PCB	MoCBs	Median	N.D.	7.4
		Range	N.D. ～ 430	3.0 ～ 89
	DiCBs	Median	100	200
		Range	N.D. ～ 800	100 ～ 620
	TrCBs	Median	920	400
		Range	210 ～ 3,700	180 ～ 1,400
	TeCBs	Median	6,400	750
		Range	650 ～ 33,000	230 ～ 4,100
	PeCBs	Median	18,000	930
		Range	1,900 ～ 140,000	130 ～ 8,200
	HxCBs	Median	87,000	980
		Range	12,000 ～ 670,000	100 ～ 14,000
	HpCBs	Median	62,000	420
		Range	10,000 ～ 520,000	37 ～ 7,500
	OcCBs	Median	13,000	71
		Range	2,600 ～ 110,000	4.1 ～ 1,100
	NoCBs	Median	1,300	11
		Range	370 ～ 6,600	1.1 ～ 91
	DeCB	Median	630	6.0
		Range	220 ～ 2,500	0.74 ～ 50
	Total PCB	Median	190,000	5,100
		Range	31,000 ～ 1,400,000	820 ～ 35,000
DDT	o,p'-DDD	Median	N.D.	39
		Range	N.D. ～ 500	4.1 ～ 550
	p,p'-DDD	Median	730	380
		Range	N.D. ～ 5,000	19 ～ 4,900
	o,p'-DDE	Median	200	27
		Range	N.D. ～ 1,100	4.8 ～ 210
	p,p'-DDE	Median	120,000	1,600
		Range	17,000 ～ 1,000,000	240 ～ 8,200
	o,p'-DDT	Median	600	66
		Range	N.D. ～ 4,500	8.5 ～ 1,400
	p,p'-DDT	Median	6,100	300
		Range	1,100 ～ 29,000	28 ～ 7,600
Chlordane	*cis*-Chlordane	Median	100	490
		Range	N.D. ～ 800	63 ～ 1,400
	trans-Chlordane	Median	N.D.	170
		Range	N.D. ～ 400	41 ～ 800
	Oxychlordane	Median	10,000	95
		Range	1,600 ～ 43,000	22 ～ 340
	cis-Nonachlor	Median	3,700	130
		Range	600 ～ 29,000	10 ～ 950
	trans-Nonachlor	Median	23,000	440
		Range	3,000 ～ 110,000	59 ～ 2,100
Drins	Aldrin	Median	All N.D.	N.D.
		Range		N.D. ～ 5.2
	Dieldrin	Median	3,200	510
		Range	1,300 ～ 40,000	71 ～ 1,800
	Endrin	Median	All N.D.	69
		Range		N.D. ～ 200
Hexachlorobenzene (HCB)		Median	14,000	630
		Range	3,400 ～ 39,000	160 ～ 2,100

□Table 15-2. Statistics for blood POPs concentrations and the intake of POPs from food (2)

Chemical compounds		Statistics	Blood concentration FY 2011(n=86)	Intake from food FY 2011(n=15)
		Unit	pg/g-fat	pg/kg bw/day
Heptachlor	Heptachlor	Median	All N.D.	13
		Range		4.5 ～ 47
	cis-Heptachlor epoxide	Median	1,800	110
		Range	600 ～ 6,500	63 ～ 430
	trans-Heptachlor epoxide	Median	All N.D.	All N.D.
		Range		
Toxaphene	parlar-26	Median	790	52
		Range	N.D. ～ 3,500	N.D. ～ 340
	parlar-50	Median	1,100	98
		Range	N.D. ～ 4,300	1.5 ～ 550
	parlar-62	Median	N.D.	73
		Range	N.D. ～ 3,400	N.D. ～ 430
Mirex		Median	1,800	14
		Range	400 ～ 6,600	2.2 ～ 190
PBDE	TeBDEs	Median	520	290
		Range	180 ～ 1,100	160 ～ 1,500
	PeBDEs	Median	210	150
		Range	N.D. ～ 870	63 ～ 710
	HxBDEs	Median	800	36
		Range	N.D. ～ 2,600	8.9 ～ 510
	HpBDEs	Median	All N.D.	N.D.
		Range		N.D. ～ 40
	OcBDEs	Median	300	25
		Range	N.D. ～ 3,400	N.D. ～ 110
	NoBDEs	Median	N.D.	36
		Range	N.D. ～ 2,000	N.D. ～ 120
	DeBDEs	Median	700	230
		Range	N.D. ～ 5,100	72 ～ 980
	Total PBDEs	Median	2,600	780
		Range	500 ～ 8,600	530 ～ 3,000
Pentachlorobenzene		Median	300	63
		Range	40 ～ 1,500	31 ～ 220
HCH	α -HCH	Median	120	160
		Range	N.D. ～ 1,200	64 ～ 1,000
	β -HCH	Median	27,000	250
		Range	2,800 ～ 240,000	48 ～ 2,000
	γ -HCH	Median	N.D.	47
		Range	N.D. ～ 1,000	23 ～ 430
	δ -HCH	Median	All N.D.	14
		Range		3.7 ～ 29
Chlordecone		Median	N.D.	All N.D.
		Range	N.D. ～ 1.0	
Hexabromobiphenyl		Median	N.D.	N.D.
		Range	N.D. ～ 700	N.D. ～ 6.3
Endosulfan	α - Endosulfan	Median	1,300	570
		Range	N.D. ～ 3,700	390 ～ 1,300
	β - Endosulfan	Median	N.D.	280
		Range	N.D. ～ 1,200	130 ～ 810
HBCD	α -HBCD	Median	N.D.	N.D.
		Range	N.D. ～ 10	N.D. ～ 9.0
	β -HBCD	Median	All N.D.	All N.D.
		Range		
	γ -HBCD	Median	N.D.	All N.D.
		Range	N.D. ～ 3.4	
	δ -HBCD	Median	All N.D.	All N.D.
		Range		
	ε -HBCD	Median	All N.D.	All N.D.
		Range		

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Supplementary Information

Overview of the Survey on the Accumulation of Dioxins and other chemical compounds in Humans (FY 2002–2010)

(1) Nationwide survey

● Blood dioxin concentrations

☐ Table 16. Blood dioxin concentrations according to the fiscal year of the study

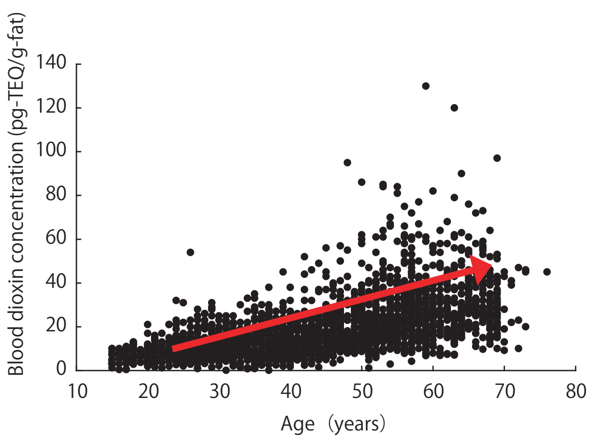
(unit: pg-TEQ/g-fat)

Survey year	FY 2002	FY 2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010	Nine-year average
Participants (N)	259	272	264	288	291	282	256	178	174	Total:2,264
Age (years)										
Average	44.4	41.7	45.2	44.3	43.0	44.2	47.6	46.3	44.4	44.5
Range	16〜72	15〜69	15〜70	15〜70	15〜72	15〜69	17〜70	18〜76	16〜70	15〜76
PCDDs+PCDFs Co-PCBs										
Average	22	19	19	22	17	20	21	17	14	19
Standard deviation	14	12	13	15	12	15	15	12	13	14
Median	19	17	16	17	14	16	17	14	11	16
Range	0.96〜95	2.7〜97	0.64〜85	1.5〜75	0.82〜67	1.6〜120	0.43〜130	1.1〜59	0.10〜82	0.10〜130

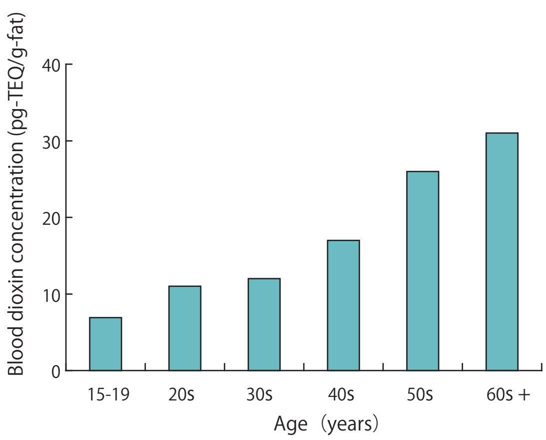
(According to WHO 2006 TEFs)

● Relationship to age

Figure 1. Relationship between age and blood dioxin concentrations



☐ Figure 2. Blood dioxin concentrations by age group



(According to WHO 2006 TEFs)

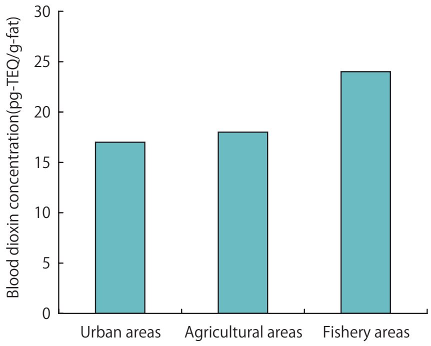
Differences in blood dioxin concentrations by area

☐ Table 17. Blood dioxin concentrations by types of survey area

	Urban areas	Agricultural areas	Fishery areas
Participants (N)	938	675	651
Average age (years)	43.5	45.4	44.8
Blood dioxin concentration (pg-TEQ/g-fat)			
Average	17	18	24
Standard deviation	11	12	17
Median	15	15	19
Range	0.11～77	0.10～97	0.43～130

(According to WHO 2006 TEFs)

☐ Figure 3. Blood dioxin concentrations by types of survey area



(According to WHO 2006 TEFs)

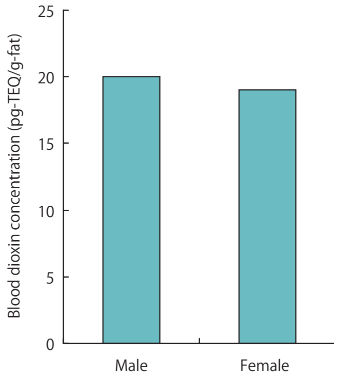
Difference in blood dioxin concentrations by gender

☐ Table 18. Blood dioxin concentrations by gender

	Male	Female
Participants (N)	1,063	1,201
Average age (years)	43.5	45.3
Blood dioxin concentration (pg-TEQ/g-fat)		
Average	20	19
Standard deviation	15	13
Median	16	16
Range	0.64～130	0.10～95

(According to WHO 2006 TEFs)

☐ Figure 4. Blood dioxin concentrations by gender



Intake of dioxin from food by survey

☐ Table 19. Intake of dioxin from food according to the fiscal year of the study

Survey year	FY 2002	FY 2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010	Nine-year average
Participants (N)	75	75	75	75	75	75	75	50	50	Total: 625
Dioxin intake from food (pg-TEQ/kg bw/day)										
Average	1.1	1.1	0.89	0.89	0.57	0.75	0.68	0.79	0.44	0.82
Standard deviation	1.1	0.92	0.66	0.89	0.44	0.90	0.75	1.2	0.42	0.86
Median	0.75	0.91	0.68	0.59	0.41	0.46	0.39	0.43	0.34	0.56
Range	0.058～5.6	0.14～5.6	0.16～3.7	0.13～5.2	0.099～2.2	0.060～6.2	0.054～4.8	0.055～6.2	0.031～2.0	0.031～6.2

(According to WHO 2006 TEFs)

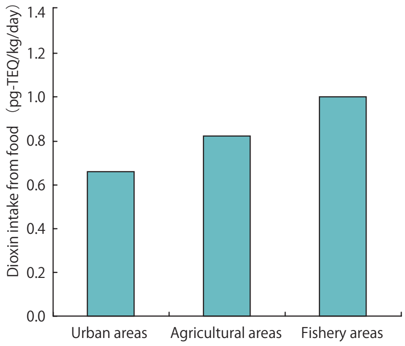
Differences in the intake of dioxin from food by area

☐ Table 20. Intake of dioxin from food by area

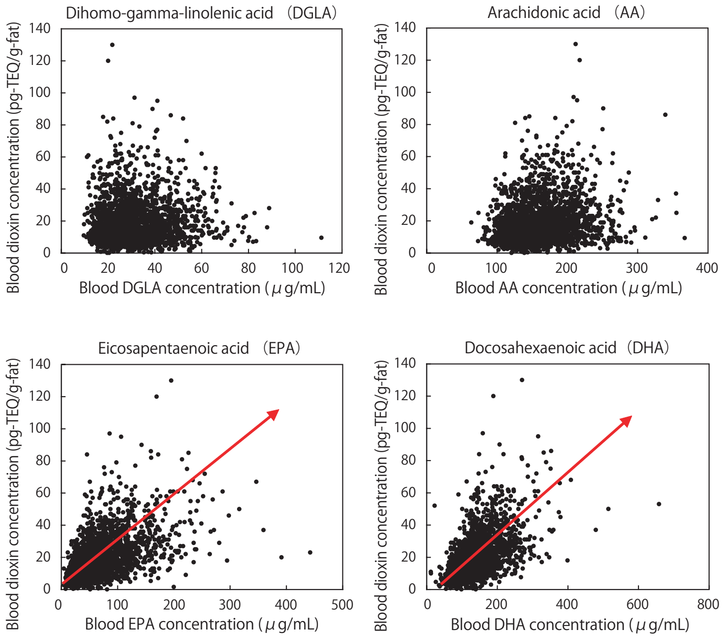
	Urban areas	Agricultural areas	Fishery areas
Participants (N)	229	201	195
Dioxin intake from food (pg-TEQ/kg wg/day)			
Average	0.66	0.82	1.0
Standard deviation	0.65	0.86	1.0
Median	0.46	0.53	0.71
Range	0.031～6.2	0.080～5.6	0.054～6.2

(According to WHO 2006 TEFs)

☐ Figure 5. Intake of dioxin from food by area

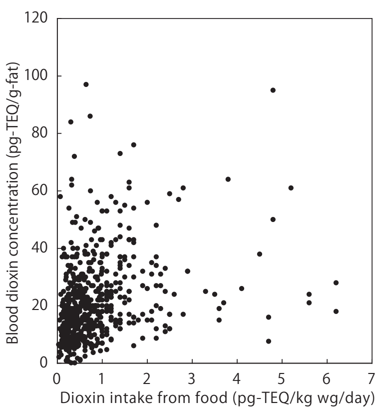


☐ Figure 6. Relationship between fatty acids and blood dioxin concentrations



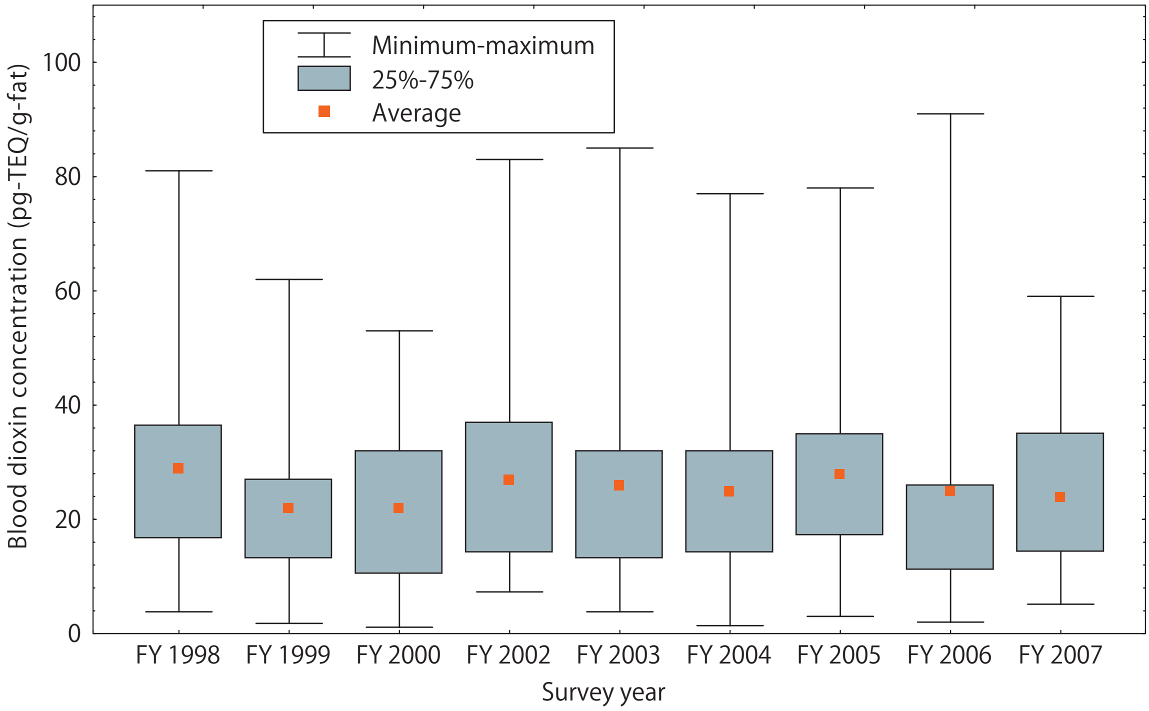
Relationship between blood concentrations and intake from food

☐ Figure 7. Relationship between dioxin intake from food and blood dioxin concentrations

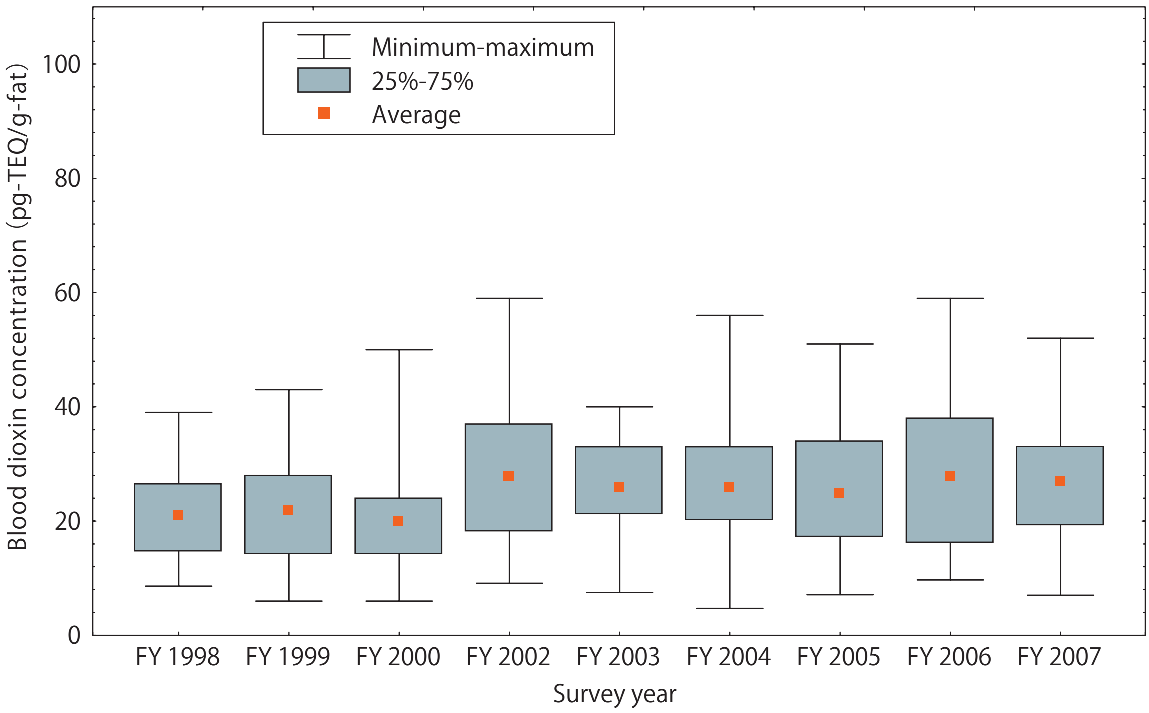


(2) Follow-up survey

☐ Figure 8. Chronological change in blood dioxin concentrations in Nose, Osaka Prefecture



☐ Figure 9. Chronological change in blood dioxin concentrations in Saitama Prefecture

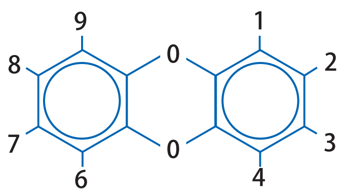


Chemical compounds measured in this survey

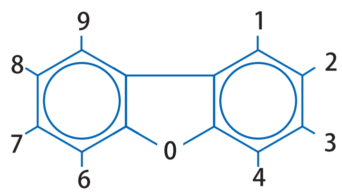
1. Dioxins

1.1 Structure of dioxins

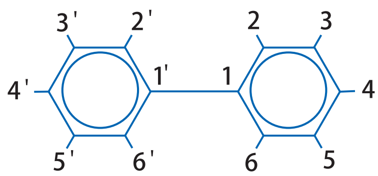
Polychlorodibenzo-p-dioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs) are collectively called dioxins. Co-planar polychlorinated biphenyls (co-planar PCBs) possess toxicity similar to those of dioxins, therefore are also known as dioxin-like compounds. Dioxins by definition include PCDDs, PCDFs, and co-planar PCBs according to Japan's Law Concerning Special Measures against Dioxins, promulgated on July 16, 1999. Accordingly, throughout this report, the term "dioxins" refers to PCDDs, PCDFs, and co-planar PCBs. The chemical structure of a dioxin molecule is generally composed of two rings of six-carbon atoms (benzene rings; the figure below) bound by oxygen atom(s) (shown as "⬡" in the figure below) with chlorine or hydrogen atoms attached (at numbered positions 1–9 and 2'–6' in the figure below). There are 75 types of PCDDs, 135 types of PCDFs, and 12 types of coplanar PCBs, and the variations depend on the numbers and locations of the attached chlorine atoms. Among these dioxins, 29 types have toxicities similar to 2,3,7,8-TCDD.



PCDDs



PCDFs



PCBs※

※ PCB compounds with two benzene rings on the same plane, are known as co-planar PCBs. Note that some PCBs without the planar structure but possess dioxin-like toxicity, are also classified as co-planar PCBs for a regulatory purpose.

1.2 Properties of dioxins

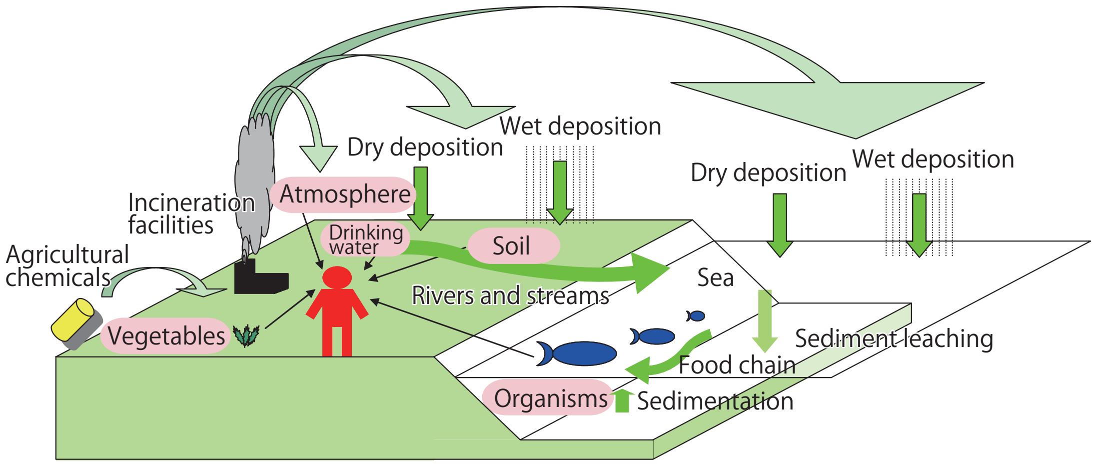
Dioxins are generally colorless solids of very low water solubility and low vapor pressure, but characteristically exhibit a high degree of solubility in fats and oils. They are generally stable, do not react easily with other compounds, acids, and alkalis, and are considered to decompose gradually in the presence of solar ultraviolet light.

1.3 Dioxin toxicity

Carcinogenicity and chronic toxicity are health risks posed by dioxins. In rats, dioxins have been reported to show carcinogenicity, such as the production of hepatocellular carcinoma, follicular adenoma of the thyroid, lymphoma, and other cancers. Dioxins are known to act as promoters for the carcinogenic mechanism; that is, dioxins do not act directly on genes, instead they promote the carcinogenic activity of other carcinogens. At present, the International Agency for Research on Cancer (IARC) and the World Health Organization (WHO) have classified 2,3,7,8-TCDD as a human carcinogen. In terms of hepatotoxicity, it is recognized to cause elevated liver enzymes and hyperlipidemia. However, for assessing the consequences of dioxin exposure during fetal stages, reproductive organ toxicity, central nervous system toxicity, and immune system toxicity received attentions when the WHO reevaluated the risks of dioxins and related compounds in 1998, as well as risk assessments that are being conducted both nationally and internationally. Shortened anogenital distance in males, congenital abnormalities in vagina, diminished learning ability, diminished resistance to viral infection, and other outcomes in laboratory animals. At present, the effects of dioxins are widely recognized to develop due to endocrine disruption through the arylhydrocarbon receptor (AhR) within cells. However, further studies are required because there is limited data available regarding the appearance of these diverse toxicities.

1.4 Generation and behavior of dioxins in the environment

Dioxins are not produced intentionally except for research purposes, such as the production of standard materials for dioxin analysis. Dioxins are by-products generated when substances containing carbon, oxygen, hydrogen, and chlorine are heated. The major source of dioxins today is waste incineration, particularly the incineration of plastic waste and other products made from fossil fuels. Dioxins are formed in combustion processes and emitted into the air when they are not captured by waste-gas mechanisms. Other sources include emissions from electric steel-making furnaces, cigarette smoke, and automobile exhaust. Some reports indicate that dioxins may have accumulated in bottom sediment in aquatic environments owing to the past use of PCBs and some types of agricultural chemicals, which contain dioxins as impurities. The behavior of dioxins in the environment is not fully known. Dioxins in the air presumably are adsorbed to particulate matter, fall to the ground, and then pollute soil and water. It is considered that over long period of time, these dioxins and others are released into the environment by various other pathways, and they ultimately accumulate in aquatic sediments and enter the food chain when ingested by plankton and fish, thereby accumulating in various organisms. Although dioxins are mostly anthropogenically produced, small amounts are generated in nature through forest fires and volcanic activities.



1.5 Brominated dioxins

Brominated dioxins have a similar structure to chlorinated dioxins, whereby some chlorines are substituted with bromines. Similar to chlorinated dioxins, brominated dioxins are not produced intentionally except for research purposes and are by-products that occur when heat is applied to organobromine compounds and in combustion processes. They are mainly produced through heating processes during the production and processing of plastics including brominated flame retardants. Their toxicity and health effects are less understood than chlorinated dioxins.

2． Organic fluorine compounds

PFOS and PFOA are organic fluorine compounds that have fluoride atom(s) bound to carbon. Carbon and fluoride are strongly bound to each other, and the compounds are highly resistant to heat and chemicals. These compounds have been used widely as “surfactants” because they are readily soluble in oil and water, and are used in water-repellent sprays, foam fire extinguishers, and until very recently, in coatings of nonstick frying pans. However, it has been reported that they are resistant to decomposition in the environment and in living organisms, and that they have substantial bioaccumulation properties. PFOS is listed as a POPs in the Stockholm Convention on Persistent Organic Pollutants. In the present survey, organic fluorine compounds including PFOS and PFOA were studied in blood and food.

☐ Table 21. Organic fluorine compounds

Chemical compound	Usage	Measurement case in Japan (average)	Standard; Tolerable intake
Fluorine compounds	Used in water-repellent sprays and foam fire extinguishers as surfactants. (PFOS, PFOA)	< Blood> PFHxA: <0.091 ng/mL (60 females; Kashino et al., 2011 ※ plasma) PFHpA: <0.079 ng/mL (60 females; Kashino et al., 2011 ※ plasma) N.D. ng/mL (14 females; Nakai et al.,2008) PFOA: 0.48 ～ 6.93 ng/mL (60 females; Kashino et al., 2011 ※ plasma) 1.72 ng/mL (14 females; Nakai et al.,2008) 4.0 ng/mL (97 males; Harada et al., 2003-2004 ※ serum) 4.4 ng/mL (103 females; Harada et al., 2003-2004 ※ serum) PFNA: 0.43 ～ 3.16 ng/mL (60 females; Kashino et al., 2011 ※ plasma) 0.87 ng/mL (14 females; Nakai et al.,2008) PFDA: 0.18 ～ 1.17 ng/mL (60 females; Kashino et al., 2011 ※ plasma) PFTeDA: N.D. ng/mL (60 females; Kashino et al., 2011 ※ plasma) PFOS : 0.86 ～ 10.96 ng/mL (60 females; Kashino et al., 2011 ※ plasma) 2.86ng/mL (14 females; Nakai et al.,2008) 18.3 ng/mL (97 males; Harada et al., 2003-2004 ※ serum) 11.7 ng/mL (103 females; Harada et al., 2003-2004 ※ serum) <Food> PFOS: 0.98 ng/kg bw/day (ND and/or below = 0) 12.1 ng/kg bw/day (ND and/or below = 1/2 ND) (Maitani et al., 2007 market-basket system; Mitani et al.) PFOA: 0.06 ng/kg bw/day (ND and/or below = 0) 11.5 ng/kg bw/day (ND and/or below = 1/2 ND) (Maitani et al., 2007 market-basket system)	※ Tolerable intake is not established.

3． Metals

Metals are widely distributed on the earth and are used for various purposes. However, some metals are potentially toxic to organisms. In the past, Japan has experienced damage to the health of people by environmental heavy metal pollution, such as Minamata disease caused by methyl mercury and Itai-Itai Disease caused by cadmium.

☐ Table 22-1. Metals studied in this survey

Chemical compounds	Usage	Measurement case in Japan (average)	Standard; Tolerable intake
Total mercury/Methyl mercury	Metal mercury is used in fluorescent lights, amalgam, batteries, catalysts, and others. Methyl mercury is produced by methylation of metal mercury. Methyl mercury have higher toxicity.	＜ Total mercury / blood ＞ 5.4 ng/mL （600 mothers; Shimada et al., 2008） 5.18 ng/mL （115 mothers; Sakamoto et al., 2007） 18.2 ng/mL （56 females; Yamauchi et al., 1994） ＜ Total mercury / food ＞ 0.225 μ g/kg bw/day （Tokyo, 2005; 10 samples by duplicated portion method） 0.17 μ g/kg bw/day （Tokyo, 2015; market-basket system） ＜ Methyl mercury / food ＞ 0.198 μ g/kg bw/day （Tokyo, 2005; 10 samples by duplicated portion method） 0.17 μ g/kg bw/day （Tokyo, 2015; market-basket method）	＜ Methyl mercury ＞ 2.0 μ g/kg bw/week
Lead	Used widely in electrodes, weight, glass products , solder, and others.	＜ Blood ＞ 10.7 ng/mL (352 people:1-15 years ;Yoshinaga et al., 2008-1010) 13 ng/mL (137 people including infant; Tokyo, 2006) ＜ Food ＞ 0.129 μ g/kg bw/day (319 samples by duplicated portion method; Food safety commission of Japan, 2006-2010) 0.17 μ g/kg bw/day (Tokyo, 2015; maket-basket method)	※ Tolerable intake is not established.
Cadmium	Used in watch batteries, plating materials , and others. Cadmium is produced and recovered during the zinc refinery process.	<Blood> 2.54 μ g/L （1243 females; kayama et al., 2010-2011） ＜ Urine ＞ 3.46 μ g/g Cr （1243 females; Kayama et al., 2000 – 2001） 1.26 μ g/g Cr （10753 females; Ikeda et al., 2000 – 2001） ＜ Food ＞ 0.320 μ g/kg bw/day （Tokyo, 2005 10 samples by duplicated portion method） 0.47 μ g/kg bw/day (Tokyo, 2015; market-basket method)	7 μ g/kg bw/week

☐ Table 22-2. Metals studied in this survey

Chemical compounds	Usage	Measurement case in Japan (average)	Standard; Tolerable intake
Arsenic	In the past, arsenic compounds were used in rat poisons. Organic arsenic is found in seafood (seaweeds, shrimps, and crabs) but are basically non-toxic. Inorganic arsenic is highly toxic.	＜ Total Arsenic / blood> 5.0 ng/mL (137 people including infant; Tokyo, 2006) ＜ Arsenic speciation / urine ＞ MMA: 2.01 μ g/g Cr DMA: 40 μ g/g Cr （248 residents near metropolitan area Chiba et al., 2001） As (V) 0.2 μ g/g Cr As (III) 4.0 μ g/g Cr MMA: 3.2 μ g/g Cr DMA: 38.5 μ g/g Cr AB: 71.4 μ g/g Cr （142 males; Nakajima et al., 2001） ＜ Total Arsenic / food ＞ 3.44 μ g/kg bw/day (319 samples by duplicated portion method Food safety commission of Japan, 2006-2010)	※ Tolerable intake is not established.
Copper	Used widely in electric wire, roofing, and others.	＜ Blood ＞ 950 ng/mL (145 males) 970 ng/mL (163 females) (Saitoh et al., 1980) ＜ Food ＞ 1.12 mg/day (8,047 samples; Ministry of Health, Labour and Welfare 2014)	10 mg/day (tolerable upper intake level ; males and females 18 years or older)
Selenium	Used in photo sensitive drum of copier, colorant for glass , and soil amendments for place of selenium deficiency.	＜ Blood ＞ 157 ng/g : males 157 ng/g : females (331 participants; Seki et al., 1981) ＜ Food ＞ 0.17 mg/day (39 males) 0.19 mg/day (40 females) (Duplicated portion method Chiba et al., 2003)	330 ～ 460 μ g/day (tolerable upper intake level ; males and females 18 years or older)
Zinc	Used widely in corrugated galvanised iron, pigment, alloy material and cosmetic , and others.	＜ Blood ＞ 8,540 ng/mL (145 males) 8,150 ng/mL (163 females) (Saitoh et al., 1980) ＜ Food ＞ 7.9 mg/day (8,047 samples; Ministry of Health, Labour and Welfare, 2014)	35 ～ 45 mg/day (tolerable upper intake level ; males and females 18 years or older)
Manganese	Used in Battery materials and fertilizer raw materials.	＜ blood ＞ 13.2 μ g/L (1,420 females; Ikeda et al., 2010) ＜ Food ＞ 5.53 mg/day (39 males) 6.11 mg/day (40 females) (Duplicated portion method Chiba et al., 2003)	11 mg/day (tolerable upper intake level ; males and females 18 years or older)

4. Other chemical compounds (including pesticides and plasticizers)

The summaries of pesticides, plasticizers, and others measured in this survey are shown in Table 23-1 and 23-2.

☐ Table 23-1. Pesticides, plasticizers, and others studied in this survey

Chemical compound	Usage	Measurement case in Japan (average)
Hydroxylated PCB	Metabolite of PCB.	＜ Blood ＞ 120 pg/g（128 pregnant women; Hisada et al., 2009-2011）
Phthalate monoesters	Used as plasticizer in plastic, adhesive agents, and others.	＜ Urine ＞ MBP：52.2 μ g/g Cr (48.1 ng/mL) MEHP：5.84 μ g/g Cr (4.44 ng/mL) MEHHP：10.1 μ g/g Cr (8.61 ng/mL) MEOHP：11.0 μ g/g Cr (9.2 ng/mL) MBzP：4.70 μ g/g Cr (3.46 ng/mL) (149 pregnant women; Suzuki et al., 2010) ※ median
Bisphenol A	Used as monomer or ingredients in plastic manufacturing.	＜ Urine ＞ N.D. μ g/g Cr (39 out of 56 pregnant women) 1.7 μ g/g Cr（median ; 17 out of 56 pregnant women） (Fujimaki et al., 2003)
Organophosphorous compound metabolites	Used in pesticides, disinfectant, wood preservatives, and others (metabolites were measured).	＜ Urine ＞ DMP：1.5 μ g/L（73 participants, Toyama） ：3.1 μ g/L（60 participants, Tokyo） DMTP：3.2 μ g/L（73 participants, Toyama） ：5.8 μ g/L（60 participants, Tokyo） DEP：0.8 μ g/L（73 participants, Toyama） ：1.2 μ g/L（60 participants, Tokyo） DETP：<0.5 μ g/L（73 participants, Toyama） ：<0.5 μ g/L（60 participants, Tokyo） (Nakazaki et al.,)
Pyrethroid pesticide metabolites	Used in pesticides, insecticides, and others (metabolites were measured).	＜ Urine ＞ PBA：0.40 μ g/g Cr （42 males　Toshima et al., 2010） PBA：0.73 μ g/g Cr （448 participants; Ueyama et al., 2009）
Carbamate pesticide metabolites	Used in pesticides, insecticides, and others (metabolites were measured).	—
Triclosan	Used as disinfectant	—
Acephate	A type of organophosphorus pesticides. Used widely as pesticides and insecticides, known as “Orthoran”.	—
Methamidophos	A type of organophosphorus pesticide. Used as pesticides and insecticides (banned to use in Japan).	—
Imidachloprid metabolite	Metabolite of neonicotinoid pesticide.	—
Fenitrothion metabolite	Metabolite of fenitrothion.	—
p-nitrophenol	Metabolite of pesticides.	—
Deet	Used as mosquito and mite repellent.	—

☐ Table 23-2. Pesticides, plasticizers, and others studied in this survey

Chemical compound	Usage	Measurement case in Japan (average)
Parabens	Used as antiseptic (antibacterial) agent in food, medicine, cosmetics, etc.	＜ Urine ＞ Methylparaben : 109 μ g/g Cr Ethylparaben : 8.0 μ g/g Cr Propylparaben : 33.5 μ g/g Cr Butylparaben : 0.743 μ g/g Cr (111 pregnant women; Shirai et al., 2007-2010) ※ median
Iodine	Essential element for human and is the main component of thyroid hormone. Found abundantly in sea weeds. Deficiency causes hyperthyroidism, but excessive intake also causes thyroid abnormalities as well.	＜ Urine ＞ 259.5 μ g/g Cr (622 pregnant women; Orito et al., 2005-2006) ※ median
Perchloric acid	Has strong oxidizing effect. Used as analytical chemistry reagent, metal/ alloy/ mineral ore solvent, organic synthesis catalysis, and as manufacturing material of perchloric acid and its derivatives.	—
PAHs metabolites	Metabolite of PAHs, found mainly as mixtures in tar, crude oil, and in petroleum.	＜ Urine ＞ 1-Hydoroxypyrene：124 μ g/g Cr (149 pregnant women; Suzuki et al., 2010) ※ median
Cotinine	Metabolite of nicotine found in tobacco.	＜ Urine ＞ 16 μ g/g Cr（smoking parents) 12 μ g/g Cr (Only the mother smokes) 3 μ g/g Cr (only the father smokes) 1 μ g/g Cr (non-smoking parents) (927 three year old children; Tateishi et al.) 3,048 μ g/g Cr (smoking) 28.7 μ g/g Cr (non-smoking and passive smoking) 33.9 μ g/g Cr (non-smoking and non- passive smoking) (504 adults; Sakanashi et al., 2009)
8-OHdG	8-OHdG is generated when DNA is exposed to UV, radiation, and/or chemical substances.	＜ Urine ＞ 15.4 μ g/g Cr (248 healthy people; Yamauchi et al., 2001)
Caffeine	Naturally derived organic compound found abundantly in coffee, tea, and chocolate.	—
Benzophenone-3	Used in sunscreen cosmetics due to its ultraviolet absorption effect.	—
Phytoestrogens	Found abundantly in leguminous plants (bean plants) such as soy beans, and act as female hormone .	＜ Urine ＞ Daizein: 1,000 μ g/g Cr Genistein: 860 μ g/g Cr (80 adult women; Tsukane et al.)

5. POPs

POPs is the abbreviation of Persistent Organic Pollutants and have the following properties:

○ they remain intact for exceptionally long period of time,
○ they accumulate in bodies of organisms,
○ they can be transported long distances and are widely distributed on the earth,
○ they have toxic effects within organisms.

The Stockholm Convention on Persistent Organic Pollutants is an international treaty. Initially, 12 POPs were recognized, which has now added up to 26. These compounds include those produced and used intentionally as pesticides and others. On the other hand, there are compounds like dioxins, which could be produced in the process of combustion or manufacturing of other chemicals. In the Convention, each member State is to prohibit the production, use, import and export of POPs, and to take every measure possible to eliminate and reduce the unintentional production of compounds. Furthermore, each member State is encouraged to undertake measures for POPs under the Stockholm Convention. Considering this, monitoring surveys on the environment and biological samples are conducted by Ministry of the Environment, Japan. In the present survey, POPs listed in Table 24 were measured in blood and food.

☐ Table 24. POPs studied in this survey

Chemical compounds	Usage
Dioxins	Produced unintentionally due to combustion, as well as during the manufacture of chlorinated substances
PCBs	Used as heat exchange fluids, in electric transformers, and as additives in carbonless copy papers and such
DDT	Used as hygiene pesticides and insecticides
Chlordane	Used to control termites and as pesticides
Aldrin	Used as pesticides
Dieldrin	Used as pesticides, insecticides, and termite control
Endrin	Used as pesticides
Hexachlorobenzene (HCB)	Used as material for herbicide manufacturing
Heptachlor	Used as pesticide and termite control
Toxaphene	Used as pesticides overseas
Mirex	Used as pesticides overseas
PBDE	Used as fire-retardant
Pentachlorobenzene	Used as chemical intermediate of agricultural fungicides
HCH	Used as pesticides
Chlordecone	Used as insecticides overseas
Hexabromobiphenyl	Used as fire-retardant
Endosulfan	Used as pesticides and insecticides
HBCD	Used as fire-retardant

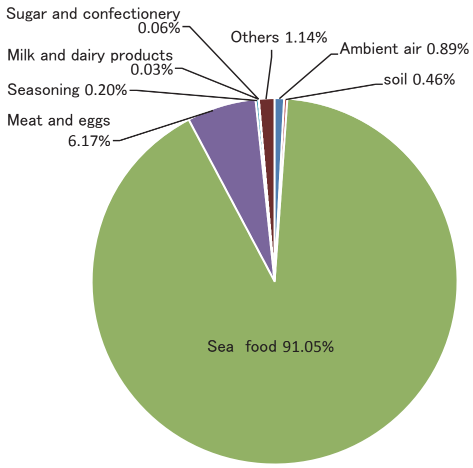
6. Dioxin intake

In Japan in June 1999, the TDI of dioxins was set at 4 pg-TEQ/kg bw/day based on the available scientific information at the time. The safety of the total amount of dioxins ingested by humans is evaluated by comparisons with this value.

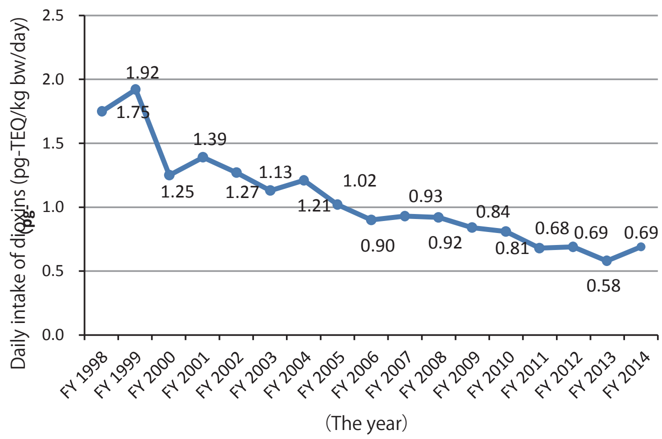
On average, the total daily intake of dioxins by the Japanese people is estimated to be approximately 0.70 pg-TEQ/kg bw/day. These levels are below the TDI and therefore considered to be below the level that can cause adverse effects on human health. Conceivable routes of intake include food, ambient air, and soil, but the intake from food is estimated to account for the largest portion (Figure 10). Figure 11 shows the chronological change in estimated total daily intake of dioxins by the Japanese people using the results of "Survey on the Daily Intake of Dioxins from Food" (Ministry of Health, Labour and Welfare, Japan). Enforcement of the "Law Concerning Special against Dioxins (January, 2000)" has greatly decreased emission of dioxins to environment. Dioxin concentrations in food and the environment (ambient air and soil) have also has decreased. As a result, the total daily intake of dioxins by the Japanese people showed a trend of decrease.

It is anticipated that the total daily intake will be reduced further owing to continuous measures against reduced emissions of dioxins.

□ FIgure 10 Specifications for the average daily intake of dioxins by the Japanese people Note1



□ Figure 11 Chronological change in the average daily intake of dioxins by Japanese people Note2



Note 1 : Graphed by MOE from the data of "FY 2014 Environmental Survey of Dioxins" (MOE) and "FY 2014 Survey on the Daily Intake of Dioxins from Food, Health and Labour Sciences Research" (Ministry of Health, Labour, and Welfare, Japan).
Note 2 : "FY 2014 Survey on the Daily Intake of Dioxins from Food, Health and Labour Sciences Research."(MHLW).

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