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Cadmium and Lead Residue Control in a Hazard Analysis and Critical Control Point (HACCP) Environment

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In 2003−2004, the U.S. Department of Agriculture Food Safety and Inspection Service (FSIS) conducted an exploratory assessment to determine the occurrence and levels of cadmium and lead in randomly collected samples of kidney, liver, and muscle tissues of mature chickens, boars/stags, dairy cows, and heifers. The data generated in the study were qualitatively compared to data that FSIS gathered in a 1985−1986 study in order to identify trends in the levels of cadmium and lead in meat and poultry products. The exploratory assessment was necessary to verify that Hazard Analysis and Critical Control Point plans and efforts to control exposure to these heavy metals are effective and result in products that meet U.S. export requirements. A comparison of data from the two FSIS studies suggests that the incidence and levels of cadmium and lead in different slaughter classes have remained stable since the first study was conducted in 1985−1986. This study was conducted to fulfill FSIS mandate to ensure that meat, poultry, and egg products entering commerce in the United States are free of adulterants, including elevated levels of environmental contaminants such as cadmium and lead.

KEYWORDS: Cadmium; lead; Hazard Analysis and Critical Control Point (HACCP)

INTRODUCTION

Cadmium (Cd) and lead (Pb) are chemical elements that are ubiquitous in the environment. The use of these chemical elements in industrial processes has affected their distribution pattern and their concentrations in soils, plants, and other environmental media. Cd and Pb accumulate in specific organs of the human body, and as is the case with other heavy metals, humans and animals have difficultly eliminating these compounds. Cd and Pb are considered to be cumulative poisons; thus, health effects from the exposure to Cd and Pb are rarely observed after a single exposure. Health effects from Cd and Pb exposure are chronic events, taking time and repeated exposure for the heavy metals to bioaccumulate to toxic levels.

Cd and Pb are bioaccumulative metals. Therefore, animals with longer life spans have high concentrations of Cd and Pb in their tissues. As a result of this bioaccumulation, the consumption of meat from older animals could represent an increased risk for ingestion of Cd and Pb. This bioaccumulation factor is demonstrated by results of the 1985−1986 Food Safety and Inspection Service (FSIS) study in which young chickens had lower levels and lower frequencies of detection for Cd and Pb than mature chickens (*1*). The contribution of the bioaccumulation factor to the overall exposure to Cd and Pb is diminished by the fact that Americans consume more young chickens than mature chickens. For instance, the consumption ratio of young to mature chickens was 56/1 in the calendar year 2004 (*2*); see **Table 1**.

Cadmium is classified as a human carcinogen by the International Agency for Research on Cancer (IARC), and exposure to Cd has also been associated with renal dysfunction and bone diseases (*3*). In food, Cd generally exists in complexes with ligands, including proteins such as metallothionein (*4*−*6*). Cadmium−metallothionein complexes are found in relatively high levels in organ meats (i.e., liver and kidney). Approximately 5% of the total ingested Cd from food is absorbed in the gastrointestinal tract. Cadmium concentrates in the human body in liver and kidney organs, with Cd levels in the kidney exceeding the levels in the liver following prolonged exposure. The excretion of Cd from the human body is a very slow process; the elimination half-life of Cd from the human body ranges from 10 to 30 years (*7*).

In the 1980s, the adult intake of Cd from food in the United States was estimated to be 30 μg/day based on the Food and Drug Administration's Total Diet Study, with the largest contribution from grain, cereal products, potatoes, and other vegetables (*8*). In addition, Thornton reported in 1992 a typical dietary intake of 0.23 mg/week of Cd, which is equivalent to a daily consumption of 33 μg/day (*9*). In 2004, the Codex Committee on Food Additives and Contaminants decided to discontinue work on establishing maximum residue levels

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Table 1. Domestic Consumption Data for Calendar Year 2004 (From FSIS 2004 National Residue Program Data)

production class	total pounds (dressed weight)	percent estimated relative consumption
bulls	503 985 982	0.493
beef cows	1 647 968 270	1.611
dairy cows	1 439 617 354	1.407
heifers	7 533 940 391	7.366
steers	12 860 188 767	12.573
bob veal	20 164 725	0.020
formula-fed veal	119 754 530	0.117
nonformula-fed veal	10 644 200	0.010
heavy calves	16 972 800	0.017
subtotal, cattle	24 153 237 019	23.614
market hogs	19 084 910 910	18.659
roaster pigs	38 517 010	0.038
boars/stags	70 997 832	0.069
sows	1 045 856 756	1.023
subtotal, swine	20 240 282 508	19.789
sheep	173 646 159	0.170
lambs	9 502 746	0.009
goats	27 935 150	0.027
subtotal, ovine	211 084 055	0.206
horses	32 600 000	0.032
bison	15 989 930	0.016
total, all livestock	44 653 193 512	43.657
young chickens	46 330 185 120	45.296
mature chickens	816 717 608	0.798
young turkeys	6 810 785 188	6.659
mature turkeys	75 276 157	0.074
ducks	174 223 959	0.170
geese	3 633 664	0.004
other fowl (includes ratites)	2 477 071	0.002
subtotal, poultry	54 213 298 767	53.004
rabbits	1 716 220	0.002
egg products	3 413 857 390[a]	3.338
grand total	102 282 065 889	100

[a] For fiscal year 2004.

(MRLs) for Cd in livestock and poultry because the foods from these production classes were not significant contributors to Cd intake.

The World Health Organization (WHO) established a provisional tolerable weekly intake (PTWI) for Cd at 7 μg/kg of body weight. This weekly value corresponds to a daily tolerable value intake of 70 μg for a 70 kg person. However, recent studies found clinical manifestations of Cd toxicity at exposure levels below the limits established by the WHO (*10*, *11*).

As for Pb, the IARC classified inorganic Pb compounds as probably carcinogenic to humans (*12*). Organic Pb compounds are not classified as carcinogenic since evidence of their carcinogenicity is not sufficient in humans and is limited in experimental animals. Exposure to Pb has been associated with reduced cognitive and neurobehavioral development in children and with cardiovascular diseases such as high blood pressure in adults. The WHO has set a PTWI of 25 μg/kg of body weight for people in all age groups.

The most frequently reported sources of high Pb concentrations in foods are ceramic-glazed storage containers. The typical absorption rate of Pb in adults is 10% (*13*−*14*). Absorbed Pb is transported in the blood and is initially distributed to soft tissues throughout the body. Subsequently, lead is deposited in bone, where it accumulates. The half-life of Pb in blood and other soft tissues is 28−36 days (*15*). Of the absorbed inorganic Pb, 90% is stored in bone while the organic Pb is oxidatively dealkylated in the human body and excreted in the urine (*16*).

FSIS conducted an exploratory assessment to determine the occurrence and levels of Cd and Pb in the kidney, liver, and muscle tissues of livestock and poultry during 2003−2004. In 2003, the kidney, liver, and muscle of 48 dairy cows and 48 heifers were sampled; in 2004, the same tissues were collected from 169 dairy cows, 41 boars/stags, and 200 mature chickens. All of the animals sampled were healthy and randomly selected at slaughter. Exploratory assessments are sampling plans designed to investigate compounds with violation rates above 1% and provide information on the prevalence of compounds without established tolerances, when suggested by intelligence from the field. This exploratory assessment on the occurrence and levels of Cd and Pb was designed to address the growing concern on the dietary exposure to these metals.

MATERIALS AND METHODS

FSIS inspectors collected kidney, liver, and muscle samples from randomly selected animals at slaughter establishments. Poultry samples consisted of tissue composites from six birds to attain the amount of tissue necessary to conduct the laboratory analyses. Samples were frozen prior to shipment to the FSIS Eastern Field Service Laboratory in Athens, GA. At the laboratory, the sample's condition, including temperature, was verified to ensure suitability for analysis using FSIS Method CLG-TM3.00, Determination of Cd and Pb by ICP-MS (inductively coupled plasma mass spectrometry). Tissue samples were then chopped, homogenized, and stored frozen until analysis. The homogenized tissue, 0.5 g for muscle and 0.5−1.0 g for liver and kidney, was mixed with concentrated nitric acid and microwave digested at 180 °C for 10 min. The digestion was followed by microwave evaporation at 120 °C for 3.5 min to remove residual nitric acid, a strong oxidizing agent from the sample. The resulting extract was prepared for ICP-MS analysis, including the addition of internal standards indium and terbium. Prior to sample analysis, the ICP-MS Agilent model 7500a was tuned according to the manufacturer's specification and calibrated using standard linear regression and a calibration blank and quality control standard. The standard solutions were prepared from commercially available reference standard materials. The ions monitored for Cd were 106, 108, 110, 111*, 112, 113, 114, and 116. The ions monitored for Pb are 204, 206, 207, and 208* (*denotes ions used for quantitation). A sample set for ICP-MS analysis consisted of one tissue blank (negative control), one or more fortified blanks (positive controls) prepared using the same tissue used for the negative control, and the samples for analysis. The Quality Assurance Plan for the FSIS Method CLG-TM3.00 identified the following as acceptable recoveries: 70−100% for Cd levels below 25 ppb and 80−100% for Cd or Pb levels equal to and greater than 25 ppb.

The minimum proficiency level (MPL) of the analytical method is the minimum amount of the analyte identified and quantified with a predicted coefficient of variation for reproducibility (CV) less than or equal to 20%, and an upper 90% confidence level for the predicted CV is less than 30%. This regulatory definition for MPL is stated in the Title 9 of the Code of Federal Regulations (9 CFR 318.21 and 9 CFR 381.153). The MPL for Cd is 10 ppb, and the MPL for Pb is 25 ppb.

Results from analyses with acceptable recoveries and with analyte levels detected and quantified at or above the MPL were reported by the FSIS Eastern Field Service Laboratory and were included in this study. The results were reported in nanograms of analyte per grams of homogenized tissue sample (ng/g or ppb).

The range of the residue levels, the arithmetic mean of the residue levels, and the standard deviation of the mean values were calculated using Microsoft Excel for the tissue samples collected in each production class under study. In addition, the percent of positive samples and the 95th percentile were also calculated for the tissue samples collected. The percent of positive samples is the proportion of samples with detectable and quantitatable Cd or Pb levels to the total number of collected samples in each production class multiplied by 100. The 95th percentile is a value that divides the data or population into two parts: the lower 95% of the values and the upper 5% of the values for the collected samples with detectable and quantitatable Cd or Pb levels in each production class.

Table 2. Results for the Testing of Cd and Pb in Kidneys from Different Production Classes, 2003–2004 Study

			positive samples[a]					
trace metal	production class	no. of samples	no. of positives	%	range (ppb)	mean	SD	P95[b]
Cd	boars/stags	41	41	100	48–1602	301	358	1038
Cd	mature chickens	200	200	100	17–11400	627	995	1454
Cd	heifers	48	48	100	25–651	174	147	489
Cd	dairy cows	218	218	100	42–3428	483	504	1190
Pb	boars/stags	41	16	39.0	26–775	100	184	101
Pb	mature chickens	200	40	20.0	25–671	58	101	44
Pb	heifers	4837	27.1	25–293	47	53	136	
Pb	dairy cows	218	138	63.3	25–880	64	83	104

[a] Concentration is equal or higher than minimum proficiency level. [b] 95th percentile is for all sampled kidneys in this production class.

Table 3. Results for the Testing of Cd and Pb in Livers from Different Production Classes, 2003–2004 Study

			positive samples[a]					
trace metal	production class	no. of samples	no. of positives	%	range (ppb)	mean	SD	P95[b]
Cd	boars/stags	41	41	100	10–302	65	66	213
Cd	mature chickens	200	199	99.5	27–1820	177	214	464
Cd	heifers	48	44	91.7	12–124	36	27	86
Cd	dairy cows	218	216	99.1	11–415	82	59	186
Pb	boars/stags	41	18	43.9	26–814	100	135	136
Pb	mature chickens	200	15	7.5	25–1293	176	221	32
Pb	heifers	48	15	31.2	25–109	15	26	68
Pb	dairy cows	218	80	36.7	25–401	62	57	93

[a] Concentration is equal or higher than minimum proficiency level. [b] 95th percentile is for all sampled livers in this production class.

RESULTS

The results and corresponding statistics are summarized in **Tables 2−4**. Cadmium was detected in 507/507 (100%) kidney samples; Pb was detected in 231/507 (46%) kidney samples (**Table 2**). Cadmium was detected in 500/507 (99%) liver samples, while only 128/507 (25%) of the liver samples analyzed were positive for Pb (**Table 3**). Among the liver samples, mature chickens have the lowest percent of positive liver samples for Pb at 7.5 vs 31.2−43.9% for sampled meat products (**Table 3**). Cadmium was detected in 1.5% of the mature chicken muscle samples, whereas Cd was not detected in muscle samples from boars/stags, dairy cows, or heifers (**Table 4**). Analyses of muscle tissue detected Pb in 5.0% of the boars/stags samples, 0.92% of the dairy cow samples, and 2.5% of the mature chicken samples (**Table 4**). Lead was not detected in the muscle of the sampled heifers (**Table 4**).

Partial results from the FSIS study conducted in 1985−1986 are summarized in **Tables 5−7**. These results were generated using an analytical method based on atomic absorption spectroscopy with a MPL of 0.025 ppm (25 ppb) for Cd and 0.50 ppm (500 ppb) for Pb. The current method, ICP-MS, reliably detects and quantitates Cd levels at least 2.5 times lower and Pb levels at least 20 times lower than the atomic absorption method. Therefore, the sampling design employed in the 1985−1986 study is similar but not identical to the sampling used in the more recent study. In addition, some of the sampled production classes are the same in both studies, and other production classes are pooled using different but overlapping sampling frames (i.e., boars/stags vs boars/sows). Because

Table 4. Results for the Testing of Cd and Pb in Muscles from Different Production Classes, 2003–2004 Study

			positive samples[a]					
trace metal	production class	no. of samples	no. of positives	%	range (ppb)	mean	SD	P95[b]
Cd	boars/stags	40	0	0	*c*	*c*	*c*	*c*
Cd	mature chickens	200	3	1.5	13–31	20	19	0
Cd	heifers	47	0	0	*c*	*c*	*c*	*c*
Cd	dairy cows	217	0	0	*c*	*c*	*c*	*c*
Pb	boars/stags	40	2	5.0	59–91	75	22	3
Pb	mature chickens	200	5	2.5	31–75	55	18	0
Pb	heifers	47	0	0	*c*	*c*	*c*	*c*
Pb	dairy cows	217	2	0.9	33–80	56	33	0

[a] Concentration is equal or higher than minimum proficiency level. [b] 95th percentile is for all muscle samples in this production class. [c] Not applicable.

Table 5. Cd and Pb in Kidney, 1985–1986 Study

			positive specimens (samples)[a]					
trace metal	production class	no. of specimens (samples)	no. of positives	%	range (ppb)	mean	SD	P95[b]
Cd	boars/sows	281	277	98.6	100–4400	650	560	1500
Cd	mature chickens	306	303	99	100–3600	1030	700	2500
Cd	heifers/ steers	288	281	97.6	100–9600	380	620	840
Cd	bulls/cows	95	95	100	130–32000	1520	3370	3800
Pb	boars/sows	279	6	2.2	510–1700	970	540	0
Pb	mature chickens	304	5	1.6	500–940	630	190	0
Pb	heifers/ steers	283	5	1.8	500–760	580	100	0
Pb	bulls/cows	93	2	2.2	690–720	700	20	0

[a] Concentration is equal or higher than minimum proficiency level. [b] 95th percentile for all specimens.

Table 6. Cd and Pb in Liver, 1985–1986 Study

			positive specimens (samples)[a]					
trace metal	production class	no. of specimens (samples)	no. of positives	%	range (ppb)	mean	SD	P95[b]
Cd	boars/sows	282	205	72.7	100–1400	210	140	390
Cd	mature chickens	309	284	91.9	100–131000	710	7760	440
Cd	heifers/ steers	289	105	36.3	100–17000	300	1650	190
Cd	bulls/cows	95	85	89.5	100–910	240	140	490
Pb	boars/sows	280	4	1.4	540–910	700	170	0
Pb	mature chickens	307	1	0.3	540–540	540		0
Pb	heifers/ steers	285	1	0.4	1000–1000	10000		
Pb	bulls/cows	93	0	0				

[a] Concentration is equal or higher than minimum proficiency level. [b] 95th percentile for all specimens.

reliable statistical data analysis requires that the same parameters be employed in the data generation, the evaluation of the results between the two studies is limited to generalizations on the incidence of Cd and Pb in the different production classes. Comparisons between these two data sets, further than generalizing on the incidence of Cd and Pb, are difficult because the lower MPL of the method used in the 2003−2004 study would weight average levels detected and the 95th percentile toward lower values.

The acquisition of a more sensitive method by the FSIS laboratories in 2003 resulted in several advantages for the current

Table 7. Cd and Pb in Muscle, 1985–1986 Study

trace metal	production class	no. of specimens (samples)	positive specimens (samples)[a] no. of positives	%	range (ppb)	mean	SD	P95[b]
Cd	boars/sows	281	1	0.4	130–130	130		0
Cd	mature chickens	308	3	1	100–140	120	20	0
Cd	heifers/ steers289	1	0.3	130–130	130		0	
Cd	bulls/cows	95	1	1.1	120–120	120		0
Pb	boars/sows	279	0	0.0				
Pb	mature chickens	306	0	0.0				Pb
heifers/ steers	285	1	0.4	520–520	520			
Pb	bulls/cows	93	1	1.1	580–580	580		

[a] Concentration is equal or higher than minimum proficiency level. [b] 95th percentile for all specimens.

and future studies. For instance, the lower MPL of the ICP-MS method allowed the detection of Pb at lower concentrations, resulting in the detection of a higher number of Pb-positive samples. This allowed the calculation of a more accurate 95th percentile than the previous FSIS study. For example, the findings of the two boar/stag muscle samples with the highest Pb levels averaged almost 75 ppb, which is much lower than the 500 ppb MPL for Pb in the earlier study.

The comparison of the results of the previous and current FSIS studies allows the recognition of general trends in the Cd and Pb levels in meat and poultry products during the last two decades. The results demonstrate that Cd levels have remained higher in the kidneys and livers of boars, mature chickens, heifers, and dairy cows. The data also illustrate that muscle samples from the surveyed production classes still contain low levels of Cd and Pb.

DISCUSSION

FSIS has a responsibility to ensure that meat, poultry, and egg products entering commerce in the United States are free of adulterants, including elevated levels of environmental contaminants such as Cd and Pb. To fulfill this mandate, FSIS provides permanent and constant inspection at slaughter and processing establishments. Under the Federal Meat Inspection Act and the Poultry Products Inspection Act, slaughter establishments are responsible to ensure that that their products are not adulterated. According to the section 9 CFR 417, slaughter and processing establishments must conduct hazard analyses to determine what food safety hazards are reasonably likely to occur within the establishment before and during slaughter or processing and implement a system of preventive measures to ensure the safety of products. The elevated levels of Cd in the kidneys of mature chickens have been identified as a food safety hazard reasonably likely to occur for more than 20 years. In view of that, the Hazard Analysis and Critical Control Points (HACCP) regulation requires that establishments demonstrate that their operating HACCP systems can determine when poultry kidneys constitute a hazard (66 FR 1762, Jan 9, 2001; 66 FR 1764, Jan 9, 2001). Consequently, the kidneys of mature chickens are often removed under an establishment's HACCP plan.

Although there are no MRLs or tolerances established in the United States for Cd or Pb in poultry and livestock edible tissues, FSIS periodically assesses the residue levels of Cd and Pb in the edible tissues of poultry and livestock. The generated data have guided the development and implementation of new policies and have supported current policies aimed to protect public health.

Table 8. European Union and CODEX MRLs for Pb and Cd [From Commission Regulation (EC) No. 466/2001, CODEX STAN 230-2001, Rev. 2003]

	EU and Codex		EU[a]		
	lead (ppb)		cadmium (ppb)		
species	meat	offal	meat	liver	kidney
bovine	100	500	50	500	1000
sheep	100	500	50	500	1000
pig	100	500	50	500	1000
poultry	100	500	50	500	1000
horse			200		

[a] In 2004, the Codex Committee on Food Additives and Contaminants decided to discontinue work on establishing Cd MRLs in livestock because these foods are not significant contributors to Cd intake.

This study found that in each production class tested, levels of Cd and Pb were higher in kidney and liver samples than in the muscle samples. None of the muscle samples contained Cd and Pb levels exceeding the MRLs established by other countries or international organizations. There are sporadic cases in which liver samples from mature chickens and boars/stags contained elevated Cd or Pb levels; however, the 95th percentile and the mean residue levels for liver samples were below the MRLs established by other countries or international organizations. In boars/stags, mature chickens, and dairy cows, the Cd levels for the 95th percentile of kidney samples (see **Table 2**) were above internationally accepted levels, exceeding the MRL (1000 ppb) established by the European Union. Boars/stags, mature chickens, and dairy cows products with Cd levels above 1000 ppb are classified as violative in EU countries; see **Table 8**.

The results of the current and previous FSIS studies (**Tables 2−7**) show that the incidence (percent of positive samples) and levels of Cd in kidney, liver, and muscle did not increase between 1985 and 2004. The 95th percentile and the mean Pb levels of positive kidney and liver samples in the current study were both far below the MPL (500 ppb) of the analytical method employed in the earlier FSIS study. The apparent increase in the prevalence of Pb in liver and kidneys in the recent survey can be attributed to the significantly lower MPL. The data suggest that the levels of Pb in the surveyed production classes have not increased and that the contribution of animal foods to the overall exposure to Cd and Pb in the U.S. population has not increased in the last 20 years. Other factors that contribute to this stabilization in the contribution of animal foods to the exposure of Cd and Pb are (i) the domestic decline in the consumption of organ meats (*17*) and (ii) the HACCP-based determination that allows only kidneys from mature chickens and turkeys without hazardous Cd levels into commerce.

Recent research studies, however, suggest that the risk for kidney damage exists at lower levels of Cd exposure than previously thought (*18−20*). This particularly affects special groups of the population such as pregnant women and their fetuses. For instance, Semczuk et al. identified microintoxication with Cd and Pb as a danger to human fetuses due to their lack of regulatory mechanisms to protect against these metals (*21*). These findings warrant more research studies and close assessment of Cd and Pb in all food commodities.

In conclusion, the results of this study demonstrate that the risk of human exposure to Cd and Pb in meat and poultry is low and that the levels of Cd and Pb in the edible tissues of boars, mature chickens, dairy cows, and heifers have not increased since an earlier FSIS study conducted in 1985–1986. The majority of the poultry and livestock samples conform to the current international MRLs, although elevated levels for one or both metals were detected. This is especially evident in the results of Cd levels in the kidneys from boars/stags, mature chickens, and dairy cows. However, in the case of Cd in dairy cow kidneys, it is noted that the average residue level is 483 ppb and the median, the midpoint of the distribution, is 325 ppb. Both the median and the mean are far below the EU MRLs for Cd in kidney.

It is recommended that the current practice of analyzing Cd and Pb in the edible tissues of different production classes on a periodic basis be continued, because this allows the detection of trends in the levels of these heavy metals over time. This is a significant indicator of the level of protection of the public health, especially for sensitive groups of the population.

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LITERATURE CITED

(1) Coleman, M. E.; Elder, R. S.; Basu, P. Trace metals inedible tissues of livestock and poultry. *J. AOAC Int.* **1992**, *75*, 615–625.

(2) Food Safety and Inspection Service, U.S. Department of Agriculture. 2004 FSIS National Residue Program Data; http://www.fsis.usda.gov/Science/2003_Red_Book/index.asp.

(3) International Agency for Research on Cancer (IARC). *Summaries and Evaluations, Cadmium and Cadmium Compounds*; IARC: Lyon, France, 1993; Vol. 58, p 119.

(4) Crews, H. M.; Dean, J. R.; Ebdon, L. Application of high-performance liquid chromatography-inductively coupled plasma mass spectrometry to the investigation of cadmium speciation in pig kidney following cooking and *in vitro* gastrointestinal digestion. *Analyst* **1989**, *114*, 895–899.

(5) Groten, J. P.; Sinkeldam, E. I.; Luten, J. B. Comparison of the toxicity of inorganic and liver-incorporated cadmium: A 4-week feeding study in rats. *Food Chem. Toxicol.* **1990**, *28*, 435–441.

(6) Nordberg, M.; Nuottaniemi, I.; Cherian, M. G. Characterization studies on the cadmium-binding proteins from two species of New Zealand oysters. *Environ. Health Perspect.* **1986**, *65*, 7–62.

(7) Jarup, L.; Berglund, M.; Elinder, C. G.; Nordberg, G.; Vahter, M. Health effects of cadmium exposure—A review of the literature and a risk estimate. *Scand. J. Work Environ. Health* **1998**, *24* (Suppl. 1), 1–51.

(8) Gartrell, M. J.; Craun, J. C; Podrebarac, D. S. Pesticides, selected elements, and other chemicals in adult samples. *J. Assoc. Off. Anal. Chem.* **1986**, *69*, 146–161.

(9) Thornton, I. Sources and pathways of cadmium in the environment. *IARC Sci. Publ.* **1992**, *118*, 149–162.

(10) Jarup, L. Cadmium overload and toxicity. *Nephrol., Dial., Transplant.* **2002**, *17* (Suppl. 2), 35–39.

(11) Satarug, S.; Moore, M. R. Adverse health effects of chronic exposure to low-level cadmium in foodstuffs and cigarette smoke. *Environ. Health Perspect.* **2004**, *112*, 1099–1103.

(12) International Agency for Research on Cancer (IARC). *Inorganic and Organic Lead Compounds*; IARC: Lyon, France, 2006; Vol. 87.

(13) O'Flaherty, E. J. Physiologically based models for bone-seeking elements. V. Lead absorption and disposition in childhood. *Toxicol. Appl. Pharmacol.* **1995**, *131*, 297–308.

(14) World Health Organization (WHO). *Food Additives Series 44. International Programme on Chemical Safety*; World Health Organization: Geneva, 2000.

(15) World Health Organization (WHO). *Environmental Health Criteria 165: Inorganic Lead, Geneva. International Programme on Chemical Safety*; World Health Organization: Geneva, 1995.

(16) International Agency for Research on Cancer (IARC). Inorganic and organic lead compounds. *Monogr. Eval. Carcinog. Risks Hum.* **2004**, *87*, 10–17.

(17) Food Availability Data, Economic Research Service, U.S. Department of Agriculture; http://www.ers.usda.gov/data/foodconsumption/FoodAvailSpreadsheets.htm.

(18) Centers for Disease Control and Prevention. *Third National Report on Human Exposure to Environmental Chemicals*; CDC: Atlanta, GA, 2005.

(19) Jarup, L.; Hellstrom, L.; Alfven, T.; Carlsson, M. D.; Grubb, A.; Persson, B. Low level exposure to cadmium and early kidney damage: The OSCAR study. *Occup. Environ. Med.* **2000**, *57*, 668–672.

(20) Suwazono, Y.; Kobayashi, E.; Okubo, Y.; Nogawa, K.; Kido, T.; Nakagawa, H. Renal effects of cadmium exposure in cadmium nonpolluted areas in Japan. *Environ. Res.* **2000**, *84*, 44–55.

(21) Semczuk, M.; Semczuk-Sikore, A. New data on metal intoxication (Cd, Pb and Hg in particular) and Mg status during pregnancy. *Med. Sci. Monit.* **2001**, *7*, 332–340.

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