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Lead, cadmium and aluminum in Canadian infant formulae, oral electrolytes and glucose solutions

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Lead (Pb), cadmium (Cd) and aluminum (Al) were determined in 437 individual samples of infant formulae, oral electrolytes and 5% glucose solutions available in Canada. In the electrolytes, Cd and Pb concentrations were all below 0.01 and 0.041 $ng\,g^{-1}$, respectively. In the 5% glucose solutions, Pb and Cd levels averaged 0.01 and 0.09 $ng\,g^{-1}$, respectively. Reported on an as-consumed basis, Pb levels in milk- and soya-based formulae averaged 0.90 and 1.45 $ng\,g^{-1}$, respectively, while Cd levels averaged 0.23 and 1.18 $ng\,g^{-1}$, respectively Average Al levels on an as-consumed basis were 440 $ng\,g^{-1}$ (range 10–3400 $ng\,g^{-1}$) in milk-based formulae and 730 $ng\,g^{-1}$ (range 230–1100 $ng\,g^{-1}$) in soy-based formulae. Al concentrations increased in the following order: plain formula < low-iron formula < iron-supplemented formula < casein hydrolysate formula ≈ premature formula ≤ soy formula. For example, in the powdered formulae, average Al concentrations were 18 $ng\,g^{-1}$ for plain milk-based, 37 $ng\,g^{-1}$ for low-iron, 128 $ng\,g^{-1}$ for iron supplemented, 462 $ng\,g^{-1}$ for lactose-free, 518 $ng\,g^{-1}$ for hypoallergenic and 619 $ng\,g^{-1}$ for soy-based formula. Al concentrations, as-consumed, increased with decreasing levels of concentration: powder < concentrated liquid < ready-to-use. Formulae stored in glass bottles contained between 100 and 300 $ng\,g^{-1}$ more Al than the same formulae stored in cans. The source of the increased Al did not appear to be the glass itself, because most electrolytes and glucose solutions, also stored in glass, contained less than 8 $ng\,g^{-1}$ Al. Corresponding differences in Pb and Cd levels were not observed. Al concentrations varied substantially among manufacturers; however, all manufacturers were able to produce plain milk-based formulae containing less than 50 $ng\,g^{-1}$ Al, i.e. within the range of Al concentrations found in human milk. Next to soya-based and hypoallergenic formulae, premature formulae contained among the highest concentrations of Al, ranging 851–909 $ng\,g^{-1}$ from one manufacturer and 365–461 $ng\,g^{-1}$ from another.

Keywords: infant formulae; aluminium; lead; heavy metals, cadmium

Introduction

Infants are particularly sensitive to the effects of ingested toxicants as food consumption is greater on a body-weight basis. Gastrointestinal absorption of most chemicals is substantially elevated prior to weaning and many organs, such as kidneys, are underdeveloped, while the physical development of critical organs impacting on the health of the infant throughout life is accelerated (Oskarsson et al. 1998). Infant formulae, often a single brand, may constitute a sole-source food for several months of an infant's life.

Lead is a potent neurotoxin for which no safety threshold has yet been found (US Environmental Protection Agency 2003). Exposure to Pb *in utero* and during infancy irreversibly affects development of the nervous system, causing reduced IQ and learning disabilities. Cd has estrogenic properties and causes an increased incidence of cancer in mice (Johnson et al. 2003). Chronic exposure to Cd and Pb is associated with kidney damage in adults (Navas-Acien et al. 2009). Infants, particularly those born prematurely, have reduced renal function and their developing kidneys are more susceptible to damage caused by excessive Cd and Pb in their diet. Al is a potent neurotoxin; long-term feeding of Al-containing total parenteral solutions to preterm infants caused impaired mental development at 18 months (Committee on Nutrition 1996; Klein et al. 2004). Also, excess Al in the blood is selectively incorporated into the bones of infants, resulting in a weakened bone structure (Bernardo et al. 2010). Al can only be removed from blood via the kidneys, and severe renal disorders can result in accumulation of Al in the blood, a situation potentially exacerbated by the action of higher levels of Cd and Pb on the kidneys. Finally, nothing is known about potential synergism between Al and Pb neurotoxicity. Thus, the monitoring of these elements in infant formulae is a high priority, internationally (Riolfatti and Veronese 1990; Baxter et al.

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1990, 1991; Sahin et al. 1995; Eklund and Oskarsson 1999; MAFF UK 1999; Rodriguez Rodriguez 1999; Tripathi et al. 1999; Ikem et al. 2002; Navarro-Blasco and Alvarez-Galindo 2003; Ursinyova and Masanova 2005; Hafez and Kishk 2008; US FDA 2008; Wojciechowska-Mazurek et al. 2008; Winiarska-Mieczan 2009; Al Khalifa and Ahmad 2010; Burrell and Exley 2010).

To optimize infant development, ingredient requirements for infant formulae are regulated and are sometimes country-specific. As a result, country-to-country variations in the concentrations of contaminants are to be expected. Previous studies have shown that typical Pb concentrations in all types of infant formula are in the order of $1–10 \, ng \, g^{-1}$ as-consumed (Dabeka 1989; Tripathy et al. 1999; Ikem et al. 2002), although levels as high as $143 \, ng \, ml^{-1}$ (Hafez and Kishk 2008) and $450 \, ng \, g^{-1}$ (Winiarska-Mieczan 2009) have been reported.

Cadmium concentrations, in addition to varying with country (Ikem et al. 2002), are usually less than $1 \, ng \, g^{-1}$ for milk-based formulae and slightly over $1 \, ng \, g^{-1}$ for soy-based formulae (Dabeka 1989; Eklund and Oskarsson 1999; Rodriguez et al. 1999; Ursinyova and Masanova 2005; Wojciechowska-Mazurek et al. 2008). Cd levels as high as $15 \, ng \, g^{-1}$ have been reported for soy formula in the UK (MAFF UK 1999).

Aluminum concentrations are known to vary widely, from an average of $58 \, ng \, g^{-1}$ in formulae from Nigeria (Ikem et al. 2002) up to $5600 \, ng \, g^{-1}$ for a soy-based formula in the UK (MAFF UK 1999). Also, in Canada, soy-based formulae consistently contained higher Al concentrations than milk-based formulae (Dabeka and McKenzie 1990).

The purpose of this survey was to establish whether the concentrations of Pb, Cd and Al in infant formulae sold in Canada have changed since previous surveys (Dabeka 1989; Dabeka and McKenzie 1990). The ultimate goal was to ensure that concentrations of trace elements in infant formulae are equivalent to or lower than those found in human milk. Electrolytes and 5% glucose solutions were also analysed because these are often fed to infants with diarrhoeal dehydration.

Experimental

Samples

Infant formulae, electrolytes and 5% glucose solutions were obtained by the Canadian Food Inspection Agency from retail stores, medical centres and hospitals between January 1999 and May 1999. An attempt was made to obtain three different lots of each product. Samples ($n = 243$) were stored at room temperature until analysed. Analyses were performed in the Quebec Regional Laboratory of the Health Products and Food Branch of Health Canada.

Reagents

Demineralized water was used wherever water is specified. Baker Ultrex-grade high-purity nitric and perchloric acids were used for digestions. Reagent-grade acids were used for washing flasks. Certified standard solutions of the elements traceable to the US National Institute of Standards and Technology were purchased from SCP Science (Montreal, Quebec, Canada). Other chemicals were reagent-grade.

Contamination control

Special contamination control measures were required to accurately quantify the background concentrations of Pb, Cd and Al in the reagent blanks in the absence of a clean room.

New glassware was soaked in 5% Decon detergent solution, rinsed with water, soaked in 5% nitric acid solution and again rinsed with water. Quartz Erlenmeyer digestion flasks were cleaned by boiling concentrated nitric acid in them until interior side and rim were wetted. The outer rim mouth of the flask was immersed in warm concentrated nitric acid. This step was critical in reducing contamination from residues on the outer rim of the flask when solution was poured from the flask. Used vessels were washed as above without soaking in Decon. Flasks were stored in dilute nitric acid solution and rinsed directly with deionized water just prior to use.

Polyethylene gloves were washed with liquid detergent and worn at all times when handling flasks and utensils. Body movements over open vessels were avoided to prevent dust or particulate contamination. When not in use, vessels were covered with plastic film (Saran Wrap™). The exterior of all vessels, including reagent bottles, was kept clean by rinsing with water and wiping dry with lint-free cellulose wipes (Kimberly Clark Kimwipes®). Teflon-FEP acid bottles were used to store high purity acids, and were stored in polyethylene bags. Except for fume-hood digestions, most sample manipulations were made under a clean air canopy.

During initial analyses, several problems were encountered with Pb and Cd contamination. A Brinkman plunger-type acid dispenser was found to be a source of Pb contamination, with the first 25-ml portion of pumped acid containing $0.15 \, ng \, ml^{-1}$ Pb while subsequent portions yielded acid with less

than $0.025 \, \text{ng ml}^{-1}$. Thus, acids were dispensed using a graduated cylinder instead of an acid dispenser.

Al method

Samples (as sold) (20 g electrolyte, 20 g ready-to-use, 10 g concentrated liquid or 3 g powdered concentrate) were digested with 25 ml nitric acid and 20 ml perchloric acid (Dabeka and McKenzie 1986), and the solutions were diluted to about 80 ml with water. Internal standard (1 ml $60 \, \text{ng ml}^{-1}$ yttrium (Y)) was added to a 5-ml sample aliquot.

Measurements were made on a VG-PlasmaQuad-2 (VG-Elemental, Winsford, UK) inductively coupled plasma mass spectrometer (ICPMS) fitted with a Teflon V-groove nebulizer and Gilson 222 autosampler. Standard operating conditions were: argon (Ar) 99.998% purity; plasma power 1350 W; spray chamber temperature 5°C. Ar gas flows were: coolant $13.5 \, \text{l min}^{-1}$, auxiliary $1.1 \, \text{l min}^{-1}$ and nebulizer $0.860 \, \text{l min}^{-1}$. Solution uptake rate was $1 \, \text{ml min}^{-1}$. The ICPMS was operated in scanning mode (30 sweeps, 500 µs) with one 57-s integration measurement for each solution. Isotopic measurements were made on ^{27}Al using ^{89}Y as internal standard.

Fifteen batches were run. Each consisted of 10 standards (0, 1, 2, 5, 10, 25, 50, 100, 200, $400 \, \text{ng ml}^{-1}$), seven reagent blanks, one or two reagent blank spikes, two unspiked sample replicates, two spiked sample replicates and about 20 samples, each analysed in duplicate, per batch. The spike added was 10,000 ng ($500 \, \text{ng g}^{-1}$ for 20 g ready-to-use formula) for both the blank and sample spikes.

Pb and Cd determinations

Samples (20 g electrolyte, 20 g ready-to-use, 10 g concentrated liquid, or 3 g powdered formula) were digested with nitric and perchloric acids, and Pb and Cd were coprecipitated with ammonium pyrrolidine dithiocarbamate according to the method of Dabeka and McKenzie (1986). The precipitate was dissolved (16 h) off the filter using 1 ml of 25 % HNO_3, then 0.5 ml internal standard containing $20 \, \text{ng ml}^{-1}$ each of indium (In) and rhenium (Re) were added, followed by 3.5 ml water. Cd and Pb were measured by ICPMS using the instrument and conditions described above for Al, except that the ICPMS was operated in peak jumping mode (175 sweeps, 3 channel per mass, 0.02 amu spacing, 15,000 µs dwell time) with one 57-s integration measurement for each solution. Isotopic measurements were made on ^{111}Cd and ^{208}Pb using ^{115}In and ^{185}Re as internal standards. No isobaric interference correction algorithm was applied.

The samples were run in 16 analytical batches. Each analytical batch consisted of 10 standards (0, 0.05, 0.1, 0.25, 0.5, 1.0, 2.0, 5.0, 10 and $20 \, \text{ng ml}^{-1}$, seven reagent blanks, one or two reagent blank spikes, two unspiked sample replicates, two spiked sample replicates, duplicates of a milk powder SRM (NIST 1545) and duplicates of about 20 samples.

Reporting results

Reported levels are based on an as-consumed basis for the ready-to-use, concentrated liquid and powder formulas. Label instructions were used to convert the concentrated liquid and powdered formulae concentrations to an as-consumed basis. All results less than the limit of detection (LOD) were reported as numeric value of the LOD.

Statistical comparisons

SigmaStat Version 3.11 for Windows was used for statistical calculations. The data were first checked for normality, then differences between selected groups were tested using a multiple *t*-test.

Results and discussion

Quality control results

For aluminum determinations, blank spike recoveries averaged 95% (range 81–109%). Sample spike recoveries averaged 98% (range 71–156%). The average limit of detection, defined as three times the standard deviation of the 7 reagent blanks in each batch divided by the sample weight, was $3.5 \, \text{ng g}^{-1}$ (range 1–$11 \, \text{ng g}^{-1}$).

For lead and cadmium measurements, blank spike recoveries averaged 95% (range 86–103%) for Pb, and 85% (range 77–94%) for Cd. Sample spike recoveries averaged 97% (range 87–109%) for Pb and 88% (range 78–98%) for Cd. Pb levels in the SRM (mean $16 \, \text{ng g}^{-1}$, range 14–$19 \, \text{ng g}^{-1}$) were slightly less than the certified level of $19 \pm 3 \, \text{ng g}^{-1}$. Cd levels in the SRM (mean $0.45 \, \text{ng g}^{-1}$, range 0.13–$0.77 \, \text{ng g}^{-1}$) were much less precise, but the average agreed with the certified level of $0.5 \pm 0.25 \, \text{ng g}^{-1}$.

Element concentration results

Table 1 summarizes the concentrations of the elements found in each oral electrolyte, glucose solution and infant formula by type.

Table 1. Summary of Pb, Cd and Al concentrations (ng g^{-1}) in formulae and electrolytes (as-consumed).

Type of formula	No.	Aluminum (ng g^{-1})					Cadmium (ng g^{-1})					Lead (ng g^{-1})				
		Mean	Median	SD	Min.	Max.	Mean	Median	SD	Min.	Max.	Mean	Median	SD	Min.	Max.
Electrolyte	13	48	5	78	3	263	0.01	0.01	0.00	0.01	0.01	0.16	0.14	0.10	0.04	0.41
Electrolye, flavoured	8	39	5	98	3	283	0.01	0.01	0.00	0.01	0.01	0.16	0.16	0.07	0.03	0.24
5% glucose	6	73	6	106	5	239	0.01	0.01	0.00	0.01	0.01	0.09	0.08	0.03	0.05	0.15
Conc. liquid milk-based	44	131	61	198	2	796	0.13	0.04	0.32	0.02	2.03	0.32	0.29	0.17	0.06	0.85
- plain	12	33	29	26	2	74	0.04	0.03	0.02	0.03	0.07	0.26	0.25	0.07	0.18	0.38
- with iron	22	90	71	79	2	228	0.08	0.04	0.09	0.02	0.36	0.28	0.29	0.11	0.06	0.54
- low iron	3	37	37	3	34	39	0.29	0.13	0.40	0.03	0.88	0.40	0.32	0.22	0.25	0.73
- lactose free	7	467	643	310	136	796	0.37	0.07	0.73	0.06	2.03	0.50	0.32	0.27	0.20	0.85
Conc. liquid soya-based	12	706	798	274	266	1047	1.12	0.96	0.34	0.76	1.70	1.19	1.14	0.24	0.88	1.54
- plain	9	688	806	318	266	1047	1.18	1.07	0.37	0.76	1.70	1.25	1.23	0.25	0.90	1.54
- with iron	3	757	792	71	675	804	0.93	0.95	0.03	0.89	0.95	1.03	1.07	0.13	0.88	1.14
Powdered, milk-based	57	177	44	230	2	1004	0.17	0.06	0.23	0.01	1.21	0.65	0.34	0.67	0.16	3.46
- plain	15	18	11	16	2	48	0.04	0.03	0.02	0.01	0.07	0.23	0.21	0.06	0.17	0.42
- with iron	24	128	49	139	2	463	0.10	0.07	0.08	0.01	0.31	0.46	0.34	0.34	0.16	1.39
- low iron	3	37	38	3	33	39	0.04	0.03	0.02	0.03	0.06	0.39	0.31	0.15	0.30	0.56
- added rice	2	30	30	8	24	35	0.05	0.05	0.01	0.04	0.05	0.87	0.87	0.10	0.80	0.94
- lactose free	6	462	404	309	174	1004	0.48	0.27	0.41	0.19	1.21	1.50	1.05	1.19	0.46	3.46
- hypoallergenic	6	518	538	87	394	628	0.53	0.51	0.19	0.32	0.80	1.58	1.39	0.50	1.06	2.20
- digestible fat modified	1	686	686		686	686	0.40	0.40		0.40	0.40	1.48	1.48		1.48	1.48
Powdered, whey-based	2	39	39	37	13	65	0.84	0.84	0.57	0.44	1.24	0.58	0.58	0.06	0.54	0.62
Powdered, soya-based	15	733	713	348	199	1461	1.56	1.39	0.60	1.07	3.47	1.32	1.27	0.35	0.79	1.90
- plain	9	619	713	332	199	1068	1.72	1.75	0.74	1.07	3.47	1.42	1.46	0.40	0.91	1.90
- with iron	6	905	818	323	598	1461	1.31	1.29	0.16	1.11	1.57	1.16	1.20	0.20	0.79	1.38
Powdered, amino acid modified	1	774	774		774	774	0.34	0.34		0.34	0.34	0.86	0.86		0.86	0.86
Powdered, protein-free	1	542	542		542	542	0.30	0.30		0.30	0.30	1.01	1.01		1.01	1.01
RTU, milk-based	67	437	365	485	10	3442	0.23	0.11	0.27	0.03	1.26	0.90	0.84	0.54	0.14	2.46
- plain	19	379	255	306	10	955	0.21	0.07	0.22	0.03	0.68	0.96	0.60	0.76	0.23	2.46
- with iron	28	372	247	624	11	3442	0.12	0.08	0.09	0.03	0.38	0.73	0.62	0.45	0.14	1.80
- low iron	4	242	181	172	110	494	0.08	0.07	0.03	0.05	0.11	0.91	0.79	0.27	0.74	1.31
- lactose-free	6	622	598	229	371	896	0.20	0.21	0.08	0.07	0.28	1.10	1.17	0.14	0.86	1.22
- hypoallergenic	10	814	792	296	458	1310	0.67	0.71	0.40	0.16	1.26	1.12	1.03	0.38	0.49	1.78
RTU, soya-based	14	730	769	277	234	1121	1.18	1.06	0.55	0.71	2.95	1.45	1.36	0.32	1.10	2.10
RTU, whey	1	510	510		510	510	0.15	0.15		0.15	0.15	0.74	0.74		0.74	0.74
RTU, modified fat supplement	1	72	72		72	72	0.25	0.25		0.25	0.25	1.85	1.85		1.85	1.85

Note: RTU, ready-to-use.

Table 2. Comparison of current Al, Pb and Cd levels in ready-to-use formula with previous Canadian surveys.

	Al, ng g^{-1}, mean (range)		Pb, ng g^{-1}, mean (range)		Cd, ng g^{-1}, mean (range)	
	1990[a]	This study	1989[b]	This study	1989[b]	This study
Milk-based	130	440	1.58[c]	0.90	0.35	0.23
	(10–360)	(10–3400)	(0.36–6.08)	(0.14–2.46)	(0.032–3.4)	(0.03–1.26)
Soya-based	1980	730		1.45	3.39	1.18
	(400–6400)	(230–1100)		(1.1–2.1)	(3.12–14.8)	(0.71–2.95)

Notes: [a]Dabeka and McKenzie (1990).
[b]Dabeka (1989).
[c]Pb values for 1989 survey include both milk- and soya-based formulae.

Lead and cadmium

In the electrolytes, Cd and Pb concentrations were all below 0.01 and 0.41 ng g^{-1}, averaging 0.01 and 0.16 ng g^{-1}, respectively (Table 1). In the 5% glucose solutions, Pb and Cd levels averaged 0.01 and 0.09 ng g^{-1}, respectively.

For the infant formulae, lower Pb, Cd, and Al concentrations were observed relative to results obtained in an earlier survey (Dabeka 1989; Dabeka and McKenzie 1990) (Table 2). The average 1989 Pb level of 1.58 ng g^{-1} (range 0.36–6.08 ng g^{-1}) in both milk and soya ready-to-use formulae decreased to 1.45 ng g^{-1} for ready-to-use soya-based formulae and to 0.90 ng g^{-1} for ready-to-use milk-based formulae. Average Cd levels decreased from 0.35 to 0.23 ng g^{-1} in ready-to-use milk-based formulae and from 3.39 to 1.18 ng g^{-1} in soya-based formulae.

Average levels of Pb and Cd were generally lower than or comparable to levels reported in the literature. Pb in milk-based formulae in Italy were found to vary from <4 ng ml^{-1} for mature formula to 95 ng ml^{-1} for premature formula (Riolfatti and Veronese 1990). In the same study, average Cd concentrations varied from 0.06 ng ml^{-1} for milk-based adapted formula to 1.31 ng ml^{-1} for hypoallergenic formula. In the UK, powdered formulae contained between <1 and 3 ng g^{-1} (milk-based) and 14 ng g^{-1} Cd (soy-based, $n = 1$), and <10–20 ng g^{-1} Pb. Ready-to-use milk-based formulae contained <1 to 1 ng g^{-1} Pb, and <0.1 ng g^{-1} to 2.9 ng g^{-1} Cd (MAFF UK 1999). In India, geometric mean trace element concentrations varied by milk type, ranging 1.7–3.35 ng g^{-1} for Pb and 0.07–0.10 ng g^{-1} for Cd (Tripathi et al. 1999). Powdered milk formula in Saudi Arabia contained 18 ng g^{-1} Pb and 7 ng g^{-1} Cd (Al Khalifa and Ahmad 2010). In Spain, average levels of Pb and Cd in reconstituted powdered formulae were 11.5 and 6.8 ng g^{-1}, respectively (Rodriguez Rodriguez 1999). Cd concentrations in formulae sold in Poland varied with formula type from 0.4 to 2 ng g^{-1}, consistent with levels found in Canada. Pb concentrations in

Polish formulae were considerably higher (Winiarska-Mieczan 2009), averaging 198–450 ng g^{-1}, over 100 times higher than those found in this study. Another Polish study found a higher average concentration of Cd (4 ng g^{-1}), but a lower concentration of Pb (31 ng g^{-1}) (Wojciechowska-Mazurek et al. 2004). In the Slovak Republic, formulae contained 0.4 ng g^{-1} Cd and 5 ng g^{-1} Pb (Ursinyova and Masanova 2005). Similar mean concentrations of 0.67 ng g^{-1} Cd and 5.94 ng g^{-1} Pb were found in formulae from the Czech Republic (Ursinyova and Hladikova 1997). A comparison of formulae from Nigeria, UK and USA found very low levels of both Pb and Cd. Average Pb concentrations varied from "not detected" in US formula to 0.8 ng g^{-1} in UK formula, while Cd varied from "not detected" in Nigerian and US formula to 0.3 ng g^{-1} in UK formula (Ikem et al. 2002). In Swedish formulae, average Cd concentrations ranged 1.1–22 ng g^{-1} depending on formula type (Eklund and Oskarsson 1999). While sample-type variations were also found in this study, the levels and concentration differences were substantially lower. For example, among the powdered formulae in this study, mean Cd levels ranged from 0.04 ng g^{-1} for plain milk-based formula to 0.48 ng g^{-1} for lactose-free, 0.53 ng g^{-1} for hypoallergenic, 0.84 ng g^{-1} for whey and 1.56 ng g^{-1} for soya-based formula (Table 1). In Australia, the geometric mean Pb concentration in infant formulae was 1.6 ng g^{-1} (range 0.07–11.4 ng g^{-1}) (Gulson et al. 2001). In Taiwan, Pb and Cd averaged 8 and 5 ng g^{-1}, respectively (Ding 2008). Nineteen samples of "since birth" formula powders sold in Saudi Arabia contained means of 18 ng g^{-1} Pb and 7 ng g^{-1} Cd (Al Khalifa and Ahmad 2010).

In Canadian human milk sampled in 1981, average levels of Pb and Cd were about 1.04 and 0.08 ng g^{-1}, respectively (Dabeka et al. 1986). Thus, levels of Pb in milk-based formulae are, on average, marginally lower than levels found previously in human milk, while Cd levels are slightly higher. The concentrations of lead in the formulae are all well below the

regulatory limits of $80 \, \text{ng} \, \text{g}^{-1}$ for ready-to-serve formula and $150 \, \text{ng} \, \text{g}^{-1}$ for concentrated liquid formula (Department of Justice 2011) in Canada, $20 \, \text{ng} \, \text{g}^{-1}$ for ready-to-serve formula in Europe (Commission of the European Communities 2001).

Aluminum

Aluminum levels in 26% of the electrolyte and glucose solutions were less than $8 \, \text{ng} \, \text{g}^{-1}$ (Table 1). Among the electrolytes sampled (various brands from three manufacturers), the highest concentrations of Al were found in a brand that has since been discontinued ($263 \, \text{ng} \, \text{g}^{-1}$ in unflavoured, and $283 \, \text{ng} \, \text{g}^{-1}$ in the flavoured version of the same discontinued brand). Of seven brands of electrolytes from a second manufacturer, four contained $<5 \, \text{ng} \, \text{g}^{-1}$ Al, while three contained 97, 98 and $119 \, \text{ng} \, \text{g}^{-1}$ Al. In the case of 5% glucose solutions, two samples from one manufacturer contained 175 and $239 \, \text{ng} \, \text{g}^{-1}$ Al, while the samples from two other companies contained $<6 \, \text{ng} \, \text{g}^{-1}$ Al. Considering that electrolytes can be given to premature infants as well as to infants who are ill, Al concentrations should be kept as low as possible. The results indicate that manufacturers are, with careful manufacturing practices, capable of producing electrolyte and glucose solutions with Al concentrations below $10 \, \text{ng} \, \text{g}^{-1}$.

In concentrated liquid milk-based infant formulae, average Al levels were $131 \, \text{ng} \, \text{g}^{-1}$, and, by formula type, were $33 \, \text{ng} \, \text{g}^{-1}$ for plain, $37 \, \text{ng} \, \text{g}^{-1}$ for low-iron, $90 \, \text{ng} \, \text{g}^{-1}$ for iron-supplemented, and $467 \, \text{ng} \, \text{g}^{-1}$ for lactose-free formulae (Table 1). Soya-based concentrated liquid formulae contained substantially higher Al concentrations (average $706 \, \text{ng} \, \text{g}^{-1}$) than milk-based formulae (average $131 \, \text{ng} \, \text{g}^{-1}$). Iron-supplemented concentrated liquid soy-based formulae contained an average of $757 \, \text{ng} \, \text{g}^{-1}$ Al, slightly higher than the non-supplemented formulae ($688 \, \text{ng} \, \text{g}^{-1}$).

The average Al concentration in all the milk-based powdered formulae was $177 \, \text{ng} \, \text{g}^{-1}$. Levels varied by formula type from $18 \, \text{ng} \, \text{g}^{-1}$ for plain formulae to $462 \, \text{ng} \, \text{g}^{-1}$ for lactose-free, and $518 \, \text{ng} \, \text{g}^{-1}$ for hypoallergenic (Table 1). Two powdered whey-based formulae contained a mean of $39 \, \text{ng} \, \text{g}^{-1}$ on an as-consumed basis. Al concentrations in an amino-acid modified formula and a protein-free formula were 774 and $542 \, \text{ng} \, \text{g}^{-1}$, respectively. Soya-based powdered formulae contained an average of $733 \, \text{ng} \, \text{g}^{-1}$, with the plain formulae containing less Al ($619 \, \text{ng} \, \text{g}^{-1}$) than those fortified with iron ($905 \, \text{ng} \, \text{g}^{-1}$).

There are large variations of Al concentrations reported for infant formula from other countries. A comparison of levels (as consumed) in powdered formula found average concentrations of $58 \, \text{ng} \, \text{g}^{-1}$ in Nigerian formulae, 92 and $101 \, \text{ng} \, \text{g}^{-1}$ in UK, and, in the US, 150 and $460 \, \text{ng} \, \text{g}^{-1}$ in milk- and soy-based formula, respectively (Ikem et al. 2002). Powdered formula imported from Europe into Turkey contained $1211–10,925 \, \text{ng} \, \text{g}^{-1}$ Al as-sold (Sahin et al. 1995). In Saudi Arabia, "since birth" and follow-on powdered formulae contained (as-sold) mean concentrations of 1944 and $1600 \, \text{ng} \, \text{g}^{-1}$, respectively (Al Khalifa and Ahmad 2010). On a ready-to-use basis, powdered milk- and soya-based formula in the UK in 1990 contained 40–200 and $640–1340 \, \text{ng} \, \text{g}^{-1}$, respectively (Baxter et al. 1990). A recent UK survey (Burrell and Exley 2010) found different types of ready-to-use milk-based formula contained average concentrations ranging from 175 to $700 \, \text{ng} \, \text{g}^{-1}$ Al. While the highest reported concentration of $863 \, \text{ng} \, \text{g}^{-1}$ Al in the UK study (Burrell and Exley 2010) was lower than the maximum concentration of $3442 \, \text{ng} \, \text{g}^{-1}$ found in this study (Table 1), the lowest concentration of $131 \, \text{ng} \, \text{g}^{-1}$ in an organic formula was much higher than the $10 \, \text{ng} \, \text{g}^{-1}$ Al found in the present study. Average Al levels in the other ready-to-use formulae were $730 \, \text{ng} \, \text{g}^{-1}$ for the soya-based, $510 \, \text{ng} \, \text{g}^{-1}$ for the whey-based and $72 \, \text{ng} \, \text{g}^{-1}$ for a modified fat supplement (Table 1).

Al levels were generally higher in the milk-based ready-to-use formulae (average $437 \, \text{ng} \, \text{g}^{-1}$) than in either powdered (average $177 \, \text{ng} \, \text{g}^{-1}$) or concentrated liquid ($131 \, \text{ng} \, \text{g}^{-1}$) formulae, suggesting a contribution of the manufacturing process to increased Al. For plain milk-based formulae as-consumed, the Al concentration increased from the powder ($18 \, \text{ng} \, \text{g}^{-1}$) to the concentrated liquid (mean $33 \, \text{ng} \, \text{g}^{-1}$) to the ready-to-use (mean $379 \, \text{ng} \, \text{g}^{-1}$).

Al levels in the soya-based infant formulae were substantially lower (mean $730 \, \text{ng} \, \text{g}^{-1}$, range $230–1100 \, \text{ng} \, \text{g}^{-1}$) than in our Canadian 1990 results (Dabeka and McKenzie 1990) (mean $1980 \, \text{ng} \, \text{g}^{-1}$, range $400–6400 \, \text{ng} \, \text{g}^{-1}$), and it is clear that efforts to reduce Al levels in these products have been successful (Table 2). The mean level of Al in soya-based formulae in this study was slightly higher than that of $640 \, \text{ng} \, \text{ml}^{-1}$ reported for Britain (Baxter et al. 1991), and $573 \, \text{ng} \, \text{ml}^{-1}$ (range $313–3479 \, \text{ng} \, \text{ml}^{-1}$) reported for Spain (Navarro-Blasco and Alvarez-Galindo 2003). In the milk-based formulae, however, average levels in this study were about three times higher than in 1990 (Table 2). This appeared to be partially due to the introduction of many more complex formulae and, in some cases, to what appears to be inadequate controls over source materials or manufacturing processes. For example, the highest concentration of Al ($3400 \, \text{ng} \, \text{g}^{-1}$) was found in a milk-based formula fortified with iron rather than in a soya-based formula. Other milk-based products from this manufacturer contained much

lower concentrations of Al, as did all of the soya-based products.

Improved manufacturing practices

As noted in the Introduction, the fundamental goal for both manufacturers and health authorities is to ensure that contaminant levels in infant formulae are lower than or of the same order of magnitude as levels present in human milk.

While this goal has been met with respect to Pb and Cd in most of the milk-based formula products, lot-to-lot variations in Pb and Cd concentrations of the same product suggest that, with judicious control over ingredients, concentrations of Pb and Cd in some of the formula products can be reduced even further. For example, of four lots of a brand of lactose-free concentrated liquid formula from one company, one contained $2.04 \, \text{ng} \, \text{g}^{-1}$ Cd, while the other three contained $0.07–0.15 \, \text{ng} \, \text{g}^{-1}$. Of three lots of a lactose-free powdered formula from another company, one contained $3.5 \, \text{ng} \, \text{g}^{-1}$ Pb while the other two contained 2.4 and $0.8 \, \text{ng} \, \text{g}^{-1}$.

In the case of Al, while there were individual products and lots with relatively high concentrations of Al, there is sufficient evidence that, with adequate controls, all manufacturers can lower Al concentrations significantly. All manufacturers were able to produce milk-based formulae which were very low in Al. For milk-based formulae stored in cans, ready-to-use formulae from one company consistently contained low Al concentrations ($11 \, \text{ng} \, \text{g}^{-1}$ Al). The same company produced six lots of concentrated liquid formula containing $2–9 \, \text{ng} \, \text{g}^{-1}$ and three lots of powdered formula contained $2–47 \, \text{ng} \, \text{g}^{-1}$ Al, as-consumed. Low Al levels were found in powdered milk-based formula products from two other manufacturers, with three lots from each containing $9–18 \, \text{ng} \, \text{g}^{-1}$, and between 6 and $11 \, \text{ng} \, \text{g}^{-1}$. Thus, it should be possible for manufacturers to consistently produce milk-based infant formulae containing less than $50 \, \text{ng} \, \text{g}^{-1}$ Al.

Al is an environmentally ubiquitous element and one would generally expect some increase in Al concentrations of formulae fortified with iron or other ingredients. However, even with these more complex formulae, manufacturers have demonstrated the ability to control contamination. For example, three lots of concentrated liquid formula fortified with iron from one company contained $70–74 \, \text{ng} \, \text{g}^{-1}$. From another company, both the concentrated liquid and powdered formulae fortified with iron contained, respectively, $15–28$ and $7–25 \, \text{ng} \, \text{g}^{-1}$. Two lots of powdered formula with added rice starch from a third company contained 24 and $35 \, \text{ng} \, \text{g}^{-1}$ Al. From the same company, three lots of each of two

Table 3. Variation in Al levels in plain soya-based infant formulae by manufacturer.

Manufacturer[a]	Type	n	Mean ($\text{ng} \, \text{g}^{-1}$)	SD ($\text{ng} \, \text{g}^{-1}$)
Company B	Ready-to-use	4	781	57
Company A		6	939	153
Company C		4	367[a]	156
Company B	Concentrated liquid	3	831	59
Company A		3	956	102
Company C		3	279[a]	16
Company B	Powdered	3	702[b]	75
Company A		3	945	113
Company C		3	209[a]	16

Notes: [a]Statistically lower ($p \leq 0.003$) than either Company B's or Company A's product of the same type.
[b]Statistically lower ($p = 0.036$) than Company A's powdered soya formula.

different formulations of powdered formula fortified with iron contained, respectively, $12–17$ and $33–74 \, \text{ng} \, \text{g}^{-1}$ Al. Thus, with manufacturing controls over the Al content of ingredients, the above data indicate that it should be possible to consistently keep Al concentrations in milk-based iron-fortified formulae below $100 \, \text{ng} \, \text{g}^{-1}$.

Soya-based formulae usually contain higher concentrations of Al than milk-based formulae (Baxter et al. 1990), but there is evidence that some manufacturers can lower concentrations of Al in soy-based formulae even further. Table 3 indicates that, of three manufacturers with ready-to-use, powdered and concentrated liquid soya-based infant formula, Company A's products consistently contained statistically lower ($p \leq 0.003$ for each of the concentrated forms) concentrations (mean $293 \, \text{ng} \, \text{g}^{-1}$, range $199–568 \, \text{ng} \, \text{g}^{-1}$) of Al than the other two companies: mean $772 \, \text{ng} \, \text{g}^{-1}$ (range $693–898 \, \text{ng} \, \text{g}^{-1}$) and mean $944 \, \text{ng} \, \text{g}^{-1}$ (range $730–1121 \, \text{ng} \, \text{g}^{-1}$). In addition, the Al concentration in Company B's powdered soy formula was significantly ($p = 0.036$) less than Company A's soy formula powder. Two formulations (regular and follow-up) of one brand of soya-based powdered formulae from Company D also contained higher Al concentrations than Company C's products, averaging over three lots each, 658 and $1152 \, \text{ng} \, \text{g}^{-1}$, respectively. The same brand of the regular formulation (as opposed to follow-up), but sold as a concentrated liquid formula, contained $757 \, \text{ng} \, \text{g}^{-1}$, as-consumed. Thus, for the same formula types, there is greater variation in Al concentrations among companies than among lots within each company. Based on a comparison of results from company to company, it appears that, by controlling the ingredients used in preparation of their soya-based formulae, Al concentrations in many of these could be reduced by at least 50%. Soya-based formulae are not

Table 4. Impact of container material on levels of Al in ready-to-use[a] infant formulae.

Manufacturer, product type	Company B, soya-based		Company B, milk-based		Company A, soya-based		Company A, milk-based		Company C, soya-based[b]	
Container	Glass	Metal	Glass	Metal	Glass	Metal	Glass	Metal	Glass	Metal
Individual lot concentrations (ng g⁻¹)	859	725	362	99	997	836	405	109	568	234
		759		93	1084	864	457	189		412
		779		76	1121	730	442	118		253
				89		810		139		300
Mean (ng g⁻¹)	859	754	362		1067		435		568	
Glass container contribution (ng g⁻¹)	105		273		257[c]		295[c]		268	

Notes: [a]Ready-to-use formulae were the only ones sold in both glass and metal containers.
[b]For Company C, the soya-based products in glass and cans differed by caloric content, and the differences in Al concentration may also have been due to the different formulations.
[c]Differences between glass and metal containers for Company A were statistically significant ($p \leq 0.009$) for both soy- and milk-based formula. For all other manufacturers and formula types, the single concentration value for aluminum in the glass bottled container exceeded the upper 95% confidence interval for the corresponding formula stored in metal containers.

recommended for feeding to preterm infants (Committee on Nutrition 1998) or to infants with milk allergies (Canadian Paediatric Society, Dietitians of Canada and Health Canada 2005); thus, the risks associated with the higher Al concentrations in these formulae are minimal.

In general, additional processing is required to produce lactose-free and hypoallergenic formulae, and Al concentrations in these formulae can be expected to be somewhat higher than in regular milk-based formulae. However, similar to soya-based formulae, there are substantial differences among manufacturers in terms of ability to control Al concentrations in these specialty formulae. For example, for concentrated liquid lactose-free formula, three lots of Company A's product contained 136–149 ng g^{-1} Al, whereas four lots of Company B's lactose-free product contained 643–796 ng g^{-1}, 4–5-fold more. Similarly, for ready-to-use casein hydrolysate formula stored in cans, three lots of Company B's product contained 458–572 ng g^{-1} Al, whereas three lots of Company A's product contained significantly more: 801–984 ng g^{-1}. It was reported that consumption of protein hydrolysate formula containing 773 ng ml^{-1} (95% CI 632–914 ng ml^{-1}) compared with human milk containing 9.2 ng ml^{-1} (95% CI 5.6–12.7 ng ml^{-1}) resulted in a statistically significant ($p = 0.028$) increase in plasma Al concentrations for infants with normal kidney function (Hawkins et al. 1994). While no corresponding health effects associated with this increase have been found, additional steps to reduce the levels of Al in these products would be prudent.

As reported for a previous Canadian survey (Gruskin 1991), formula stored in glass bottles had higher concentrations of Al than the same formula stored in metal cans (Table 4). On average, the glass bottled formulae contained 100–300 ng g^{-1} more Al than the same formulae stored in cans. Thus, it can be surmised that additional Al is entering the formula at one or more of the following points: glass containers used for storing formula (washing, leaching), the lids (leaching), and/or equipment and processes used for filling the glass containers. Al contamination of glass-stored formulae appears common to more than one manufacturer, but the magnitude of the contamination is product-dependent in some cases. The low concentrations of Al in most of the glass-stored electrolyte and glucose solutions suggest that elimination of the contamination source is technologically possible.

Infants born prematurely generally have weakened kidney function, and premature formula given to these infants should have as low concentrations of Al as technologically feasible using good manufacturing practices, i.e. substantially less than 100 ng g^{-1}. Three different formulations (one sample each) of Company B's premature formula, all sold under the same brand name (not tabulated), contained, respectively, 851, 955 and 909 ng g^{-1} Al. These are among the highest concentrations found for any of the milk-based formulae and are substantially higher than two premature formulations, sold under the same brand name by Company D: a single sample of the first formulation contained 365 ng g^{-1} Al, while three lots of the second formulation contained 449–461 ng g^{-1} Al. The above formulae are all stored in glass and it may be possible to lower a portion of the Al present in them by finding and eliminating the Al contamination source(s) related to storage in glass (Table 4). Based on the differences in Al concentrations between the tested premature formulae manufactured by Company D and those premature formulae manufactured by Company B, screening of ingredients and processes for Al contamination may also lower the Al content.

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