

March 13, 1996

Chemistry Review Branch, HFS-247

Cumulative exposure estimates for bisphenol A (BPA), individually for adults and infants, from its use in epoxy-based can coatings and polycarbonate (PC) articles. Verbal request of 10-23-95.

Division of Product Manufacture and Use, HFS-245

Attention: G. Diachenko, Ph. D.

This memorandum is in response to your verbal request for cumulative dietary exposure estimates to bisphenol A (BPA), individually for both adults and infants, from its use in epoxy-based can enamels (coatings) and polycarbonate (PC) articles. In developing our exposure estimates, you specifically requested that we use the results of: 1) studies conducted by the Chemistry Methods Branch (CMB) on BPA migration from PC infant bottles under conditions simulating actual consumer use, and 2) a study conducted at the University of Granada, Spain (denoted as the "Spanish" study), involving BPA levels in food packed in epoxy-coated cans.<sup>1</sup> We have also used selected information on: 1) BPA migration from can enamels obtained by an industrial consortium, the Society for Plastics Industries Inter-Industry Group on Bisphenol A and Alkyl Phenols (SPI-IGBAP)<sup>2</sup>, and 2) a survey conducted by CMB on BPA levels in infant formula packed in epoxy-coated cans.

### **Background**

A purported link between the weak estrogen-like physiological activity of certain organic compounds (often referred to as environment estrogens, estrogen mimics, or xenoestrogens) and reproductive effects of certain animals (e.g., birds and alligators) has raised speculation on the possible effects of human exposure to these substances. The substances in question originate from several sources, occurring both in nature (phytoestrogens) and in industrial products (such as components for cosmetics, pesticides, and food-packaging).<sup>3</sup>

One particular substance with estrogen-like physiological activity in vitro, BPA, is used as a monomer in the manufacture two types of polymers used for food-contact articles, i.e., PC polymers and epoxy-based can enamels. PC-based polymers are manufactured by the reaction of BPA with phosgene or diphenyl carbonate and are, for the most part, intended for repeated contact with food. Typical uses include food processing equipment, such as

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<sup>1</sup> Brotons, J. A.; Olea-Serrano, M. F.; Villalobos, M.; V. Pedraza, and Olea, N., "Xenoestrogens Released from Lacquer Coatings in Food Cans," *Environmental Health Perspectives*, **1995**, *103*, 609-612.

<sup>2</sup> The SPI-IGBAP study on can coatings is contained in a report submitted to FMF 580 entitled "Report on Potential Exposure to Bisphenol A from Epoxy Can Coatings," Epoxy Resin Can Coating Work Group, SPI-IGBAP, September, 1995.

<sup>3</sup> Larkin, M. "Estrogen, Friend or Foe?," *FDA Consumer*, April 1995, pp. 25-29.

popcorn makers, and water and infant bottles. Epoxy-based coatings derived from BPA and epichlorohydrin are used in a variety of canned food and beverage applications.

We have previously presented an estimate of cumulative exposure to BPA. A chemistry memorandum dated 5-2-94 on FAP 3B4361 (S. Carberry to J. Smith), responding to a Division of Health Effects Evaluation (DHEE) request of 1-26-94, estimated cumulative dietary exposure to BPA at 0.8 mg/p/d. (Assuming a daily intake of 3 kg food, this corresponds to a dietary concentration of 0.27  $\mu\text{g}$  BPA/g food, or 0.27 ppm.) This estimate was developed by "summing" the individual dietary exposures for several coating and polymer applications listed under Parts 175 and 177 of 21 CFR. This estimate is somewhat exaggerated and, in light of the new migration data, may be refined to give a more realistic estimate of exposure.

### **Approach to a "Realistic" Cumulative Exposure**

The CMB and SPI-IGBAP have each been involved in developing additional data that may be used in providing a realistic estimate of dietary exposure to BPA from its use in epoxy-based can enamels and PC infant bottles. Specifically, studies by CMB have focused on BPA migration from PC infant bottles *and* BPA levels in vegetables<sup>4</sup> and infant formula<sup>5</sup> packed in epoxy-coated cans. Studies by SPI-IGBAP have focused on BPA migration from both PC articles<sup>6</sup> and epoxy-coated cans.<sup>2</sup>

We will use selected results reported by CMB and SPI-IGBAP, in addition to the Spanish study, to develop estimates of cumulative dietary exposure to BPA, for both infants and adults, from the use of epoxy-based can enamels and PC articles. In estimating cumulative exposure to BPA for *adults*, we will consider exposure from the use of both epoxy-based can enamels and reusable PC articles. Exposures to BPA from the use of epoxy-based can

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<sup>4</sup> A summary of CMB's studies on BPA migration from PC infant bottles and BPA level in vegetables was provided to the Chemistry Review Branch (CRB) on 9-26-95 by CMB (Henry Hollifield) in a draft report entitled "Bisphenol-A: Status Summary Report."

<sup>5</sup> CMB's studies on BPA levels in infant formula are described in a CMB memorandum dated 3-5-96 (J. Biles to G. Diachenko).

<sup>6</sup> The SPI-IGBAP study on PC articles is contained in a report submitted to FMF 580 entitled "Report on Potential Exposure to Bisphenol A from Food-Contact Use of Polycarbonate Resins," Polycarbonate Work Group, SPI-IGBAP, November, 1995.

enamels will be based on both migration studies (SPI-IGBAP) and BPA levels in food (CMB and Spanish studies). In estimating cumulative BPA exposure for *infants*, we will consider two primary sources of BPA exposure:

- 1) epoxy-based can enamels used to contain infant formula (liquid). Exposure to BPA will be based, in part, on the results reported by CMB on BPA levels in infant formula (liquid).
- 2) PC infant bottles used by the consumer to prepare infant formula and milk. Exposure to BPA will be based on the results reported by CMB on BPA migration from PC infant bottles.

The results of the CMB, SPI-IGBAP, and Spanish studies are summarized below.

## **Results**

### **CMB Studies**

CMB conducted migration studies on reusable PC infant bottles under conditions simulating actual household use in the preparation of infant formula. PC-based infant bottles are of interest since they contact a considerable portion of an infant's diet and, as such, represent a major route of potential exposure. In addition, CMB surveyed selected canned vegetables and infant formula for levels of BPA.

#### *PC Infant Bottles*

Residual levels of BPA in commercially available PC infant bottles were reported to range from 7 to 30 ppm. PC bottles were tested according to two migration protocols, provided by CRB,<sup>7</sup> designed to model "common" and "worst case" use scenarios in the preparation of infant formula (see Appendix I). The results are summarized below.

For the common protocol, PC bottles were sterilized in boiling water (5 minutes), filled with a food-simulating liquid (FSL), water or 10% ethanol, and stored at room temperature for up to 72 h. (This test procedure is in agreement with the "common" protocol suggested by CRB). The test solutions were then analyzed for BPA by high performance liquid chromatography (hplc) with fluorescence detection. BPA was not detected in any sample at a limit of detection (LOD) of 5 ppb in the FSLs. Using a FSL volume-to-sample surface area ratio of 3.4 mL/in<sup>2</sup> and our standard assumption of 10 g food per in<sup>2</sup>, this corresponds to a BPA migration to food of less than 1.7 ppb.<sup>8</sup>

For the worst-case protocol, PC bottles (containing 46 ppm residual BPA)<sup>9</sup> were sterilized in boiling water (5 minutes), filled with the FSLs water or 10% ethanol, heated to 100°C for 0.5 h, cooled to room temperature, and stored in the refrigerator for 72 h. The test solutions were analyzed for BPA by hplc with fluorescence detection. BPA was not detected at a LOD of 5 ppb in the FSLs, corresponding to a migration to food of less than 1.7 ppb. We will use this value in developing an estimate of infant exposure to BPA from the use of PC infant bottles.

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<sup>7</sup> These protocols were provided to CMB in 1/95.

<sup>8</sup> The PC samples were reported to be 6 cm x 4 cm, corresponding to a 2-sided surface area of 7.4 in<sup>2</sup>. Using a FSL volume of 25 mL, the FSL volume-to-sample surface area ratio is 3.4 mL/in<sup>2</sup> (John Biles, CMB, personal communication).

<sup>9</sup> See the reference cited in footnote 3.

*Can Enamels (Vegetables)*

CMB surveyed BPA levels in select canned vegetables purchased in local (Washington, D.C. area) supermarkets and packed in several different can types (imported and domestic) and epoxy-based coating enamels. No information on the exact breakdown of can construction (i.e., 2- or 3-piece; identity of end and body coating) was reported by CMB. The test samples consisted of canned mushrooms, tomatoes, artichokes, and mixed vegetables and included both the pureed vegetable and liquid. The test samples were analyzed for BPA by hplc. CMB reported BPA levels ranging from 5-39 ppb in vegetables, with an *average* value of 16 ppb for all six (6) samples (see Table 1).

Table 1: BPA Levels in Canned Vegetables as reported by CMB

Vegetable	BPA Level (ppb)
mushrooms (3 samples)	6, 12, 15
tomatoes	18
artichokes	39
mixed vegetables	4

In the sections that follow, we will compare CMB's results on BPA levels in vegetables to those reported in the Spanish study. We will then compare actual BPA levels in vegetables (CMB and Spanish study) to BPA levels estimated based on migration studies (SPI-IGBAP studies).

*Can Enamels (Infant Formula)*

CMB surveyed BPA levels in both milk and soy infant formula (liquid concentrate) distributed by five (5) leading manufacturers (i.e., Mead-Johnson, Wyeth, Ross, Carnation, Gerber) and purchased in local (Washington, D.C. area) supermarkets. The samples consisted of both 2- and 3-piece cans with epoxy, modified-epoxy, and/or PVC-based side and lid coatings (see Table 2, below). Several lots from each manufacturer were tested in triplicate (for a total of 42 analyses). Aliquots of each test sample were loaded onto a solid-phase extraction column, with the retained BPA eluted with chloroform (CHCl<sub>3</sub>). The organic phase was evaporated to near dryness, redissolved in acetonitrile: methanol:water (1:1:1), and analyzed by hplc with fluorescence detection. BPA recoveries were reported to range from 67-106%. The results are shown in Table 2.

Table 2: BPA Levels in Infant Formula (Concentrate) as reported by CMB

Manufacturer	Lot No.	Can Type (piece)	Formula Type	Coating (end/body) <sup>a</sup>	BPA Level (ppb) <sup>b</sup>
Mead-Johnson (MJ)	MJJ04	2	milk	ep+,ep-ester	12.1
	MKJ42	2	milk	ep+,ep-ester	13.2
	CJJ88	3	milk	ep/ep+	5.1
Wyeth	1C23C	3	milk	ep/ep	4.8
	2A06C	3	milk	ep/ep	3.6
	AK27C	2	milk	ep/ep-co	8.3
Ross	10590	2	milk	ep/PVC	1.3
	10523	2	milk	ep/PVC	1.5
	73509	3	soy	ep/ep-fa	4.5
	06799	2	soy	ep/PVC	1.3
Carnation	5319	3	milk	ep/ep	0.1
	5193	3	milk	ep/ep	0.7
	5293 <sup>c</sup>	3	soy	ep/ep	3.9
Gerber <sup>d</sup>	ALJ24	3	milk	ep-co/ep-ma	9.5

*a*- ep= epoxy; ep+= epoxy plus other components; ep-ester= epoxy-ester; ep-co= epoxy-castor oil; ep-fa= epoxy-fatty acid; ep-ma= epoxy-melamine; *b*- average of triplicate analyses; *c*- this sample was reported to be ca. 3 years old; *d*- a MJ product marketed under the Gerber name.

Inspection of the data contained in Table 2 indicates BPA levels ranging from 0.1-13.2 ppb in infant formula (liquid concentrate). The *average* BPA level for all fourteen (14) samples surveyed is 5 ppb. In general, cans manufactured with modified-epoxy (e.g., epoxy-ester) coatings exhibited the highest levels of BPA. Directions on the labels of the liquid formula concentrates specify 1:1 dilution with water (v/v). Accordingly, BPA levels in *prepared* formula range from 0.05-6.6 ppb, with an average of level of 2.5 ppb. Given that an infant's diet may consist of *exclusively* one type (or brand) of infant formula, we will use the *highest* BPA level in prepared formula (i.e., 6.6 ppb) in developing an estimate of infant exposure to BPA from epoxy-based can enamels.

#### Spanish Study

The Spanish study involved a survey of BPA levels in canned vegetables purchased in U. S. and Spanish supermarkets. No information on the origin of individual cans (i.e., U. S. or Spanish) or exact breakdown on can construction (i.e., 2- or 3-piece; identity of end and body coating) was reported. The test samples consisted of the *liquid* phase from select green beans (whole), artichoke hearts, asparagus spears, corn, peas, mushrooms, palm hearts, peppers, tomatoes, and mixed vegetables. Aliquots of each test sample were extracted with CHCl<sub>3</sub>, the organic phase evaporated to dryness, the resulting residue suspended in ethanol, and

analyzed by hplc with ultraviolet detection (280 nm). The results are shown in Table 3 [taken from the reference cited in footnote 1 (Table 1)].

Table 3: BPA Levels in Canned Vegetables as reported in the Spanish Study

Vegetable	Food mass (g/can)	BPA Level ( $\mu\text{g}/\text{can}$ )	BPA Level in Food (ppb) <sup>a</sup>
peas	300	$22.9 \pm 8.8$	76
artichokes	390	$18.6 \pm 6.5$	48
green beans	400	$11.9 \pm 5.3$	30
mixed vegetables	450	$10.1 \pm 4.3$	22
corn	300	$4.5 \pm 2.6$	15
mushrooms	350	$4.2 \pm 4.1$	12
asparagus	230	ND <sup>b</sup>	-
palm hearts	500	ND	-
peppers	390	ND	-
tomatoes	390	ND	-

*a*- determined by dividing the reported *average* BPA level ( $\mu\text{g}/\text{can}$ ) by the food mass (g/can); *b*- ND= non-detect.

Inspection of the data contained in Table 3 indicates that BPA was not detected in four (4) of the ten (10) test samples. The *highest* BPA level was 76 ppb in peas. The LOD was not reported in the Spanish study. However, assuming that the Spanish investigators were able to achieve a LOD of 5 ppb (as reported in the CMB and SPI-IGBAP studies), the *average* BPA level for all ten (10) vegetables surveyed is on the order of 22 ppb.

Taken as a whole, BPA levels in food reported in this study are slightly *higher* in comparison to those reported by CMB (compare Tables 1 and 3). In estimating BPA levels in food (Table 3, column 4), we assumed that BPA levels for the vegetable (solid) would be identical to those reported for the liquid phase. In general, the liquid phase *might* be expected to exhibit *higher* BPA levels in comparison to the solid vegetable. (This, of course, assumes a somewhat less than maximum shelf life, or in other words, non-equilibrium conditions). Accordingly, BPA levels in food estimated based on the Spanish study results may tend to be *higher* in comparison to levels reported by CMB.

Given that an individual's diet typically consists a variety of canned vegetables, we believe that an *average* level of 22 ppb BPA in vegetables will be sufficiently conservative for estimating exposure to BPA from epoxy-based can enamels.

SPI-IGBAP

SPI-IGBAP conducted migration studies to address exposure to BPA from its use in epoxy-based can enamels.<sup>10</sup> SPI-IGBAP selected a total of thirteen (13) can samples chosen to represent a broad spectrum of those commercially available for packaging of food and beverages. The can samples were tested (in triplicate) with the FSLs 10%- and 95%-ethanol (EtOH) according to conditions of use A-H (as defined in Table 2 of 21 CFR 175.300(d)) depending on the representative packaging applications. The test solutions were analyzed after the initial heating phase (0.5 h or 2 h)<sup>11</sup> and at 10 days using hplc with fluorescence detection. The test parameters (i.e, can type, representative food, and condition of use) and results are summarized below in Table 4 (as taken from pp. 12 and 14, respectively, of the SPI-IGBAP report).

Table 4: BPA Migration from Can Enamels as reported by SPI-IGBAP

Can Type (piece)	Food	End Coating	FSL (% EtOH)	Test Cond.	BPA Level (ppb) <sup>a</sup>	
					24 h	240 h
2	beer/bev.	vinyl	10	D	ND <sup>b</sup>	ND
		epoxy	10	D	ND	ND
		uncoated	10	D	ND	ND
2	vegetables	epoxy	10	A	69	71
		epoxy	10	A	116	120
		uncoated	10	A	73	71
		uncoated	10	A	7	8
3	meat	uncoated	95	A	80	81
	formula	epoxy	10	A	87	121
	vegetables	epoxy	10	A	40	40

<sup>10</sup> A Division of Petition Control (DPC) letter dated 3-15-95, transmitting comments contained in our 3-15-95 memorandum (A. Bailey to D. Robertson), provided several comments on a migration protocol proposed through their agent, Keller and Heckman (K&H).

<sup>11</sup> The SPI-IGBAP report states (p. 13) that test solutions for the initial heating phase (both 0.5 h and 2 h) were actually tested after 1 day.

meat	epoxy	95	A	ND	ND
fruit juice	epoxy	10	C	83	86
tomato prods.	epoxy	10	A	25	25

*a-* average of triplicate analyses; *b-* non-detected at less than 5 ppb food.

Inspection of the data contained in Table 4 indicates that BPA was not detected (<5 ppb food) in the beer/beverage can test solutions. The 2- and 3-piece food cans gave results ranging from non-detection of BPA in meat test samples (<5 ppb food) to 121 ppb for some infant formula test samples. BPA migrations for the four test samples representative of vegetables packed in 2-piece can/coatings were (240 h) 71 ppb, 120 ppb, 71 ppb, and 8 ppb, corresponding to an average BPA migration of 68 ppb for the 2-piece can/coatings. BPA migration for the one test sample representative of vegetables packed in 3-piece can/coatings was 40 ppb. The *average* BPA migration for both 2- and 3-piece can/ coatings is 62 ppb.

#### Comparison of CMB, Spanish, and SPI-IGBPA Studies

In summary, the pertinent results of the CMB, SPI-IGBAP, and Spanish studies are shown in Table 5.

Table 5: Summary of CMB, SPI-IGBAP and Spanish Studies

Study	BPA Levels (ppb)		
	PC Bottles	Vegetables	Infant Formula
CMB	<1.7	5-39	0.05-6.6 (2.5) <sup>a</sup>
Spanish		ND-76 (22)	
SPI-IGBAP		8-120 (62)	121

*a-* values in parenthesis represent an *average* of the reported range

For canned vegetables, the SPI-IGBAP results on BPA migration from cans/coatings representative of those used to package vegetables (range 8-120 ppb; average 62 ppb) are in reasonable agreement with BPA levels in canned vegetables as reported by CMB (range 5-39 ppb; average 16 ppb; Table 1) and in the Spanish study (range ND-77 ppb, average 22 ppb; Table 3). However, for infant formula, the SPI-IGBAP result on BPA migration from a can/coating representative of that used to package infant formula (121 ppb) is considerably higher than detected BPA levels in infant formula (prepared) as reported by CMB (range 0.05-6.6 ppb; average 2.5 ppb).

CRB typically estimates dietary exposure for a proposed use based on accelerated testing protocols designed to model both the processing and storage phases encountered in the packaging of food. However, CRB prefers to base dietary exposure estimates on *actual* adjuvant levels in food, when available, as determined by analysis of commercially available samples (e.g., BPA in vegetables or infant formula). Accordingly, *we will use the results of the CMB and Spanish studies in our exposure estimates.*

#### Exposure

Given that an *adult's* diet typically consists of a variety of vegetables, only some of which are canned, we will use an *average* BPA level of 22 ppb as determined from the Spanish survey (value in parenthesis in Table 5) in estimating BPA exposure from epoxy-based can enamels. Given that an *infant's* diet may consist of exclusively one type (or brand) of infant formula, we will use the *highest* BPA level of 6.6 ppb as determined from the CMB survey (i.e., highest value in the range reported in Table 5) in estimating BPA exposure from infant formula packaged in can enamels. We will also use the results of CMB on BPA migration from PC infant bottles (<1.7 ppb BPA in infant formula and milk). Exposure estimates for both adults and infants are described in detail below.

### Adults

For adults, we will estimate cumulative exposure to BPA using an average level of 22 ppb in vegetables. We assumed that these levels are representative of all food (i.e., aqueous, acidic, alcoholic, and fatty) packed in coated cans. This is known as the "weight-averaged" concentration of BPA in food ( $\langle M \rangle$ ), i.e.,  $\langle M \rangle_{\text{average}} = 22$  ppb. Using a consumption factor (CF) of 0.17 for polymer-coated metal, as discussed in our "Recommendations" (Appendix IV, Table 1), the corresponding *average* dietary concentration of BPA from can enamels is 3.7 ppb (22 ppb x 0.17). Assuming an individual's daily intake of food is 3 kg, this corresponds to an estimated daily intake (EDI) of 11  $\mu\text{g/p/d}$ .

As noted above, PC-based polymers are intended for repeated-use by the adult consumer. Given the large quantity of food processed over the service lifetime of a typical PC-based food-contact article, dietary exposure to BPA would be insignificant in comparison to BPA exposure for can enamels. Therefore, the cumulative exposure to BPA from its use in can enamels and PC-based polymers is expected to be no greater than 11  $\mu\text{g/p/d}$  for adults.

We emphasize that this estimate is conservative since it assumes that *all* food types (including beverages) are packed in cans coated with BPA-based enamels. Although epoxy-based can enamels dominate the market, other major types of can enamels, such as oleoresinous and vinyl, are used depending on the particular packaging application.

### Infants

For infants, we will estimate cumulative exposure to BPA from two primary sources (can enamels and PC infant bottles) using the results of the CMB and Spanish studies as follows:

- 1) epoxy-based can enamels used to contain liquid infant formula. We will assume that 6.6 ppb (CMB study) represents the average BPA level in prepared infant formula.
- 2) PC infant bottles used by the consumer to prepare infant formula and milk. Exposure to BPA will be based on <1.7 ppb BPA from PC infant bottles (CMB study).

### *Comments on the Overall Dietary Intake of Infants*

Estimation of cumulative exposure to BPA from the consumption of infant formula must take into account the changes in the diet of a maturing infant. As the infant matures, formula intake will decrease and solid food intake will increase. The use of infant bottles decreases as an infant matures. Recommended feeding guidelines for infants (up to 12 months of age)

are outlined in Appendix II.<sup>12</sup> Inspection of the information contained in Appendix II suggests two observations:

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<sup>12</sup> *Textbook of Pediatric Nutrition*, 2nd Edition, R. Suskind and L. Lewinter-Suskind, Eds.; Raven Press, NY, 1993, Appendix A, p 531.

First, an infant's diet consists solely of formula up to about 3 months of age, with small amounts of soft foods and juice introduced from 3-6 months of age. These guidelines lend support to claims that infants generally do well on most soft (strained) baby foods between 3-6 months of age. Many infants are given "junior" foods between 6-9 months of age, with most children being capable of eating table foods between 9-12 months of age.<sup>13</sup>

Second, infant formula should be replaced, if not supplemented with, whole milk by 6-7 months of age. One reference states that it is generally recommended that infant formula be replaced with homogenized milk at 12 months of age.<sup>14</sup> Based on 1979 data, another reference reports that the fraction of infants using prepared formula is approximately 10% at 12 months of age.<sup>15</sup> In general, it appears that some pediatricians prefer to introduce milk into an infant's diet sometime after 6 months of age, while others prefer to wait until 12 months of age. In light of these observations, we will focus our analysis on the time period when most *infant formula* is actually consumed; *the first year of an infant's life*.

#### *Formula Consumption*

Using the TAS International Diet Research System (TAS Diet)<sup>16</sup>, the mean average-daily-consumption of infant formula (3 days, actual users) for infants up to 12 months of age is 820 g (standard deviation± 363 g). Information in Appendix II indicates that the total recommended volume of liquid (formula and milk) consumed by an infant up to 12 months of age is ca. 25-30 ounces (oz) per day (725-870 g per day), suggesting good agreement between actual and recommended formula intakes.

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<sup>13</sup> *Taking Care of Your Child: A Parent's Guide to Medical Care*, Special Federal Employee Edition; R. Pantell, J. Fries, and D. Vickery; Addison-Wesley, NY, 1990, p 62.

<sup>14</sup> *How to be Your Child's Doctor (Sometimes)*, 1st Edition; A. S. Hashim; International Graphics Printing Service, MD, 1985, Ch. 2, p 23.

<sup>15</sup> *Pediatric Nutrition Handbook*, 2nd Edition; G. Forbes and C. Woodruff, Eds.; American Academy of Pediatrics, Elk Grove Village, IL, 1985, Ch. 2, p 16.

<sup>16</sup> TAS Diet (version 3.14) is based on the combined 1989-90, 1990-91 and 1991-92 USDA Continuing Survey of Food Intake by Individuals (CSFII) survey data.

### *Cumulative Exposure*

An average EDI for BPA from epoxy-based can enamels used for infant formula may be calculated by multiplying the mean average-daily-consumption of infant formula (820 g) by the average (6.6 ppb) BPA level in infant formula. Thus, the average EDI for BPA from can enamels is 5.4  $\mu\text{g/p/d}$ . Exposure to BPA from the use of PC infant bottles was estimated at <1.7 ppb, corresponding to an EDI of <1.4  $\mu\text{g/p/d}$ . Accordingly, the average cumulative exposure to BPA is expected to be no greater than 7  $\mu\text{g/p/d}$  for infants.

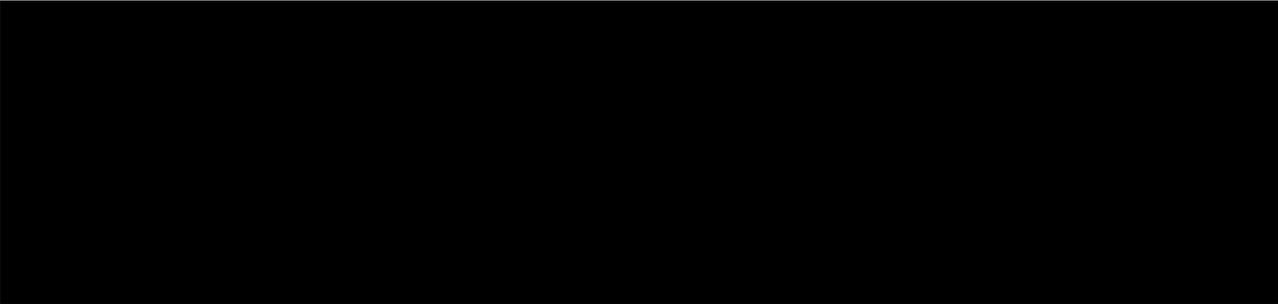
We emphasize that these estimates are conservative since we assumed that all infant formula:

1) is packed in cans coated with BPA-based enamels; and 2) is in a liquid form, specifically ready-to-feed, as used by the consumer. Powdered formula accounts for a finite portion of the infant formula market.<sup>17</sup> In contrast to liquid formula (i.e., ready-to-feed or concentrate), powdered formula would not be subjected to the rigorous temperature/time conditions needed for in-can sterilization that, ultimately, lead to measurable BPA levels in the formula.

### **Summary**

Adult cumulative exposure to BPA from its use in can enamels and PC-based polymers is expected to be no greater than 3.7 ppb, corresponding to an EDI of less than 11  $\mu\text{g/p/d}$  (based on an adult daily food intake of 3 kg). Infant cumulative exposure to BPA from its use in PC infant bottles and can enamels for infant formula is expected to be no greater than 8.3 ppb (6.6 ppb + 1.7 ppb), corresponding to an EDI of less than 7  $\mu\text{g/p/d}$  (based on an infant daily liquid intake of 820 g).

Allan B. Bailey, Ph. D.





## Appendix I

### Common Protocol

This protocol models *typical* preparation conditions recommended when sterilization is necessary, either because of poor water quality, inadequate refrigeration, or infant vulnerability. The typical method of preparation involves boiling the bottles (in water) and water (for formula) *separately* for 5 minutes in appropriate vessels. The water (for formula) is allowed to cool, followed by the addition of concentrated (or powdered) formula. Briefly, the migration protocol designed to model this use is as follows: sterilize the bottle for 5 minutes, add food or FSL, refrigerate for 24-48 h, and warm to body temperature (approximately 38°C).

### “Worst Case” Protocol

This protocol models the "terminal sterilization" method and represents the most rigorous sterilization conditions. In comparison to the common protocol, the worst-case protocol would lead to the maximum anticipated levels of BPA migration to infant formula. In terminal sterilization, both the bottles and water and/or infant formula (contained in the bottles) are sterilized *simultaneously* in a large kettle or sterilizer. (This method of preparation is known as terminal because all sterilization is performed at once, at the end). Briefly, the protocol designed to model this use is as follows: sterilize bottle for 5 minutes, add food or FSL, heat to 212°F (100°C) for 0.5 h, cool to room temperature, refrigerate for 24 h, and warm to body temperature.