DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service
Food and Drug Administration

Memorandum

Date: June 2, 2008

From: Division of Food Contact Notifications (HFS-275)
Chemistry Review Group 1
Allan Bailey, Ph.D.

Subject: Memorandum to the File. Update on cumulative exposure to BPA for infants from epoxy-based container coatings and polycarbonate (PC) bottles in contact with infant formula. Verbal request dated 4/29/08.

To: Division of Food Contact Notifications
Regulatory Group 1
Attention: M. Twaroski, Ph.D.

During the week of April 14, 2008, upon the request of the Commissioner of Food and Drugs, FDA formed an agency-wide BPA (Bisphenol A) Task Force, consisting of representatives from the various Centers, to facilitate cross-agency review of current research and new information on BPA for all FDA regulated products. As a result of this review, the Task Force will make recommendations to the Commissioner regarding next steps.

As part of the FDA Task Force effort, CFSAN's OFAS is evaluating new data concerning infant exposure to BPA from food contact materials. BPA is a monomer used in the manufacture of epoxy-based container coatings for food and beverages and polycarbonate (PC) articles, such as infant formula bottles and certain water bottles. This memorandum will:

1) provide summaries of and comments on numerous reports and studies on BPA levels in infant formula as a result of epoxy-based enamels used to coat cans containing formula and PC bottles used to prepare and serve infant formula; and,
2) update cumulative exposure, as appropriate, to BPA for infants from the use of BPA-containing articles.

<u>Background</u>

Our most recent estimate of the cumulative estimated daily intake (CEDI) of BPA for infants was contained in a memorandum dated [redacted] on [redacted]. The data and conclusions in that memorandum were taken from our 5/2/00 memorandum on FAP 9Z4681[2] and our 3/13/96 memorandum[3]. [redacted] we concluded that:

"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

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[redacted]
2 Chemistry memorandum on FAP 9Z3681 dated 5/2/00 (K. Paquette to J. Smith).
3 Memorandum to the File dated 3/13/96 (A. Bailey to G. Diachenko).

CEDI of less than 7 μg/p/d (based on an infant daily liquid intake of 820 g)".

FDA Laboratory Studies

In our 3/13/96 memorandum, we noted that our laboratories conducted two sets of pertinent studies determining: 1) BPA levels in canned infant formula (liquid concentrates), and 2) BPA migration from PC infant bottles under conditions simulating actual household use in the preparation of formula. The results of both studies have since been published[4,5].

In the first study, Biles et al. determined BPA levels in 14 samples of infant formula (liquid concentrates) representing 5 brands purchased in local (Washington, DC) supermarkets. At least one interior surface of each container (sidewall and/or ends) was found to contain a BPA-based epoxy coating. BPA levels in the formula concentrates ranged from 0.1 to 13.2 ppb, with an average of 5 ppb. Label directions specify a 1:1 dilution with water. Thus, BPA levels in prepared formula would range from 0.05 to 6.6 ppb, with an average of 2.5 ppb. We used the highest value of 6.6 ppb in our exposure estimate.

In the second study, Biles conducted migration tests with cut-up bottle strips (2-sided migration) or intact bottles (1-sided migration) in contact with various food simulants (water; 8%, 10%, 50%, or 95% ethanol; [redacted]) or real foods (infant formula or apple juice) under various time and temperature conditions designed to represent exaggerated, repeat, typical and "extreme" typical uses. Only the typical tests were deemed to simulate *normal use* of baby bottles:

1) Intact bottles were held in boiling water for 5 minutes, filled with apple juice or formula, and refrigerated at 4ºC for 24 hrs. BPA was not detected at a detection limit (DL) of 100 ng/mL (100 ppb).
2) Bottle pieces were placed in the simulants, heated at 100ºC for 0.5 h, then refrigerated (4ºC) for 72 h. The BPA level in the 10% ethanol and water food simulants was about 2 μg/kg (2 ppb), after correction for the food mass-to-surface area typical of baby bottles. The DL was 2 ng/mL (2 ppb). (The high DLs for formula and juice were attributed to matrix effects of real foods vs simulants.)

As noted in our 3/13/96 memorandum, migration experiments on PC infant bottles at room temperature (RT) for 72 h ("common" protocol) and 100ºC/0.5 h, then 4ºC/3 d ("worst-case" protocol) both resulted in non-detection of BPA at a DL of 5 ppb. Using the simulant volume-to-sample surface area (3.4 mL/sq in) and our standard assumption (10 g food/in^2) corresponds to a BPA migration to food of <1.7 ppb. We used a value of <1.7 ppb in our exposure estimate.

FAP 9Z4681

4 Biles, J., McNeal, T., Begley, T., Hollifield, H., "Determination of Bisphenol-A in Reusable Polycarbonate Food-Contact Plastics and Migration to Food-Simulating Liquids, *Journal of Agricultural and Food Chemistry*, Vol. 45, No. 9, 1997, pp. 3541-3544.
5 Biles, J., McNeal, T., Begley, "Determination of Bisphenol-A Migrating from Epoxy Can Coatings to Liquid Infant Formula Concentrates," *Journal of Agricultural and Food Chemistry*, Vol. 45, No. 9, 1997, pp. 4697-4700.

In our 5/2/00 memorandum on FAP 9Z4681[2], we commented on literature information submitted by the National Environmental Trust (NET) on BPA migration from can coatings, PC infant bottles and tableware. The information consisted of discussions of migration tests conducted by Biles (above), Consumers Union[6], Takao[7] and Iguchi[8].

We noted that although we had already seen the results of Biles's studies, NET provided three new studies on the migration of BPA from epoxy-coated cans and PC articles into food. Of these three studies, only the Takao study included data that had been published and peer-reviewed. Nevertheless, our analysis of the Takao data and NET's summary of the CU data indicated that the BPA migration levels were comparable to those published by Biles and used in our 1996 exposure estimates. At that time we concluded that there was no reason to revise the exposure estimate for BPA given in our 3/13/96 memorandum.

Need for a Revised Estimate and Approach

Since our last review of BPA exposure, numerous studies relating to infant exposure to BPA have appeared in the open literature, as well as reports or evaluations from advocacy groups and government bodies. For the most part, the studies in the open literature, as well as some unpublished studies, have been discussed and considered in the reports and evaluations from advocacy groups, such as the Environmental Working Group (EWG), and government bodies, such as Health Canada (HC) and the European Food Safety Authority (EFSA). Along with the re-evaluation of BPA toxicity by the National Toxicology Program (NTP)[9], these reports and evaluations have prompted the Agency's review of infant exposure to BPA from the use of epoxy-based can enamels to package formula (liquid and powdered formula) and the use of PC infant bottles to prepare and serve formula. Reports and evaluations from EFSA, EWG and HC are briefly discussed below

In addition, in order to provide some guidance on the appropriate BPA levels to use based on the numerous studies since our previous estimates, we reviewed recommendations from several organizations on "infant formula feeding."

Finally, while it is unlikely that infant formula consumption has changed significantly since our previous evaluation, we used updated food consumption databases to determine infant formula consumption for several age groups up to 12 months of age.

Pertinent Reports and Evaluations

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6 "Baby Alert: New Findings About Plastics," *Consumer Reports*, May 1999, pp. 28-29.
7 Takao, Y., Lee, H. C., Ishibashi, Y., Kohra, S., Tominaga, N., Arizono, K., "Fast Screening Method for Bisphenol A in Environmental Water and in Food by Solid-Phase Microextraction (SPME)," *Journal of Health Science*, Vol. 45, 1999, p. 39.
8 Cited by NET as unpublished results by Iguchi of Yokohama City University, Japan.
9 NTP Draft Brief published on April 14, 2008 by the U.S. National Institutes of Health. (NIH)

The EFSA, EWG and HC reports discussed below are not the only reports and evaluations that have come to our attention. Rather, they are ones that contain the most extensive discussions on the chemistry aspects of this issue.

For the most part, the studies discussed in these reports have focused on BPA levels in infant formula as a result of BPA migration from epoxy-based container coatings and PC infant bottles. By far the majority of these studies have involved testing of PC infant bottles under “typical” and “non-typical” scenarios.

ESFA Report (2006)

In 2006, ESFA[10] re-evaluated the use of BPA in articles intended to contact food, with particular attention given to infant exposure. EFSA noted that previous evaluations included an EU Risk Assessment Report (RAR) on BPA in 2003 and a Scientific Committee for Food (SCF) opinion on BPA in 2002. The information pertinent to infant formula for both epoxy-based can coatings and PC bottles is summarized below (pp. 16-20 of the EFSA report).

Several pertinent studies were discussed in the EFSA report. The first three studies cited evaluated BPA migration levels from PC bottles after one use, while the next three cited evaluated BPA migration levels from PC bottles after several uses or cycles. The final study cited evaluated BPA levels in powdered formula, but no studies involving liquid infant formula were discussed. These studies are described in more detail below.

PC bottles- one-time use. In the first study by Simoneau[11], bottles filled with water or 3% acetic acid (50ºC), agitated and cooled to RT gave BPA levels <10 µg/L (DL). In the second, unpublished study by Hanai[12], bottles filled with water (95ºC), cooled and stored at RT overnight gave BPA levels ranging from 3 to 55 µg/L (DL ~2 µg/L). In the third study by Earls[13], bottles filled with water or 3% acetic acid (100ºC), stored in the refrigerator (24 h) and heated to 40ºC gave BPA levels ranging from 20 to 50 µg/L.

PC bottles- repeated use. In the fourth study by Brede[14], new bottles filled with water (100ºC, 1 h) analyzed and washed for a number of cycles gave mean BPA levels as follows: 0.23 µg/L (new), 8.4 µg/L (after 51 cycles) and 6.7 µg/L (after 169 cycles). In the fifth study by Tan and

10 “Opinion of the scientific panel on food additives, flavourings, processing aids and materials in contact with food on a request from the Commission related to 2,2-bis(4-hydroxyphenyl)propane (Bisphenol A), Question number EFSA-Q-2005-100”, *The EFSA Journal*, Vol. 428, 2006, pp. 1-75.
11 Simoneau, C., Roeder, G., Anklam, E., “Migration of bisphenol-A from baby bottles: effect of experimental conditions and European survey.” 2nd International Symposium on Food Packaging: Ensuring the Safety and Quality of Foods (ILSI conference), Vienna, Austria, 8-10 November 2000.
12 Cited in the report as: Hanai, Y., “Bisphenol-A Eluted from Nursing Bottles,” Unpublished Data, Environmental Science Research Center, Yokohama National University, 1997.
13 Earls, A., Clay, C., Braybrook, J., “Preliminary Investigation into the Migration of Bisphenol-A from Commercially-Available Polycarbonate Baby Feeding Bottles”. LGC Technical Report LGC/DTI/2000/005.
14 Brede, C., Fjeldal, P., Skjevrak, I., Herikstad, H., “Increased migration levels of bisphenol A from polycarbonate baby bottles after dishwashing, boiling and brushing”, *Food Additives and Contaminants, Vol.* 20, 2003, pp. 684-9.

Mustafa[15], new and "used" (i.e., in service for >3 months) bottles filled with water (80ºC, holding time not stated) resulting in BPA levels in water ranging from <DL to 1 µg/L (new) and 0.1 to 22 µg/L (reuse). In the last study by UK's Central Science Laboratory (CSL)[16], new bottles were filled with 10% EtOH or 3% acetic acid (70ºC, 1 h) and the simulants analyzed for BPA. The bottles were then washed for a number of cycles and migration experiment repeated. Mean BPA levels as follows: <1 µg/L (new), <1 to 4.5 µg/L (20 cycles, 10% EtOH) and <0.3 to 0.7 µg/L (20 cycles, 3% acetic acid).

PC bottles- summary. EFSA concluded that (p. 17) "…BPA migrates from feeding bottles and that migration can increase with repeated use of the bottle due to cleaning treatments (dishwashing, sterilization, brushing, etc.)." They assumed that a "typical" migration level was 10 µg/kg and an "upper limit" level was 50 µg/kg in formula from contact with PC bottles. Using the highest ratio of food intake to body weight (a 95th percentile consumption of 1060 mL/p/d and a mass of 6.1 kg), EFSA estimated exposure to BPA of 1.7 µg/kg-bw/d (typical) and 8.7 µg/kg-bw/d (upper limit) for the contribution from PC bottles only.

EFSA also noted that in the SCF opinion on BPA in 2002[17], BPA migration from PC infant bottles into water and infant formula was in the range of <10 to 20 µg/kg. For infants 0-4 months, the SCF estimated exposure from the use of PC infant bottles using a migration of 10 µg/kg and the highest ratio of food intake to body weight (a formula intake of 0.7 L/p/d and a mass of 4.5 kg).

EFSA also noted that in the EU RAR[18] in 2003, a comprehensive review of the literature conducted at the time indicated that BPA levels may be as high as 50 µg/L (50 µg/kg). The EU RAR used this value in their exposure estimates for PC infant bottles.

Powdered formula. In a study by Kuo[19], analysis of six brands of canned infant formula and milk (both powdered) available in Taiwan gave BPA levels ranging from ND (non-detected as a DL of about 1 ppb) to 113 µg/kg. The samples consisted of two infant formulas (lactose-free, ND; soy-based 45 ppb) and four powdered milks (3 normal, 44, 113 and 57 ppb; 1 hypoallergenic, 57 ppb). Based a reported reconstitution ratio of 135 g/L, a level of 100 µg BPA/kg powdered formula, and the assumptions above for infants, EFSA calculated an exposure of 2.3 µg/kg-bw/d for the contribution from powdered formula only.

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15 Tan, B., Mustafa, A. M., "Leaching of bisphenol A from new and old babies bottles, and new babies feeding teats", *Asia Pacific Journal of Public Health,* Vol. 15, 2003, pp. 118-23.
16 "A study of the migration of bisphenol A from polycarbonate feeding bottles into food simulants", Central Science Laboratory Test Report L6BB-1008 for the Boots Group, 2003 (available at www.boots-plc.com/environment/library/250.pdf).
17 European Commission (2002), "Final opinion of the Scientific Committee on Food on Bisphenol A," April 17, 2002, SCF/CS/PM/3936 (http://ec.europa.eu/food/fs/sc/scf/out128_en.pdf).
18 European Union Risk Assessment Report. Bisphenol A, CAS No: 80-05-7. Institute for Health and Consumer Protection, European Chemicals Bureau, European Commission Joint Research Centre, 3rd Priority List, Luxembourg: Office for Official Publications of the European Communities.
19 Kuo, H., Ding, W., "Trace determination of bisphenol A and phytoestrogens in infant formula powders by gas chromatography-mass spectrometry", *Journal Chromatography A,* Vol. 1027, 2004, pp. 67-74.

Summary. Based on the information available on BPA migration levels from epoxy-based canned formula (powder) and PC infant bottles, EFSA concluded that (p. 20):

"….the potential dietary exposure in infants 0-6 months fed from PC bottles with infant formula previously packed in food cans with epoxy-phenolic coating based on a migration value of 50 µg/L of infant formula would be 11 µg BPA/kg-bw/day (8.7 + 2.3 µg/kg bw/day). This is the estimate of dietary exposure in infants fed every day with PC bottles leaching BPA at the highest concentration observed in realistic conditions of use. A more typical scenario, based on a migration value from PC bottles of 10 µg/L of infant formula would lead to a dietary exposure of 4 µg BPA/kg bw/day (1.7 + 2.3 µg BPA/kg bw/day)."

EWG Report (dated 3/5/07)

The Environmental Working Group (EWG)[20] reported on a survey of ninety-seven (97) cans of food, representing 27 national brands and three store brands, purchased in the US (Georgia, California and Connecticut). The 10 types of canned food included concentrated liquid soy- and milk-based infant formula (two brands, six cans). BPA levels were determined by the Southern Testing and Research Division of Microbac Laboratories, Inc., a contract laboratory based in North Carolina. Only minimal details on the laboratory method are provided in the EWG report and are insufficient for detailed evaluation or comment.

Part 2 of the EWG report summarizes the results for each food type (Table 1), the results for studies conducted by other groups (Table 2) and each individual analysis (Table 3). From Table 1 of the report, BPA levels in infant formula (liquid concentrates) ranged from ND (<2 ppb) to 17 ppb, with an average level of 2.4 ppb. Table 2 of the EWG report summarizes the expected range of BPA levels in infant formula based on the results of studies conducted by Biles[5,6] (liquid concentrates) and Kuo[18] (powder) (both discussed above) and Goodson[21]. In the Goodson study, analysis of four cans of infant formula (powder[22]) gave BPA levels near the DL (three were ND at 2 ppb and one was reported as 2.9 ppb). Two of the cans originated from the United Kingdom, one from France and the origin of the other was not stated.

Part 5 of the EWG report discusses their approach to "exposure" assessment for both acute and chronic exposure. We will not comment on EWG's exposure estimates due to their convoluted approach.

Health Canada's Chemicals Management Plan ("The HC Report," Draft dated 4/2008)

Under the Government of Canada's Chemicals Management Plan (CMP), an external Challenge Advisory Panel (CAP) on BPA recently issued a draft summary report[23] containing a human

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20 "A Survey of Bisphenol A in US Canned Foods," dated 3/5/07 (available on the EWG website).
21 Goodson, A., Summerfield, W., Cooper, I., "Survey of bisphenol A and bisphenol F in canned foods", *Food Additives and Contaminants*, Vol. 19, 2002, pp. 796-802.
22 Personal communication between A. Bailey and T. Begley (HFS-706), May 2008.
23 "Draft Screening Assessment for Phenol, 4,4'-(1-methylethylidene)bis- (80-05-7) April 2008," Government of

health section addressing dietary intake (pp. 35-43 and 52 of the report). The CAP report focused on exposure to BPA from two sources: epoxy-based container coatings (pp. 35-38) and PC repeat-use containers (pp. 38-43). A summary of the report as it pertains to BPA exposure for infants is described below.

Epoxy-based container coatings. The CAP Report provided a summary of the residue studies and exposure estimates on infant formula (liquid only) provided by the Health Products Food Branch (HPFB) in the Food Directorate of HC's Bureau of Chemical Safety. (We note that a draft of the HPFB report was provided to us through HPFB.) These studies involved BPA levels in liquid infant formula collected from one Canadian city (Ottawa) in 2007. The samples consisted of 21 cans (eight brands) of liquid infant formulas (ready-to-drink and concentrate). BPA was detected in all 21 products at levels ranging from 2.3 to 10.2 ppb (average of 4.6 ppb), but no further analytical details were provided. These levels were consistent with those reported by Biles[5] where BPA levels ranged from 0.1 to 13.2 ppb, equivalent to 0.05 to 6.6 ppb in prepared formula.

PC infant bottles. The CAP Report summarized many of the recent studies on PC bottles conducted to date, with an emphasis on those that simulated "realistic exposure conditions." The summarized studies are reported below.

Four studies of bottles obtained from the Canadian market were available. In 2000, HC conducted a series of limited migration studies as described in unpublished studies by Page[24]. No BPA was detected in milk simulant (50% ethanol) following storage in PC bottles for up to 7 days at 4 or 22ºC (DL <0.1 µg/kg). In additional trials, bottles were subjected to the following storage conditions:

a) 7 days at 4ºC, 7 days at 22ºC, then 6 days at 70ºC;
b) 7 days at 22ºC, 7 days at 4ºC, then 6 days at 70ºC; and
c) 6 days at 70ºC.

BPA levels were determined after 1, 2, 3 and 6 days and were reported to range from 0.4 to 1 ppb at 1 day for all three storage conditions. BPA levels reportedly increased on subsequent days at 70ºC, but no further details were provided.

Cao and Corriveau[25] evaluated BPA migration from three PC infant bottles and two refillable drinking bottles marketed in Ottawa in 2007. The bottles were filled to capacity with boiling water (100ºC), allowed to cool to RT and held at RT for 24 hours. BPA levels in the water ranged from 1.7 to 4.1 µg/L (ppb).

Canada (http://www.ec.gc.ca/substances/ese/eng/challenge/batch2/batch2_80-05-7_en.pdf).
24 Page, D., Lacroix, G., Lalonde. P., Feeley, M., "Bisphenol A (BPA) content of commercial polycarbonate (PC) baby bottles," Health Canada Science Forum Book of Abstracts. 2006.
25 Cao, X. Corriveau J., "Migration of bisphenol A from polycarbonate baby and water bottles into water under severe conditions", 2008 [Manuscript in preparation].

The CAP reported on preliminary data from a study conducted by HC in 2008[26]. Fourteen brands of PC infant bottles available in Canada were evaluated for BPA migration with water and 50% ethanol. The bottles were incubated at 40°C for 8, 24 or 240 hours to simulate use at RT. BPA levels were in the range of 0.095 µg/L (ppb) in water after 8 hrs, to 2.05 µg/L in 50% ethanol after 240 hours. CAP stated that the most realistic use consisted of filling bottles with the 50% ethanol and incubating them for 8 hours at 40ºC, resulting in an average BPA level of 0.15 µg/L.

Canada's Environmental Defence[27], a Canadian advocacy group, conducted a study on nine new PC infant bottles available on the Canadian market. The bottles were filled with water, sealed and allowed to sit for 24 hours at RT. In a second experiment, the bottles were heated at 80ºC presumably for 24 hours. Treatment at 80ºC was considered by the study authors to simulate repeat washing of bottles (i.e., 60-100 washes), but the CAP did not consider this treatment to represent a realistic migration from a single use. Results from the RT trials ranged from below the limit of detection (reported as 0.05 ng; not as a concentration) to 0.063 ppb. Results from the 80ºC trial ranged from 4.3 to 8.3 ppb.

Maragou[28] conducted a study on 31 new PC infant bottles (from 6 different brands), available on the Greek market, under a variety of conditions. Bottles were cleaned (by dishwasher or hand-washing with brushing), rinsed, sterilized, filled with water and incubated at 70ºC for 2 hours. This "cycle" was repeated several times. The authors concluded that a) repetitive cleansing of bottles, either with a dishwasher or hand-washing with brushing, does not lead to detectable BPA migration, and b) BPA was not washed from the surface of the bottles. BPA migration was only detected when bottles were filled with boiling water (100ºC). Specifically, five repeat cycles of cleaning the bottles by hand-washing with brushing and detergent, sterilizing in boiling water for 10 minutes, then filling with boiling water (100ºC) and leaving at ambient temperature for 45 minutes resulted in BPA levels ranging from DL (2.4 ppb) to 14.3 ppb, with an average BPA level of 10 ppb.

The Norwegian Food Safety Authority (Biedermann-Brem[29]) investigated the effect of extreme washing conditions, such as strong alkali detergents and time/temperature washing conditions (80ºC for 1 hour, followed by drying of unrinsed bottles at 90ºC for 30 minutes), on PC bottles with respect to BPA migration. They concluded that even after aggressive washing, BPA levels in the liquids stored in the bottles are unlikely to exceed 10 µg/L (ppb).

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26 The reference was cited as: HC, Safe Environment Programme, HECSB, personal communication, 3/6/08, unreferenced.
27 "Toxic baby bottles in Canada,: 2008, Environmental Defence (available at http://www.toxicnation.ca/files/toxicnation/report/ToxicBabyBottleReport.pdf).
28 Maragou, N., Makri, A., Lampi, E., Thomaidis, N., Koupparis, M., "Migration of bisphenol A from polycarbonate baby bottles under real use conditions, " *Food Additives and Contaminants*, Vol. 25, issue 3, 2008, pp. 373-383.
29 Biedermann-Brem, S., Grob, K., Fjeldal, P., "Release of bisphenol A from polycarbonate baby bottles: mechanisms of formation and investigation of worst case scenarios," Norwegian Food Safety Authority, 2007 (available in German at http://matportalen no/Matportalen/artikler/2007/11/taateflasker_av_polykarbonat_er_trygge_i_bruk).

Ehlert[30] recently conducted a study on PC infant feeding bottles available on the European market. Bottles containing water were heated to 100ºC during three microwave cycles. BPA levels in water were reported to be in the range of <0.1 to 0.7 µg/L (ppb)

Miyamoto and Kotake[31] reported that new, unwashed PC bottles exposed to water at 95ºC for 30 minutes gave BPA levels ranging from 0.05 (DL) to 3.9 ppb.

Le et al.[32] reported on recent studies on PC (new and used) and HDPE (new, as control) bottles obtained in the New Jersey area. The "used" PC bottles were collected from anonymous donors and were reportedly used under normal conditions from 1 to 9 years. Bottles (3 new, 5 used) were filled with water (100 mL) and stored at 22ºC for 7 days with agitation. Samples were collected on 1, 3, 5 and 7 days and analyzed for BPA. For the new PC bottles, BPA levels ranged from 0.08 to 0.36 ppb (day 1) and 0.73 to 1.33 ppb (day 7) depending on the bottle. For the new HDPE controls, BPA levels ranged from 0.01 to 0.08 ppb (day 1) and 0.08 to 0.19 ppb (day 7). For the used PC bottles, BPA levels ranged from ND to 0.29 ppb (day 1) and 0.34 to 0.93 ppb (day 5). (We note that detection of BPA in the controls may indicate a flaw in this study. Therefore, although the detected levels of BPA do not seem unreasonable, we will not use these values in our general assessment.)

BPA intake from epoxy-based coatings and PC bottles. The intake values for BPA based on levels in infant formula from epoxy-based container coatings is shown in Table 12 (pp. 37-38) of the report. The intake values were determined for both "average" and "maximum" BPA levels (4.6 ppb, 10.2 ppb) as well as "average" and "maximum" formula intakes for infants of different age groups (assuming a constant body weight). The intakes based on an "average" BPA level and "average" formula intake are also shown in Tables 19a and 19b (column 2) of the report. We have included Tables 19a and 19b as Attachment 1 to this memorandum.

The intake values for BPA based on levels in infant formula from PC bottles is shown in Table 14 (p. 42) of the report. As above, the intakes values were determined for both "average" and "maximum" BPA levels (RT, 0.24 ppb; boiling, 10 ppb) as well as "average" and "maximum" formula intakes for infants of different age groups (constant body weight). These intakes are also shown in Tables 19a and 19b (columns 3 & 4) of the report (see Attachment 1).

The intakes from both epoxy-based coatings (Table 12) and PC bottles (Table 14) were used to estimate an aggregate exposure from all sources of BPA. This is tabulated in Tables 19a and 19b (see columns 2-4 of Attachment 1). Additional details on the assumptions used in deriving

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30 Cited in the report as: Ehlert, K., Beumer, C., Groot, M., "Migration study of bisphenol A into water from polycarbonate baby bottles during microwave heating", 2008 (in press).
31 Miyamoto, K., Kotake, M., "Estimation of daily bisphenol A intake of Japanese individuals with emphasis on uncertainty and variability", *Environmental Science*, Vol. 13, Issue 1, 2006, pp.15-29.
32 Le, H., Carlson, E., Chue, J., Belcher, S., "Bisphenol A is released from polycarbonate drinking bottles and mimics the neurotoxic actions of estrogen in developing cerebellar neurons," *Toxicology Letters*, Vol. 176, 2008, pp. 149-156.

the exposure estimates are in the footnotes to the table. Other studies reported on in the literature were not discussed in the report.

Comments on the EFSA, EWG and HC Reports

Below we summarize the collective results from the three reports for BPA migration from PC infant bottles and epoxy-based can coatings in contact with liquid and powdered formula.

PC bottles. The PC bottles studies summarized in the EFSA, EWG and HC reports are tabulated in Attachment 3 to this memorandum. As with EFSA's analysis, we concur that only those studies on PC infant bottles that used time/temperature conditions that are representative of "realistic exposure conditions" are useful in estimating exposure. Based on the results summarized in Attachment 3, we conclude that the following BPA migration levels will be adequate to *represent BPA levels in infant formula from PC infant bottles*:

1) <0.5 μg/kg under normal, RT use conditions;
2) <10 μg/kg under use conditions as high as 100ºC.

Liquid infant formula. The EWG study reported BPA levels in infant formula (liquid concentrates collected in the US) ranging from ND (<2 ppb) to 17 ppb, with an average level of 2.4 ppb. These values correspond to BPA levels in prepared formula ranging from <1 to 8.5 ppb, with an average level of 1.2 ppb. In the HC report, BPA levels in infant formulas (ready-to-drink and concentrates collected in Canada) ranged from 2.3 to 10.2 ppb (average of 4.6 ppb). From the information available in the HC report, we can only say that this range and average includes both ready-to-drink and concentrates.

Powdered infant formula. The EFSA report noted that BPA levels in infant formula (powders collected in Taiwan) were ND (lactose-free) and 45 ppb (soy-based). On the other hand, BPA levels in infant formula (powder collected in the UK and France) were on the order of 2 to 3 ppb. Using a reconstitution ratio of 135 g/L as given above, BPA levels in prepared formula would be on the order of 0.3 to 0.4 ng/g. The reason for the high value of 45 ppb BPA from soy-based powdered formula in Taiwan was not clear from the reports.

Infant Formula Feeding Practices

In order to determine the appropriate BPA migration levels to use for evaluation of BPA exposure based on the numerous studies (discussed above) that have appeared in the literature since our previous estimates, we reviewed some of the recommendations from several organizations on "infant formula feeding."

In our original analysis[3], we used the BPA migration levels obtained from testing PC infant bottles at RT for 72 h (common protocol) and 100ºC/0.5 h, then 4ºC/3 d (worst-case protocol), both of which resulted in non-detection of BPA at a DL of 5 ppb (<1.7 ppb in formula). As discussed in the 3/13/96 memorandum, the "worst-case" protocol was designed to model the practice of "terminal sterilization" in infant formula preparation. Thus, we searched the web for information addressing the need to employ "terminal sterilization" (aka "terminal heating") in the preparation of infant formula.

CFSAN Website

General information for consumers, industry and other interested parties on infant formula is available through CFSAN's Office of Nutrition, Labeling and Dietary Supplements (ONLDS)[33] website Much of the information under the heading "General information and other resources" was taken from various FDA Consumer articles. The recommended practices pertinent to this analysis are summarized below.

1) the American Academy of Pediatrics currently recommends boiling water for infant formula.
2) water for infant formula (including bottled water) should be heated to a rolling boil, boiling continued for 1-2 two minutes, and then cooled before putting the water in the bottle.
3) dishwashers may be used to sterilize bottles and nipples or they can be placed in a pan of boiling water for 5 minutes.
4) prepared formula should be refrigerated and used right away.
5) bottles should not be heated in the microwave oven but may be warmed by placing the bottle in a pot of water on the stove.

Powdered formula instructions

As a representative example, the Mead-Johnson Nutritionals website has a section[34] with instructions for the preparation, storage and use of each of their products for infants, toddlers, children and adults. The preparation instructions for many of their infant products specify pouring the desired amount of cool water (35-75°F) into a bottle, adding the appropriate amount of powder, attaching the nipple, ring, and disc or nipple cover, and shaking for about 5 seconds. Prepared infant formula can spoil quickly, so the formula should be used immediately or covered and refrigerated at 35-40°F (2-4°C) for no longer than 24 hours. Prepared formula left unrefrigerated for more than 2 hours should not be used, nor should prepared formula be frozen.

Neither the ONLDS nor the Mead-Johnson websites, as well as several other websites (see Attachment 2 to this memorandum), *explicitly* address any need to employ "terminal sterilization" in the preparation of infant formula.

Additional information

According to Sara Fein[35], a Consumer Science Specialist at CFSAN, the need for sterilization of equipment and water is controversial. Most consumer education materials reportedly

33 CFSAN's "Infant formula" page at www.cfsan.fda.gov/~dms/inf-toc html.
34www meadjohnson.com/app/iwp/HCP/Content2.do?dm=mj&id=/HCP_Home/Product_Information/Instructions_for_Preparation.
35 Fein, S. B., Falci, C. D., 1999, "Infant Formula Preparation, Handling, and Related Practices in the United States", *Journal of the American Dietetic Association*, Vol, 99, No. 10, p. 1234.

recommend sterilization, but a 1990 review article[36] indicated that sterilization is not necessary when "…water that has safe levels of bacteria is available." Also, boiling water for formula is thought to increase lead (Pb) levels in the reconstituted formula. On the other hand, the contamination of Milwaukee's water with the parasite *Cryptosporidium* in 1993 raised some concern about using water that has not been sterilized.

According to another position statement by the European Society for Pediatric Gasteroenterology, Hepatology and Nutrition (ESPGHAN) Committee on Nutrition:

"The FAO and WHO recently convened an expert meeting on *E. sakazakii* and other microorganisms in powdered infant formulae. One of their recommendations was that whenever possible, sterile liquid formula or reconstituted powder formula that has undergone an effective decontamination step (such as mixing with boiled water or heating) should be used for high-risk infants. *The ESPGHAN Committee on Nutrition disagrees with the use of boiling water and of heating of reconstituted formula to temperatures close to the boiling point because of possible adverse effects on nutrients such as vitamins*."

The WHO website contains a section entitled "Guidelines for the safe preparation, storage and handling of powdered infant formula" that contains several publications intended for parents and health care professionals[37]. According to the introductory discussion, the concern with contamination of formula with harmful bacteria, from either non-sterile powdered infant formula or inappropriate preparation practices during reconstitution, led Codex Alimentarius to revise the International Code of Hygenic Practice for Food for Infants and Children based on guidance from FAO and WHO. All of the FAO/WHO publications on the website generally recommend boiling the water for formula and "…taking care to avoid scalds, pour the correct amount of boiled water into a cleaned and sterilized bottle. The water should be no cooler that 70ºC, so do not leave it for more than 30 minutes after boiling."

According to one reference text[38], formula preparation requires extreme care and cleanliness, especially in the first 3 months of an infant's life. The author concedes that there is some controversy about the need for this process at all, given the safe nature of the water supply throughout most communities in the US. Certainly this method should be used in any household in which the risk of contamination of food is likely. According to another reference[39], terminal sterilization should be used for formula preparation when using well or non-chlorinated water.

According to the American Dietetic Association[40], terminal sterilization is not recommended for formula preparation in health care facilities. Also, only chilled, sterile water is recommended for

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36 The Fein publication referenced Schumna, A, "Pediatrics 1990: Facts and fantasies, myths and misconceptions", *Clinical Pediatrics*, Vol. 29, 1990, pp. 558-564.
37 Available at www.who.int/foodsafety/publications/micro/pif2007/en/.
38 "Pediatrics for Medical Students," 2nd Edition, D. Bernstein and S. P. Shelov, Lippincott, Williams & Wilkins, Puablished 2003 (ISBN 0781729416), Ch. 4, p. 88.
39 "Caring for Your Baby & Young Child: from Birth to Age 5," S. Shelov, Oxford University Press, 1998 (ISBN 0192627783), Ch. 4, p. 101.
40 Available at www.eatright.org/cps/rde/xchg/ada/hs.xsl/nutrition_1562_ENU_HTML htm

infant formula preparation and single-use containers are recommended for dispensing in health care facilities.

According to another reference[41], the need to boil water is not clear. While most brands of baby formula once recommended boiling as a part of their instructions, they now often recommend "asking your baby's doctor" or "local health department" instead. The American Academy of Pediatrics does not offer any formal advice on the subject. The author notes that a recent book on newborns[42] does say that "…..you may want to use boiled or purified (bottled or filtered) water, at least in the first month or two." The author claims there is no research which indicates that doing anything special to the water that one uses for a baby's formula "in the first month or two" is helpful or does anything at all. The author states that that this advice is likely based on the fact that younger babies are simply assumed to have weaker immune systems.

Based on the available information, we assess that terminal sterilization may be used by some consumers in the first 2 months of an infants life. It might also be used in areas where water contamination with microorganisms is of concern. However, it is not a commonly recommended practice. In support of our conclusion, the analysis by HC described in the HC report noted that the label directions for the preparation of infant formula (concentrate and powder) typically specify that water be sterilized and allowed to cool to RT before addition to the PC bottles.

Infant Formula Consumption

In our 3/13/96 memorandum, we calculated our CEDI based on an infant daily formula intake of 820 g (eaters-only). For this update, we consulted our newest updated food consumption databases to determine infant formula consumption for several age groups up to 12 months of age.

Mean daily intakes for various infant age groups using food consumption databases from the USDA 1994-96 & 1998 Continuing Survey of Food Intakes by Individuals (CSFII) and National Health and Nutrition Examination Survey (NHANES 2003-2004) using the Exponent Food Analysis and Residue Evaluation (FARE) software (version 8.12; NFCS food code #117 for infant formula). The mean, per capita and eaters-only intakes, as well as male and female body masses, for various age groups for both databases are shown below in Table 1.

Table 1: Mean infant formula consumption and body mass up to 12 months

Consumption (g/p/d)	Age Range (months)											
	0-1	1-2	2-3	3-4	4-5	5-6	6-7	7-8	8-9	9-10	10-11	11-12	0-12
CFSII, 1994-96, 98												
Per capita	512	603	759	808	773	703	669	696	671	614	460	62	334

41 "Preparing baby formula" by V. Iannelli, MD on About.com: Pediatrics (http://pediatrics.about.com/od/weeklyquestion/a/0707_bby_formla htm).
42 "Heading home with your newborn,", Jana, L. and Shu, J., American Academy of Pediatrics, 2005.

Eaters-only	827	889	957	972	930	862	864	846	824	794	751	624	839
NHANES 2003-2004													
Per capita	542	732	819	766	712	736	657	715	745	649	383	35.5	
Eaters-only	705	882	923	916	853	832	736	772	798	717	564	435	
%-eaters	77	83	89	84	83	88	89	93	93	90	68	8	
Mass-F (kg)[a]	3.80	4.54	5.23	5.86	6.44	6.97	7.45	7.90	8.31	8.69	9.04	9.36	
Mass-M (kg)[a]	4.00	4.88	5.67	6.39	7.04	7.63	8.16	8.64	9.08	9.48	9.84	10.16	
a- infant body masses taken from CDC (http://www.cdc.gov/nchs/about/major/nhanes/growthcharts/datafiles.htm)													

Inspection of the tabulated data leads to several observations. First, as one would expect, the mean, eaters-only intakes are *somewhat higher* than the mean, per capita intakes. This being said, NHANES reports a high percentage of eaters (>75%) for the mean, eaters-only intakes for almost all age ranges, the exceptions being months 10-11 and 11-12 when larger amounts of solid food are consumed. Second, by 12 months of age a high percentage of infants have stopped consuming liquid formula.

Revised Exposure Estimate

In our 3/13/96 memorandum, we noted that any 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, body mass and food intake will increase, with a decrease in formula intake and an increase in solid food intake. As the intake of solid food increases, the use of infant bottles will decrease. Our 1996 analysis focused on the period when the most *infant formula* is actually consumed, i.e., *the first year of an infant's life*. We see no reason to alter our original approach, although we have made some minor refinements as follows.

With regard to *PC bottles*, the available information suggests that terminal sterilization may be used by some consumers in the first 2 months of an infant's life, if it is used at all. According to the survey by S. Fein[35] of infant feed practices in the US, "…mothers were more likely to sterilize bottles, nipples, and water for 2-month-old infants than for older infants." Thus, in our revised exposure analysis, we will use BPA levels of:

a) <10 µg/kg to represent BPA levels from PC bottles from the use of terminal sterilization in the preparation of infant formula in months 1-2, and,
b) <1 µg/kg to represent BPA levels from the use PC bottles from the use of typical heating in the preparation of infant formula in months 3-12.

With regard to *liquid infant formula* studies, the EWG study reported BPA levels in prepared (reconstituted) formula ranging from <1 to 8.5 ppb, with an average level of 1.2 ppb. In the studies conducted in our laboratories, BPA levels in prepared formula ranged from 0.05 to 6.6 ppb, with an average of 2.5 ppb. We will use the average value of 2.5 ppb in our updated analysis.

With regard to the *powdered infant formula* studies, the EFSA report noted that BPA levels in four powdered infant formulas available in the UK and France resulted in BPA levels on the order of 0.3 to 0.4 ng/g (ppb) in prepared formula. Inspection of *powdered infant formula* cans available in the US[43] indicates that they are composite cans made of paper and aluminum foil and, as such, would not be expected to contain any BPA-based coatings. Because there is no BPA to migrate into formula, we will not include a BPA contribution from powdered infant formula.

We used the mean, eaters-only infant formula consumptions from the most recent source, the NHANES 2003-2004 food consumption database (Table 1), to estimate exposures for each age group.

Table 2: BPA exposure for infants up to 12 months												
	Age Range (months)											
	0-1	1-2	2-3	3-4	4-5	5-6	6-7	7-8	8-9	9-10	10-11	11-12
BPA level in formula from PC bottles (ng/g)	<10	<10	<1	<1	<1	<1	<1	<1	<1	<1	<1	<1
BPA level in formula from can coatings (ng/g)[a]	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Maximum total BPA level in formula (ng/g)	12.5	12.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5
Eaters-only consumption (g/p/d)	705	882	923	916	853	832	736	772	798	717	564	435
BPA exposure (μg/p/d)	**8.8**	**11**	**3.2**	**3.2**	**3**	**2.9**	**2.6**	**2.7**	**2.8**	**2.5**	**2**	**1.5**
a- BPA in prepared formula from ready-to-feed and liquid concentrates, not powder.												

The estimates presented above in Table 2 are conservative since we assumed that *all* infant formula was:

1) packed in cans coated with BPA-based enamels.

As noted above, inspection of powdered infant formula available in the US indicates that it is

43 Results from W. Limm (HFS-706) on two brands of infant formula packaged in composite containers indicates that the linings not based on epoxy chemistry. Memorandum dated 5/28/08, W. Limm to A. Bailey.

packaged in paper-aluminum foil composite cans that do not contain epoxy-based linings. This observation is entirely consistent with the fact that powdered formulas are not heat sterilized in the same manner as liquid formulas and, thus, would not require such linings. Moreover, liquid formula packaged in plastic containers was recently made available to consumers and is expected to begin to displace canned liquid formula in the marketplace.

2) in liquid form either as ready-to feed or concentrates.

According to two documents available at FDA dockets[44], powdered infant formula accounts for approximately half (49%) of the infant formula market in the US in 1999. In many other countries, most infant formula is sold in powdered form.

3) prepared and fed to infants using PC bottles.

It is well known that a certain fraction of the infant formula bottle market is made up of polypropylene (PP) and, to a lesser extent, poly(ethersulfone) bottles. Other feeding bottles use a polymeric liner that does not contain BPA.

4) the BPA migration levels from PC bottles were expressed on a daily basis.

Although a PC bottle is a repeat-use article, our approach to estimating exposure assumed that either <10 µg/kg (<two months old) or <1 µg/kg (>2 months old) was present in infant formula every time the PC bottle was used by the consumer. This scenario would occur if there was a non-steady state concentration of BPA, e.g., from depolymerization of PC to BPA monomer. This is a worst-case assumption.

Conclusion

Information collated from a review of the relevant literature pertaining to BPA migration levels into infant formula in contact with epoxy-coated containers and PC bottles, as well an information on infant feeding practices and formula consumptions, was used to update exposure estimates for BPA for infants of various age groups up to 12 months of age.

Allan B. Bailey, Ph.D.

44 www.fda.gov/ohrms/dockets/AC/03/slides/3939s1_Anderson.ppt;
www fda.gov/ohrms/dockets/ac/03/briefing/3939b1_tab4c_coversheet.pdf .

[redacted]

Attachment 1 (taken from HC Report[23])

Table 19a. Aggregated average estimates of exposure for formula fed infants aged 0-18 months (µg/kg-bw per day).

Age group (months)	Intake from infant formula[1,2]	Intake from migration from polycarbonate bottles		Total estimated dietary intake[5]		Intake from environmental media[6]	Total estimated intake	
		Filled with room temp. water[3]	Filled with boiling water[4]	Room temp. water	Boiling water		Room temp. water	Boiling water
0 to 1	0.45	0.040	1.65	0.490	2.1	0.009	0.50	2.11
2 to 3	0.50	0.047	1.95	0.547	2.450	0.009	0.56	2.46
4 to 7	0.38	0.035	1.46	0.415	1.840	0.009	0.42	1.85
8 to 12	0.21	0.020	1.07	0.230	1.03	0.02	0.25	1.05
12 to 18	0.23	0.017	0.71	0.247	0.94	0.02	0.27	0.96

[1] Based on the average concentration of BPA as measured in liquid infant formula (Health Canada, Food Directorate, HPFB, pers. comm., 2007 Dec 14, unreferenced) and an average formula intake for each age group.
[2]If drinking water is used to dilute the infant formula during preparation, it may affect the overall BPA concentrations. However as concentrations of BPA measured in drinking water were significantly lower than those measured in liquid infant formula, that source of exposure was not included in these estimates.
[3]Based on the average concentration of BPA measured in water, 0.24 ppb, that resulted from the room temperature use of PC bottles (Le et al. 2008).
[4] Based on the average concentration of BPA measured in water, 10 ppb, that resulted from filling PC bottles with boiling water (Maragou et al. 2007).
[5] Heath Canada recommends that solid food be introduced to infants after 6 months of age. For this assessment it was assumed that an infants main source of food is infant formula, however if infants consume other canned foods this may increase their total dietary exposure to BPA.
[6] Based on average concentrations measured in various environmental media.

Table 19b. Aggregated **maximum** estimates of exposure for formula fed infants aged 0-18 months (µg/kg-bw per day).

Age group (months)	Intake from infant formula[1,2]	Intake from migration from polycarbonate bottles		Total estimated dietary intake[5]		Intake from environmental media[6]	Total estimated intake	
		Filled with room temp. water[3]	Filled with boiling water[4]	Room temp. water	Boiling water		Room temp. water	Boiling water
0 to 1	1.35	0.066	2.77	1.42	4.12	0.18	1.60	4.30
2 to 3	1.31	0.064	2.67	1.37	3.98	0.18	1.55	4.16
4 to 7	1.02	0.049	2.00	1.07	3.02	0.18	1.25	3.20
8 to 12	0.55	0.026	1.07	0.58	1.62	0.44	1.02	2.06
12 to 18	0.46	0.020	0.85	0.48	1.31	0.44	0.92	1.75

[1] Based on the maximum concentration of BPA as measured in liquid infant formula (Health Canada, Food Directorate, HPFB, pers. comm., 2007 Dec 14, unreferenced) and the maximum formula intake for each age group (see Table 12).
[2]If drinking water is used to dilute the infant formula during preparation, it may affect the overall BPA concentrations. However as concentrations of BPA measured in drinking water were significantly lower than those measured in liquid infant formula, that source of exposure was not included in these estimates.
[3]Based on the average concentration of BPA measured in water, 0.24 ppb, that resulted from the room temperature use of PC bottles (Le et al. 2008) .
[4] Based on the average concentration of BPA measured in water, 10 ppb, that resulted from filling polycarbonate bottles with boiling water (Maragou et al. 2007) .
[5] Heath Canada recommends that solid food be introduced to infants after 6 months of age. For this assessment it was assumed that an infants main source of food is infant formula, however if infants consume other canned foods this may increase their total dietary exposure to BPA.
[6] Based on maximum concentrations measured in various environmental media.

Attachment 2 (Pertinent websites addressing infant feeding practices)

1. FAQs document from International Formula Council (www.infantformula.org/faqs html#8)

The American Academy of Pediatrics recommends that either breastfeeding or iron-fortified infant formula be continued during the first year of life, even after solids have been introduced.

Sterilization of all equipment and water used in preparing infant formula is commonly recommended until a health professional decides it is unnecessary.

The American Dietetic Association does not recommend preparing formula with boiling hot water due to problems with physical stability of the formula (e.g., clumping or separation) and nutrient degradation.

Liquid infant formula can be kept for up to 48 hours, if tightly covered and immediately placed in the refrigerator. Bottles of formula made from liquid should be refrigerated and used within 48 hours. Formula prepared from powder and placed in bottles for feeding should be refrigerated and used within 24 hours.

Microwave ovens should NEVER be used for heating infant formulas since there is a danger of overheating the liquid. During the microwaving process, the bottle may remain cool while hot spots develop in the formula. Overheated formula can cause serious burns to the baby.

2. "How to prepare infant formula" by H. Corley on About.com: Baby products (http://babyproducts.about.com/od/feedingdrinks/ht/prepareformula.htm)

Turn on cold water at the sink and let it run for 30 seconds to one minute before preparing baby formula. This is said to reduce the concentration of lead or other contaminants in the water.

If you have been instructed to boil water before preparing formula, be sure to bring the water to a rolling boil for 5 minutes.

Fill the baby bottle with cold water. If you have boiled the water, let it cool before pouring it into the baby bottle. Measure the water carefully before adding any formula powder. Do not add formula powder first, as the powder in the bottom of the bottle will skew the measurement of the water.

3. "Preparing baby formula" by V. Iannelli, MD on About.com: Pediatrics (http://pediatrics.about.com/od/weeklyquestion/a/0707_bby_formla htm)

Follow the directions on your baby's formula package and if using tap water, start with cold tap water. According to the U.S. Environmental Protection Agency, you should "never cook or mix infant formula using hot water from the tap."

The issue of the need to boil water is not clear. While most brands of baby formula once recommended boiling as a part of their instructions, they now often recommend "asking your baby's doctor or "local health department" instead.

The American Academy of Pediatrics doesn't offer any formal advice on the subject either. The latest book on newborns that they published, *Heading Home with Your Newborn: From Birth to Reality,* does say that "you may want to use boiled or purified (bottled or filtered) water, at least in the first month or two."

The author claims that the main problem with that statement is that purified, bottled, or filtered water isn't sterile, so isn't necessarily any safer than tap water that hasn't been boiled first. Bottled and filtered water should have fewer impurities and contaminants, including lead, but could still have harmful bacteria, which was the whole reason you were supposed to boil tap water when making baby formula in the first place.

And there is no research which states that doing anything special to the water that you use for your baby's formula "in the first month or two" is helpful or does anything at all. That advice is likely based on the fact that younger babies are simply supposed to have weaker immune systems.

If you do decide to boil the water when preparing your baby's formula, the FDA recommends that you "bring it to a very bubbly boil. Keep boiling it for a minute or two, then let it cool." Once it has cooled, you will be ready to add it to your baby's formula.

Attachment 3: Summary of PC Infant Bottles Studies

Source	Year	Substrate	Cycles	Food	Temp/time	DL	Levels
Biles	1997	Bottles					
Simoneau	2000	Bottles	1	Water/ 3% AA	50ºC→RT	10 µg/L	<10 µg/L
Hanai	1997	Bottles	1	Water	95ºC→RT, then 12 h	2 µg/L	3-55 µg/L
Earls	2000	Bottles	1	Water/ 3% AA	100ºC, then frig (4ºC) 24 h, heat to 40ºC		20-50 µg/L
Brede	2003	Bottles	1, 51, 169	Water	100ºC/1 h, then washed several cycles		0.23 µg/L (1 cycle) 8.4 µg/L (51 cycles) 6.7 µg/L (169 cycles)
Tan	2003	Bottles, new & used	1	Water	100ºC/time not specified		New: DL-1 µg/L Used: 0.1-22 µg/L
UK CSL	2004	Bottles	1, 20	10% Ethanol/ 3% AA	70ºC/1 h		<1 µg/L (1 cycle) <1-4.5 µg/L (20 cycles, 10% ethanol) <0.3-0.7 µg/L (20 cycles, 3% AA)
Page	2006	Bottles	1	50% Ethanol	4ºC/7 d; 22ºC/7 d; 70ºC/6 d	0.1µg/kg	<0.1 µg/kg (4ºC/1 d) <0.1 µg/kg (22ºC/1 d) <1 µg/kg (70ºC/1 d)
Cao	2008	Bottles & glasses	1	Water	100ºC→RT for 24 h		1.7-4.1 µg/kg
HC	2008	Bottles	1	Water/ 50% ethanol	40ºC/10 d		Water: 0.1 µg/L (8 h) 50% ethanol: 0.15 µg/L (8 h) 2 µg/L (240 h)
Canada Env. Defence	2008	Bottles	1, 60	Water	RT/24 h; 80ºC/ 24 h		DL-0.06 µg/kg 4.3-8.3 ppb
Maragou	2007	Bottles	1, 5+	Water	70ºC/2 h; then washed several cycles; 100ºC→RT for 45 min	2.4 ppb	ND 2.4-14.3 µg/L
Biedermann- Brem	2007	Bottles	1+	Water	80ºC/1 h, then aggressive conditions		<10 µg/L
Ehlert	2008	Bottles	1+	Water	Heat to 100ºC in microwave for 3 cycles		<0.1-0.7 µg/L
Miyamoto	2006	Bottles	1	Water	95ºC/0.5 h	0.05 ppb	DL-3.9 ppb
Le & Belcher	2008	Bottles, new & used	1	Water	22ºC/7 d		New: 0.08-0.36 ppb (1 d); 0.73-1.33 ppb (5 d) Old: ND-0.3 ppb (1 d); 0.34-0.93 ppb (5 d)