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## Bisphenol A in Food Cans: An Update

The can manufacturing industry and suppliers have followed closely the current research on can coatings and have conducted our own research as it relates to potential exposure to bisphenol A from can coatings. We would like to present new research findings that will amend several conclusions drawn by Nagel et al. (*1*) in *Environmental Health Perspectives*.

The paper states that the active level of bisphenol A in rodents was measured at 2 and 20 micrograms per kilogram body weight per day (µg/kg/day) and is "near or within the reported ranges of human exposure." This conclusion appears to be based on human exposure data derived from a paper by Brotons et al. (*2*) in *Environmental Health Perspectives* in 1995. New, updated data based on much more definitive analytical methodology supersedes this finding.

In late 1996, our industry's Epoxy Can Coating Work Group of the Interindustry Group on Bisphenol A and Alkylphenols completed a second study on potential human exposure to bisphenol A from epoxy lacquer-coated food cans. The first study from this work group (*3*), completed in 1995, was referenced by Nagel et al. (*1*). The second study was undertaken using the improved analytical methodology that minimizes the interferences which were observed in the first study and likely occurred in the study of Brotons et al. (*2*).

The findings of the 1996 report, "Potential Exposure to Bisphenol A from Epoxy Can Coatings" (*4*), provide new improved exposure data. This 1996 study with more accurate data was not referenced by Nagel et al. (*1*). These new data, which have now been provided to the U.S. Food and Drug Administration and the National

## Corrections and Clarifications

In the article by Munger et al. (Intrauterine Growth Retardation in Iowa Communities with Herbicide-contaminated Drinking Water Supplies) published in EHP in Volume 105, Number 3, 1997, Table 1 was incorrect. For all variables, both mean and median should be given in micrograms per liter. The corrected table is shown below.

**Table 1.** Contaminants of drinking water supplied in towns in the southern tier of Iowa counties with a population of 2,500 or fewer by source of water supply, 1984–1990

| Variable | RRWA (*n* = 13) | All water supplies in Rathbun counties excluding RRWA (*n* = 38) | Surface water supplies other than Rathbun (*n* = 21) | Groundwater from alluvial and glacial drift (*n* = 75) | Groundwater from bedrock aquifers (*n* = 42) |
|---|---|---|---|---|---|
| Alachlor (Lasso) | | | | | |
| Mean (µg/l) (SD) | <0.01 (0.1) | 0.0 (0) | 0.00 (0.00) | <0.1 (0.2) | 0.0 (0) |
| Median (µg/l) | 0 | 0 | 0 | 0 | 0 |
| Positive detection (%) | 7.7 | 0 | 0 | 4.0 | 0 |
| Atrazine | | | | | |
| Mean (µg/l) (SD) | 2.2 (0.4) | 0.7 (1.2) | 0.8 (1.1) | <0.1 (0.1) | <0.1 (<0.1) |
| Median (µg/l) | 2.1 | 0 | 0.44 | 0 | 0 |
| Positive detection (%) | 100.0 | 42.1 | 76.2 | 5.3 | 4.7 |
| Cyanazine (Bladex) | | | | | |
| Mean (µg/l) (SD) | 1.4 (0.5) | 0.3 (0.5) | 0.7 (0.9) | 0.0 (0) | 0.00 (0.00) |
| Median (µg/l) | 1.4 | 0 | 0.3 | 0 | 0 |
| Positive detection (%) | 100.0 | 26.3 | 57.1 | 0 | 0 |
| Metolachlor (Dual) | | | | | |
| Mean (µg/l)) (SD) | 0.2 (0.3) | 0.2 (0.4) | 0.1 (0.2) | <0.1 (<0.1) | 0.0(0) |
| Median (µg/l) | 0 | 0 | 0 | 0 | 0 |
| Positive detection (%) | 38.5 | 26.3 | 21 | 1.3 | 0 |
| 2,4-D | | | | | |
| Mean (µg/l) (SD) | <0.1 (<0.1) | <0.1 (<0.1) | <0.1 (<0.1) | <0.1 (<0.1) | 0.00 (0.00) |
| Median (µg/l) | 0 | 0 | 0 | 0 | 0 |
| Positive detection (%) | 7.7 | 5.3 | 4.8 | 2.7 | 0 |
| Chloroform | | | | | |
| Mean (µg/l) (SD) | 53.2 (9.3) | 57.8 (94.9) | 110.2 (81.8) | 7.92 (20.9) | 1.10 (6.0) |
| Median (µg/l) | 55.0 | 1.0 | 89 | 2.0 | 0 |
| Positive detection (%) | 100.0 | 52.6 | 95.2 | 70.7 | 16.7 |
| Bromodichloromethane | | | | | |
| Mean (µg/l) (SD) | 10.0 (3.7) | 9.6 (13.8) | 18.00 (10.3) | 5.19 (17.3) | 0.45 (1.9) |
| Median (µg/l) | 9.0 | 1 | 18 | 1.0 | 0 |
| Positive detection (%) | 100.0 | 52.6 | 90.5 | 61.3 | 14.3 |
| Dibromochloromethane | | | | | |
| Mean (µg/l) (SD) | 0.6 (0.5) | 1.32 (1.7) | 1.67 (1.2) | 3.79 (12.4) | 0.60 (1.3) |
| Median (µg/l) | 1.0 | 0 | 2 | 1.0 | 0 |
| Positive detection (%) | 61.5 | 47.4 | 81.0 | 52.0 | 26.2 |
| Bromoform | | | | | |
| Mean (µg/l) (SD) | 0.00 (0.00) | 0.9 (2.1) | 0.05 (0.2) | 1.1 (2.9) | 1.6 (5.0) |
| Median (µg/l) | 0 | 0 | 0 | 0 | 0 |
| Positive detection (%) | 0 | 25.0 | 4.8 | 28.0 | 26.2 |
| *p,m*-Xylene | | | | | |
| Mean (µg/l) (SD) | <0.1 (<0.1) | 0.2 (0.7) | 0.4 (1.1) | 0.0 (0) | 0.62 (2.90) |
| Median (µg/l) | 0 | 0 | 0 | 0 | 0 |
| Positive detection (%) | 7.7 | 10.5 | 14.3 | 0 | 9.5 |
| *o*-Xylene | | | | | |
| Mean (µg/l) (SD) | 0 | 0.05 (0.2) | 0.10 (0.3) | 0.0 (0) | 0.14 (0.8) |
| Median (µg/l) | 0 | 0 | 0 | 0 | 0 |
| Positive detection (%) | 0 | 5.3 | 9.5 | 0 | 4.8 |
| Tetrachloroethane | | | | | |
| Mean (µg/l)) (SD) | 0.0 (0) | 0.0 (0) | 0.0 0) | 0.0 (0) | 0.0 (0) |
| Median (µg/l) | 0 | 0 | 0 | 0 | 0 |
| Positive detection (%) | 0 | 0 | 0 | 0 | 0 |

Abbreviations: RRWA, Rathbun Rural Water Association; *n*, number of communities; SD, standard deviation; 2,4-D, 2,4-dichlorophenoxyacetic acid.
Communities grouped by source of drinking water supply.

Academy of Sciences Committee on Hormone-related Toxicants in the Environment, indicate that the estimate of dietary exposure is approximately 0.1 µg/kg/day under the most exaggerative conditions. Obviously, this is a level far below the lowest dietary exposure used by Nagel et al. (*1*). It is therefore quite clear that epoxy lacquer-coated metal food and beverage containers present no public health hazard.

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*Note: The final report of the Epoxy Can Coating Work Group is available by contacting Susan Howe, Society of the Plastics Industry, 1801 K Street NW, Suite 600K, Washington, D.C., 20006-1301; (202) 974-5223.*

## Corrections and Clarifications

In the news article about the BEST Program that appeared in the February issue of EHP (105:176–177), Marian Johnson-Thompson, Assistant to the Director for Education and Biomedical Research Development, was not identified as the program's chief organizer and the NIEHS BEST contact person. Additionally, Larry Champion, Laboratory of Molecular Genetics, should be identified as the individual who coined the term BEST.

Furthermore, the unique characteristic of the BEST Program that formally is a partnership between the NIEHS and Durham Public Schools engages several other important elements. These are represented by the continuous and active involvement of the school's students, parents, faculty, and staff, community-based organizations and volunteers, businesses, other RTP area federal and private scientific organizations, local and state government officials, local universities, and the N.C. School of Science and Math. Conspicuous in this innovative concept is the "It Takes a Village" approach.

Finally, since the February publication, an additional school, C.C. Spaulding Elementary School, home of the new Biosphere Magnet Center, has joined the BEST Program.

## Response

In a paper published earlier this year (*1*), we described biological effects *in vivo* on the rodent prostate caused by fetal exposure to very low doses of the environmental estrogen bisphenol A. Fetuses were exposed by feeding pregnant female mice bisphenol A at average maternal doses of 2 and 20 µg/kg maternal body weight per day (2 and 20 ppb), and these exposure levels produced enlarged prostates [similar to effects seen with low doses of estradiol and diethylstilbestrol (*2*)] measured in subsequent adulthood. Our conclusion that these doses of bisphenol A were "near or within the reported ranges of human exposure" was based on exposures to bisphenol A following application of some dental sealants as reported by Olea et al. (*3*), where up to 913 µg of bisphenol A were reported released into saliva in the first hour after application of sealant. This 913 µg of bisphenol A in a 60 kg human would be equivalent to 913 ÷ 60, or 15 µg/kg body weight, well above the lowest dose of 2 µg/kg/day at which we observed a biological effect in mice on the developing prostate. In a very recent report, Steinmetz et al. (*4*) detected biological effects of bisphenol A at a concentration down to 1 nM, or 0.23 µg/l.

In their letter addressing several conclusions drawn in our study, Hoyle and Budway noted that the Epoxy Can Coating Work Group's final report "Potential Exposure to Bisphenol A from Epoxy Can Coatings" is now available and that newer methods for measuring bisphenol A minimize interferences and therefore revise downward the estimates of exposure to bisphenol A. However, the revised value in the final report for estimated daily intake (EDI) of bisphenol A extracted from epoxy can linings, using the improved methods, was reduced only 35%, from 9.6 to 6.3 µg/person/day, compared to the preliminary report. The final report expressed the EDI as a potential exposure level of 0.105 µg/kg/day. However, a limitation to these studies is that solvents were used to simulate the effects of food to extract bisphenol A from the lining of cans, whereas in the study referred to by Hoyle and Budway in their letter, Brotons et al. (*5*) extracted bisphenol A actually present in the liquid phase of vegetables stored in cans, and values published in this study ranged from nondetectable to 23 µg bisphenol A in a can of peas.

For chemicals such as bisphenol A, the FDA calculates an acceptable daily intake (ADI), which is assumed to be safe. To calculate the ADI, safety or uncertainty factors (*6*) are applied to results from animal studies. Safety factors originate from the realization of uncertainty with regard to extrapolating from animal data to estimation of risk to humans. There are three multiplicative uncertainties that apply here: 1) a 10-fold safety factor is applied when the lowest dose used in the experiment results in an adverse effect (such as prostate enlargement) instead of no adverse effect; 2) another 10-fold safety factor is normally also applied since, in the human population, there is assumed to be a distribution of susceptibility and intake levels; and 3) because of uncertainty in extrapolating from experimental animals to humans, another 10-fold safety factor is standard. Dividing the lowest dose (2 µg/kg) in our study (that led to an adverse effect) by a safety factor of 1,000 provides an ADI of 0.002 µg/kg using current methods of risk assessment (*6*). Thus, exposure to bisphenol A at 0.105 µg/kg/day is 50-fold higher than the ADI calculated above.

For Hoyle and Budway to support the statement "It is therefore quite clear that epoxy lacquer-coated metal food and beverage containers present no public health hazard," they should have used accepted risk assessment procedures and referenced the estimated daily intake of bisphenol A from cans to an acceptable daily intake level. Instead, they referred to the lowest dose used in our study and indicated that the EDI reported by the Society of the Plastics Industry of 0.105 µg/kg/day "is a level far below the lowest dietary exposure used by Nagel et al." It is clear that the estimated daily intake of bisphenol A from cans is actually above the level that would justify the statement regarding public health.

Although the Epoxy Can Coating Work Group's report focused on exposure from cans, bisphenol A exposure may derive from a number of sources in addition to can linings, and published findings demonstrate that these other sources contribute to a higher body burden of this chemical (*3*). With regard to the public health, exposure to chemicals that act via a common mechanism (such as binding to estrogen receptors) should be viewed in the context of intake from all sources. However, even if one

accepts that each source of exposure be viewed independently, based on current risk assessment methods, to support the contention that no public health hazard exists from the use of bisphenol A to coat food and beverage cans, there would have to be a wide (>1,000-fold) margin of safety between the EDI from cans and the lowest adverse effect level in animal studies. Based on the findings of our study as well as of the Steinmetz et al. study (*4*), this clearly is not the case.

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