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...
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 exaggerated 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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REFERENCES
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2. Brotons JA, Olea-Serrano MF, Villalobos M, Pedrata V, Ola N. Xenoestrogens released from lacquer coating in food cans. Environ Health Perspect 103:608–612 (1995).
3. Society of the Plastics Industry. Report on Potential Exposures to Bisphenol A from Epoxy Can Coatings. Washington, DC; Society of the Plastics Industry, 1995.
4. Society of the Plastics Industry. Potential Exposure to Bisphenol A from Epoxy Can Coatings. Washington, DC; Society of the Plastics Industry, 1996.

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

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 55 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