Data challenges the APB on BPA

Pacific Northwest National Laboratory

BOSTON – A controversial component of plastic bottles and canned food linings that have helped make the world's food supply safer has recently come under attack: bisphenol A. Widely known as BPA, it has the potential to mimic the sex hormone estrogen if blood and tissue levels are high enough. Now, an analysis of almost 150 BPA exposure studies shows that in the general population, people's exposure may be many times too low for BPA to effectively mimic estrogen in the human body.

The analysis, presented at the American Association for the Advancement of Science's annual meeting by toxicologist Justin Teeguarden of the Department of Energy's Pacific Northwest National Laboratory, Richland, Wash., shows that BPA in the blood of the general population is many times lower than blood levels that consistently cause toxicity in animals. The result suggests that animal studies might not reflect the human BPA experience appropriately.

"Looking at all the studies together reveals a remarkably consistent picture of human exposure to BPA with implications for how the risk of human exposure is interpreted," said Teeguarden. "At these exposure levels, exposure to BPA can't be compared to giving a baby the massive dose of estrogens found in a birth control pill, a comparison made by others."

In addition to evaluating the likelihood of BPA mimicking estrogen in humans, Teeguarden also analyzed another set of BPA studies that looked at the chemical's toxicity in animals and cells in the lab. These 130 studies are significant as a group because they refer to the exposures as "low dose," implying they are very relevant to human exposures.

According to his analysis, however, the "low doses" actually span an immense range of concentrations, a billion-fold. In addition, only a small fraction of the exposures in these self-described "low dose" studies are in the range of human exposures, from 0.8 percent to 7 percent depending on the study.

"The term low-dose cannot be understood to mean either relevant to human exposures or in the range of human exposures. However, this is in fact what it has come to mean to the public, as well as many in the media," said Teeguarden.

Analysis of 150 Exposure Studies

The first analysis covered 30,000 individuals, including women and infants, in 19 countries. Human blood concentrations were calculated multiple ways using many kinds of exposure data.

Teeguarden looked to see if BPA concentrations were sufficiently high to be a

significant source of estrogen-like activity in the blood. Researchers have long known that BPA can bind to the same proteins that estrogen does — called estrogen receptors — when estrogen is doing its job in the body. However, in most cases, BPA does so much more weakly than estrogen. To trigger biological effects through receptors, BPA concentrations have to be high enough in the blood to overcome that weakness.

"Systematically testing the estrogenicity, or the bioactivity of BPA at the part per trillion concentrations we expect in human blood would seem the most scientific way to substantiate or refute this conclusion," said Teeguarden.

Teeguarden analyzed the data in these studies using multiple independent approaches applied systematically to the data from thousands of individuals. The results showed that human blood levels of BPA are expected to be too far below levels required for significant binding to four of the five key estrogen receptors to cause biological effects.

Teeguarden's analysis also confirmed the findings of many academic and government scientists that biologically active BPA is at such low concentrations in the blood that it is beneath toxicologists' current ability to detect it, raising questions about the role of sample contamination in studies reporting high levels of BPA.

Analysis of 130 Toxicity Studies

In this analysis, Teeguarden compiled all the BPA studies that included the term "low dose" as it referred to human exposure by using such terms as "low-concentration," "environmentally relevant," or "human exposure." From the 130 studies found, he and PNNL biologist Sesha Hanson-Drury compiled all the doses that were actually used in the studies.

The results showed that a small fraction of the "low doses" used in these studies are within the range of human exposures, with the vast majority being at least 10 to thousands of times higher than what humans are exposed to daily. In addition, the range of concentrations spans from upwards of 10 grams per kilogram of weight per day down to 100 picograms per kilogram of weight per day (a picogram is one millionth of a gram).

"Unfortunately, the low dose moniker has been used by some to promote the importance of selected toxicity studies, for example, in arguments to ban BPA," said Teeguarden. "For BPA and all chemicals, we need more accurate language to present these findings so the public and scientists in other disciplines can understand how human exposures compare to exposures in laboratory studies reporting toxicity."

Justin Teeguarden, Ph.D., is a senior scientist in the Systems Toxicology and Exposure Science group at the Pacific Northwest National Laboratory. This work was entirely supported by the United States Environmental Protection Agency under the Science to Achieve Results (STAR) program.

Reference: Justin Teeguarden, *Estrogen Receptor Activation Potential of Internal Concentrations of BPA in Humans*, **Feb. 16, 1:30 p.m.-4:30 p.m.**, Room 302, Hynes Convention Center.
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