





INVESTIGATING BPA

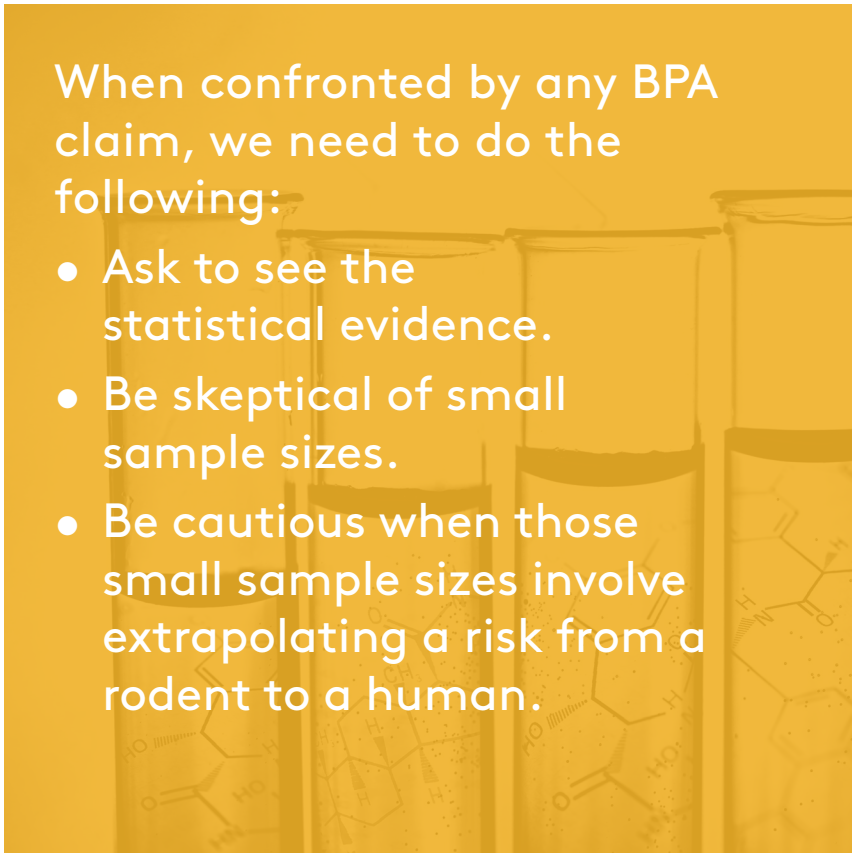
A look into how—and why—the media ignores the science confirming that BPA poses no risk to humans

By Trevor Butterworth

I recently asked three world-class statisticians to engage in a thought experiment, one that mirrored the moment bisphenol-A (BPA) entered the public's consciousness. Imagine, I wrote, that you are watching television and that I, as a scientist, appeared on a news program to say that an entire field of science had to change based on my research. That what I had found represented a paradigm inversion—a turning upside down or backwards of our understanding of the way things worked. And then imagine that the journalist interviewing me, having done her research, asked me for the statistical basis for this claim. And I answered, "Two studies, each with seven mice and 11 controls. In sum, a total of 14 dosed animals."

What would be your immediate reaction?

"At first glance, this would sound as a claim totally out of proportion versus the magnitude and type of the evidence, clearly outrageous—but maybe I am missing something," said



John Ioannidis, C. F. Rehnborg Professor in Disease Prevention in the School of Medicine at Stanford University, and one of the leading researchers into the scope and scale of error in medical research.

David Spiegelhalter, Winton Professor for the Public Understanding of Risk, at the University of Cambridge's Statistical Laboratory, and co-author (with Michael Blastland) of *The Norm Chronicles: Stories About Numbers and Danger*, expressed caution about making any judgment without more context, but he said, "I generally take a Bayesian approach to evidence, which means that extraordinary claims need extraordinary evidence." The numbers of animals in the studies were too low to amount to substantial evidence; the claim needed proper replication.

For Stanley Young, assistant director of Bioinformatics at the National Institute of Statistical Sciences, the problem was more fundamental than low numbers. "I worked for many years as the lead statistician in an industrial toxicology lab," said Young. "I've also consulted with biologists on predictive biology from animal studies. In both situations it was generally agreed, mice are generally poorer for predictions than rats; both are essentially awful for predicting humans."

Those reactions tell us a number of things. When confronted by any claim that we are at risk, we need to do the following:

- Ask to see the statistical evidence.
- Be skeptical of small sample sizes.
- Be cautious when those small sample sizes involve extrapolating a risk from a rodent to a human.

None of that is controversial: it's the kind of basic quantitative literacy that we all need to practice in a world powered by scientific claims. Or more realistically, it is the kind of literacy we need journalists to exercise on our behalf if they are going to report those scientific claims.

Questions Not Asked

But back in 1998, in an interview on PBS FRONTLINE, no such questions were asked of a University of Missouri developmental biologist, Frederick vom Saal, when he talked about how he found adverse health effects at extremely low doses of BPA that didn't occur at higher doses, how this meant that people—and especially fetuses and infants—were at risk from exposure to plastics in food packaging, and how these findings showed that "the fundamental tenets of a field of science" were wrong. Toxicology operated on the basis, first set down by Paracelsus in the 16th century, that the dose made the poison and that anything could be poisonous in high enough doses. His research represented a "paradigm inversion"—one that was so threatening to the field of toxicology, and to the billion-dollar chemical industry, that they would deny it was happening.

The producers, the reporters, the interviewer—none of them thought to ask how all of this could be reliably and robustly deduced from the weight of 14 mouse prostate glands. Instead, the claims about BPA fit into a narrative of endocrine disruption that had emerged in the 1990s focusing on the threats to wildlife from estrogenic chemicals in the environment. BPA brought the threat home to humans.

Still, neither the field of toxicology nor the chemical industry immediately dismissed vom Saal and his collaborators or their data. The National Toxicology Program called for the low dose experiments with BPA to be replicated, and

two research teams, one led by John Ashby, the other by Stuart Cagen, tried to do so. Both failed. Ashby tried to replicate another study claiming that BPA exposure reduced sperm counts in rats; he couldn't.

The clearest warning sign that all was not what it seemed in BPA research came in 2004, with the publication of Iain Purchase's Paton Prize lecture—"Fraud, errors and gamesmanship in experimental toxicology"—which reflected what this failure actually meant, and how the debate on BPA was departing from accepted scientific practice. "Gamesmanship is where the normal paradigm of the self-corrective mechanism in science, that is verification and scientific review, is not followed," he wrote. "Rather, in place of scientific criticism, the focus of the criticism is the scientist or the scientist's affiliation."

Vom Saal had warned that the chemical industry would dismiss his findings—and here you had two research teams from industry who appeared to be doing just that. The proper scientific response, wrote Purchase, was for vom Saal to do a large-scale study to confirm his hypothesis; instead, he publicly attacked the competence and integrity of Ashby and Cagen.

"The technical competence of Ashby's group was questioned, but a member of vom Saal's group trained Ashby's group in the technique of prostate dissection," wrote Purchase. "Then high levels of phytoestrogens in Ashby's laboratory diets were claimed to invalidate the results, but the phytoestrogen levels in the diets employed by vom Saal were higher." And on it went.

The Purchase paper should have been a warning to journalists covering BPA, but it never made it out of the toxicological community and into the media. Instead, over the next few years, vom Saal would be portrayed in the media as the authority on BPA (*USA Today* gave him a full-page spread) even as the scientific criticism of his work—and counter evidence to the threat of BPA—grew in leaps and bounds.

Multi-generational toxicity studies conducted for the European Food Safety Authority (EFSA) and the U.S. Environmental Protection Agency (EPA) failed to reproduce low dose effects from BPA in a variety of species, while showing that such effects occurred with the control substance. Yet the media narrative either ignored that research or labeled it as corrupted by industry funding. In the media's telling, there were hundreds of studies showing a risk, so why was the government not doing anything to ban this chemical?

The problem was that those studies either lacked statistical power or had methodological problems—such as administering BPA to rodents by injecting it straight into the bloodstream (something every regulatory agency around the world agreed was an inappropriate way to assess risk). And yet, the media, with a few exceptions, stuck to the same alarmist narrative, even when the agency that had funded much of this research—the National Institute of Environmental Health Sciences—admitted in 2008 that these studies—the studies that had driven a worldwide panic over BPA—couldn't be used for human risk assessment.

Making Sense of the Media

To give some sense of how asymmetrical the reporting on BPA was, I asked colleagues at George Mason University's Center for Media and Public Affairs (CMPA) to analyze a specific aspect of the media coverage. Again, it started

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with a simple thought experiment: What—amid a squall of claims about the chemical's safety—would be a critical piece of information that a reader would need to know to make sense of the controversy?

The answer was EFSA's 2006 risk assessment on BPA. It was the most comprehensive review of the science; it was regularly updated to evaluate new research; it was independent, conducted by scientists across the European Union; and, critically, it was conducted under the regulatory burden of the precautionary principle, something environmental activists were urging on the U.S. regulatory system as a way of protecting the public from the potential dangers of chemicals like BPA. EFSA kept finding and explaining why there was no risk to humans or infants at current exposure levels to BPA.

The pattern of coverage in the U.S. media might well have been, "never let a good risk assessment get in the way of a good story." Between January 1, 2006 and May 6, 2011, CMPA found 551 stories on BPA in a sample of the 19 top circulation newspapers in the United States. Just 35—6.4 percent—mentioned EFSA's risk assessment. A sample of national broadcast news transcripts found 104 stories, just three of which contained references to EFSA.

Things might be changing. At this year's meeting of the American Association for the Advancement of Science (AAAS), top FDA researchers presented their latest research findings on the chemical. The controversy over BPA has, in fact, stimulated groundbreaking progress in the field of toxicology, and that progress is impossible to ignore. The conclusion, of course, is still the same—the original vom Saal studies cannot be replicated in the most carefully designed study yet to try to do so. There is no evidence that BPA poses a risk to human or fetal health.

And, as a reminder of the central importance of numbers in understanding risk, two studies funded by the EPA were also previewed at AAAS. They reviewed the low dose literature that has been powering the controversy and compared the doses administered to every reliably-taken measurement of BPA in human serum from around the world. Turns out, the majority of low doses weren't low at all. If one cent equalled human exposure, the low doses ran up to 10 billion dollars. Remarkably, this time, the media paid attention.

BPA AND BOTTLED WATER

Bottled water is comprehensively regulated as a food product by the U.S. Food and Drug Administration (FDA). Plastic food and beverage containers, including polycarbonate plastic bottles made with bisphenol-A (BPA), must meet or exceed all FDA requirements. FDA approves all food-contact plastics for their intended use based on migration and safety data. The approval process includes stringent requirements for estimating the levels at which such materials may transfer to the diet. FDA's safety criteria require extensive toxicity testing for any substance that may be ingested at more than negligible levels. That means FDA has affirmatively determined that, when these plastics are used as intended in food-contact applications, the nature and amount of substances that may migrate, if any, are safe.

Polycarbonate plastic has been the material of choice for many food and beverage product containers for nearly 50 years because it is lightweight, highly shatter-resistant, and transparent. During that time, many international studies have been conducted to assess the potential for trace levels of BPA to migrate from lined cans or polycarbonate bottles into foods or beverages. The conclusions from those studies and comprehensive safety evaluations by government bodies worldwide are that polycarbonate plastic bottles are safe for consumer use.

Trevor Butterworth *is a contributor to* Forbes, The Wall Street Journal, *and many other publications. He is editor-at-large for STATS.org, an affiliate of George Mason University that examines the use of statistics in public policy or the media. For more, visit his website: www.trevorbutterworth.com.*