

## ENSAYO

# Challenges to regulate products containing bisphenol A: Implications for policy

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## Abstract

Bisphenol A (BPA), found in plastics and epoxy resins, is one of the most studied chemicals. BPA is regarded as an endocrine disruptor and has been related to adverse health effects in humans. However, some regulatory agencies around the world have concluded that BPA is safe at current human exposure levels. As the scientific community attempts to settle the debate on BPA's health effects, regulatory agencies have been put into a challenging public health policy situation. The United States has implemented no regulatory actions due to safety concerns, while Europe has used the precautionary principle to guide its regulation in the face of scientific uncertainty. In this paper, we explore the debate surrounding BPA regulation and the possibility for countries to introduce guidelines, using Mexico as an example. Policy change determinants analysis suggest that countries can and should impose regulations on BPA.

**Keywords:** Bisphenol A; government regulation; public policy; Mexico

## Resumen

El bisfenol A (BPA), presente en plásticos y resinas epoxi, es uno de los químicos más estudiados. Se considera un disruptor endocrino y se ha relacionado con efectos adversos para la salud humana. Algunas agencias regulatorias en el mundo han concluido que el BPA es seguro a los niveles de exposición humana actuales. Mientras la comunidad científica intenta resolver el debate sobre dichos efectos, las agencias regulatorias enfrentan una difícil situación de política pública. Los Estados Unidos de América no han implementado acciones reglamentarias por razones precautorias, mientras que Europa ha utilizado el principio precautorio para guiar su regulación ante la incertidumbre científica. En este documento exploramos el debate que rodea la regulación del BPA y la posibilidad de que los países introduzcan directrices, usando a México como ejemplo. El análisis de los determinantes del cambio de políticas sugiere que los países pueden y deben regular el BPA.

**Palabras clave:** Bisfenol A; regulación gubernamental; política pública; México

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**B**isphenol A (2,2-Bis [4-hydroxyphenyl]propane), commonly referred to as BPA, is a synthetic chemical with wide-spread applications in the production of polycarbonate plastics and epoxy resins that are used in food containers, baby bottles, medical devices and personal care products, among other uses. The purpose of adding BPA to polycarbonate is to increase the durability of the plastic. In epoxy resins, BPA's benefit is to line the interior of food cans. BPA was introduced into plastic manufacturing during the 1950's, and now has an estimated worldwide annual production of over six billion pounds.<sup>1,2</sup>

Humans are exposed to BPA mainly via ingestion of food and beverages that are stored in plastic and canned containers made with BPA, secondarily via inhalation and to a lesser degree by dermal exposure, dental sealants and injections.<sup>3,4</sup>

Several studies on BPA exposure in animals show effects mainly in the male reproductive system, brain development and behavior.<sup>5,6</sup> Some of these studies have been conducted in accordance with regulatory guidelines and using human-relevant exposure routes; many others lack these characteristics. As a result, there are considerable discrepancies in the nature of the effects and the levels at which these effects occur. In some studies, effects have been observed at several orders of magnitude lower dose levels than those used in studies carried out in accordance with regulatory guidelines. Although the US Food and Drug Administration (FDA) has long declared BPA as a safe compound, the controversy led the agency to reevaluate BPA exposure and its health effects. By one hand, the FDA evaluated the effects on growth, organ weight and tumor development in rats exposed during a two-year period following federal regulatory and statutory guidelines; on the other hand, non-FDA academic institutions evaluated a range of additional endpoints using the same FDA-exposed animals. The most recent publication, based on the FDA set of results, concluded that BPA exposure may have caused changes in male rat pituitary and female rat reproductive tissues at high doses, in contrast to the non-FDA results that have found adverse effects at low-level BPA exposure.<sup>7,8</sup> Furthermore, epidemiological evidence suggest harmful effects such as infertility, lower male sexual function, reduced sperm quality, changes in endogenous sex hormone concentrations, immunotoxicity, obesity, cardiovascular disease, type-2 diabetes, and neurobehavioral problems.<sup>9-11</sup> These effects have been identified at human BPA concentrations that lie below safety thresholds of government agencies. These findings, thus, call into question the frequent use of BPA-containing products and bring about concerns of adverse effects from low-dose chronic exposure.

Many countries have introduced BPA regulations and approaches vary from nation to nation, other countries like Mexico, lack BPA regulations.

We will review the approach taken by some regulatory agencies and then propose a model with specific criteria for evaluating whether or not to regulate BPA.

### **Policy background on BPA**

While adverse health effects have been found in numerous BPA studies, the weight of evidence placed on them differs by regulatory agency due to varying levels of concerns surrounding the methodologies. For example, the report from a joint Food and Agriculture Organization (FAO)/World Health Organization (WHO) expert meeting in 2010 stated that proposing a "safe" exposure level for BPA continues to be hampered by: 1) A lack of data from experimental animal studies that are suitable for risk assessment, 2) Design and analysis issues that limit their utility, 3) Controversy over the biological significance of many of the more sensitive end-points, 4) Studies that assess only conventional end-points which may not detect all potentially relevant effects.<sup>12</sup>

Global responses vary as a result of these uncertainties. Countries like Canada, Malaysia, Colombia and Brazil, among others, have banned BPA from baby bottles. Although the United States has also banned BPA from baby bottles, its BPA regulations are much more lenient than Canada's or France's.<sup>13,14</sup>

In the United States, the FDA has amended its food additive regulations to prohibit the use of BPA-based materials but only in baby bottles, spill proof cups, and infant formula packaging. These bans, however, are clearly stated by the FDA as "not based on safety". Instead, the FDA approved these bans at the request of the American Chemistry Council since consumer avoidance of BPA containers forced manufacturers to abandon BPA containing packaging and the FDA pronouncement had the benefit of clearing up market confusion as to whether BPA is present.<sup>15</sup> In addition to these bans, the FDA maintains their No Observed Adverse Effects Limit (NOAEL) of 5 mg/kg bw/day.<sup>16</sup> Likewise, the Environmental Protection Agency (EPA) has also maintained a reference dose (RfD) of 50 µg/kg bw/day, based on reduced mean body weight in a rat chronic oral bioassay.<sup>17</sup>

In order to address data gaps, the FDA is collaborating in the Consortium Linking Academic and Regulatory Insights on BPA Toxicity (CLARITY-BPA), along with the National Institute of Environmental Health Sciences (NIEHS) and the National Toxicology Program (NTP). CLARITY-BPA intends to link more effectively academic (Grantee Studies) and guideline-compliant

(Core Study) research in order to study a full range of potential health effects from BPA exposure and therefore will provide data that can be used for regulatory decisions.<sup>18</sup> Results from the CLARITY-BPA Core Study showed no impact of BPA exposure at the lowest dose, except for an increase in female rat mammary gland tumors, and effects in the female reproductive tract and in the male pituitary at the highest exposure dose. So far, based on these results, it has been concluded that the effects observed below the highest exposure dose presented several problems including non-dose-response and no clear pattern within or across organs, and that only the effects observed at the highest exposure dose may be due to BPA.<sup>8</sup> However, academic grantees have published peer-reviewed studies that found harmful effects at low-level exposures.<sup>7</sup>

The European Food Safety Authority (EFSA) maintains a similar policy position regarding BPA's toxicity as the FDA, but approaches it differently in both regulation and attitude. Like the FDA, EFSA also declares that BPA is safe and does not pose any health risks at current human exposure levels.<sup>14</sup> However, EFSA has acted clearly by continually lowering their safety threshold and making strong efforts to protect the most vulnerable on the basis that uncertainty over BPA's health effects calls for precautionary bans. EFSA has even banned BPA from products that extend beyond baby bottles, spill-proof cups and infant formula packaging, thus, ensuring that BPA will not migrate from varnishes and coatings to: follow-on formula, food for special medical purposes, milk-based drinks, processed cereal-based food, and similar young children-targeted products.<sup>19</sup>

At the conclusion of its 2015 review, EFSA decided to lower its safety threshold from 50  $\mu\text{g}/\text{kg}$  bw/day to a temporary tolerable daily intake (t-TDI) of 4  $\mu\text{g}/\text{kg}$  bw/day.<sup>14</sup> In 2018, EFSA lowered the specific migration limit (SML) of BPA from plastics in contact with food from 0.6 mg/kg to 0.05 mg/kg. The report cited that with the new indications of developmental immunotoxicity, precautionary steps should be taken to protect vulnerable populations (such as infants and young children) in which developmental effects could be irreversible. Although EFSA's evaluations maintain that exposure levels are safe, the constant reassessments of BPA in 2006, 2008, 2010, and 2011 led to bans on a precautionary basis.<sup>19</sup>

On the world stage, the approaches of the Europeans and Americans are considered opposite ends of the regulatory regimes. There are, however, countries that have evaluated the FDA and EFSA approaches and set their own policy strategies in a middle ground. For example, the uncertainty of low-level BPA exposure health effects has not stopped Brazil, a nation of signi-

ficant economic status, from demonstrating precaution and banning BPA from baby bottles and infant feeding bottles.<sup>14</sup> Like EFSA, these bans were enacted based on precautionary measures; in contrast to EFSA, these bans exclusively protect the most vulnerable, but not the entire population. The economic impact of Brazil's recent ban has not yet been fully analyzed, but initial studies indicate a decrease in BPA exposure among infants in Brazil.<sup>20</sup>

## Discussion

### Mexico case study

Most of the world's developing countries, however, have no regulatory policies on BPA. One example is Mexico, where there is evidence of the presence of BPA in the general population and in products regularly commercialized.

Urinary BPA concentrations in pregnant women from Mexico City were found to be similar to those in women in the United States and other developed countries.<sup>21</sup> However, recent Mexican immigrants had lower levels of BPA than those among low-income pregnant women of Mexican-American heritage living in the United States.<sup>22</sup> A more recent study noted that the exposure levels among Mexican pregnant women were 30 times higher than those reported in previous studies.<sup>23</sup> These studies are limited in sample size and target only pregnant women, which highlights the need for information about BPA levels in other Mexican population groups. In addition, in products commonly found in Mexican supermarkets, it has been shown that BPA migrated from the epoxy resin lining *tuna* and *jalapeño* cans into the enclosed food;<sup>24</sup> and that BPA is present in baby bottles and microwaveable plastic containers.<sup>25</sup>

The Mexican regulatory apparatus responsible for protecting population health from the effects of goods and services, environmental and occupational factors, and sanitary emergencies is the Federal Commission for Protection against Sanitary Risks (*Comisión Federal para la Protección contra Riesgos Sanitarios*, [Cofepris]), a decentralized body of the Ministry of Health.<sup>26</sup> Ever since its creation, it has recognized that the knowledge of contaminants concentrations in the environment is essential for public health interventions. However, in the last years its action plan has not taken into account BPA regulation among other important contaminants.<sup>27</sup> Cofepris' mission is addressed through the enactment of standards (*Normas Oficiales Mexicanas*, NOM), which establish specifications, characteristics and guidelines for products, processes or activities, terminology, packaging or labeling, and its compliance.<sup>28</sup> These standards are

mostly based on those guidelines dictated by international organisms in order to make recommendations for member States. A factor that contributes to this measure is the scarce analytical capacity for the determination of environmental contaminants in Mexico, represented by the National Network of Environmental Laboratories (*Red Nacional de Laboratorios Ambientales*) which does not cover the entire country.<sup>29</sup>

With the different focuses of countries that have regulated BPA in mind, countries like Mexico can approach the problem of regulating BPA through a model with specific criteria.

### Model's criteria to regulate BPA in Mexico

The main determinants for policy change are: 1) disseminating scientific evidence, 2) technological resources, 3) economic resources, 4) risk communication and public awareness, as well as 5) politics.

The scientific evidence of BPA exposure adverse health effects has been mentioned previously. Health damages associated to low levels of BPA exposure are a concern.<sup>9-11</sup> In Mexico, there is evidence of BPA exposure in pregnant women and, there is a lack of studies addressing BPA exposure in other vulnerable populations, like children. Moreover, scarce research is available regarding BPA and health damages among Mexicans, only a recent study performed by our research group, where we reported an increased risk of diabetes in relation to urinary concentrations of BPA, among women living in Northern Mexico.<sup>30</sup> In this context, it is reasonable to extrapolate the findings from other studies to enhance the plausibility of BPA exposure on health damages and initiate a dialogue with policy makers.

From the technological resources point of view, a challenge to regulate BPA in Mexico is the country's scarce analytical capacity. A few laboratories are certified to measure environmental contaminants and thus, be used as a reliable technical base for decision making.<sup>29</sup> The strengthening of a certified analytical laboratory network would be a strong step to regulate not only BPA but many other environmental pollutants.

BPA is a highly efficient and necessary component in current plastic production. In order to eliminate BPA, consideration needs to be given to other ways to acquire its beneficial properties. However, the main substitutes in BPA-free products, BPS (2,2-bis [4-hydroxyphenyl] sulfone) and BPF (2,2-bis [4-hydroxyphenyl]methane), have also been linked to adverse health effects but their toxicological data are still limited. In this regard, a review of 25 *in vitro* and seven *in vivo* studies concluded that BPS and BPF are as hormonally active as BPA, and may have additional disruptive effects.<sup>31</sup> More recently,

it has also been documented in experimental studies that these compounds may decrease basal testosterone secretion by human fetal and adult testes, induce oxidative stress in human red blood cells and change cancer-related genes methylation profiles in human breast cancer cells.<sup>2,32-34</sup> Even though these findings warrant confirmation, current packaging labeled as BPA-free, likely contains BPS and BPF which may be just as harmful. Other materials like polyesters, polypropylenes, and acrylics may be safer compounds and have started to replace BPA-containing polycarbonate in baby bottles. While the compounds are functionally viable, there are noticeable differences from BPA-containing polycarbonate bottles as acrylic bottles are opaque, and polyester bottles are more expensive.<sup>35</sup> Nonetheless, these products allow for an effective route of regulation and replacement of BPA in baby bottles.

When approaching a public health and risk governance issue like this one, it is important to keep in mind the economic effects on the country. Therefore, a cost-benefit analysis is necessary to compare the costs of banning BPA versus the potential risks that BPA poses to the population. For instance, prenatal BPA exposure in the European Union was shown to have a 20-69% probability of causing 42 400 new cases of childhood obesity annually. These cases would add up to an associated lifetime cost of 1.54 billion euros. Likewise, it has been reported that removing BPA that is in contact with food may prevent 6 236 cases of childhood obesity and 22 350 cases of incident coronary heart disease per year in the United States. This would add up to a total potential annual economic benefit of 1.74 billion dollars which could outweigh the cost of transitioning to BPA substitutes.<sup>36,37</sup> The methods used to calculate the environmentally attributable costs for multifactorial conditions, such as obesity in these studies, were created by the Institute of Medicine.<sup>38</sup> These methods could be used for similar analyses in other countries.

From a risk communication standpoint, people around the world overlook the potential harms of using plastic containers for foods and drinks. A Thai study surveyed parents and health professionals about their knowledge, attitudes, and practices towards BPA, phthalate, and styrene releasing plastic food or drink containers. Due to higher attitude scores compared to lower knowledge scores, the study suggested that people are aware of the harmful side effects yet they may have little knowledge about how to use plastics correctly with food and drink.<sup>39</sup> A public awareness campaign for BPA's effects would include dissemination of scientific evidence, preparation of guidelines to show people alternatives to BPA-containing plastics, and creation of ways for consumers to retrieve information

about the plastics they are purchasing. Until a more definitive stance is taken on BPA, the public outreach should target parents and those caring for infants so as to inform them on how to avoid BPA.

The political analysis is country-specific, in Mexico's case, we identified two guidelines for addressing BPA regulation, NOM-130-SSA1-1995 which provides maximum concentration limits for different agents in food packaging, and lists allowable substances as suitable coatings for cans;<sup>40</sup> and NOM-131-SSA1-2012 that provides maximum concentration limits for agents contained in infant formulas, foods, and beverages.<sup>41</sup> Moreover, there is record of a legislative petition initiative to regulate BPA, that has not yet resulted in public policy change.<sup>42</sup> NOMs are supposed to be reviewed every five years, however, those two NOMs have not been updated in at least seven years. Thus, this opportunity could be used to regulate BPA in Mexico.

## Conclusion

After reviewing the scientific evidence, technological and economic resources, risk awareness strategies, and politic opportunities, it is clear that countries like Mexico do in fact have the ability to and should impose regulations on BPA exposure especially among the most vulnerable populations. As policy change does not occur merely on the presentation of scientific evidence, alignment of political will with economic and institutional capacities have an important role. The development of a certified monitoring network will be essential for environmental regulation. A transition to functionally viable replacements for BPA-containing products makes potential bans possible, in the meantime, public awareness campaigns should inform the general public not only on the adverse health effects of BPA but also on the alternatives to commonly used BPA-containing products. The probable economic health savings discussed above makes regulation more appealing for any country looking to modernize its laws on BPA. While the politics of the countries will define how far and how quickly they can go to ban BPA, their commitment to these efforts can be reevaluated and safety thresholds can be adjusted as they see fit over time. However, a ban on BPA in infants' formula and baby bottles can and should be enacted, as it is the bare minimum standard in order to protect the most vulnerable.

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