Need for regulatory policies in India, on the use of bisphenol A in food contact plastic containers

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The incidence of endocrine disorders and reproductive abnormalities has been increasingly reported in the recent past. There are chemicals that cause these disorders known as endocrine disrupting chemicals. Bisphenol A (BPA) is one such compound used in the polycarbonate plastics and epoxy resins. Studies are available to demonstrate the migration of BPA from such containers to food substances under various conditions. Similarly, studies conducted using animal models have revealed that BPA interacts with steroid receptors and intereferes with lipid metabolism, glycogen metabolism, etc. Although studies are available to demonstrate the toxicity of BPA even at lower concentrations, formulation of strong regulatory policies against BPA usage in plastics is quite difficult for Government authorities, since the results are inconsistent. Considering the potential risks posed by this compound, there are about 40 countries that have adopted restrictive policies on BPA use in food contact plastics especially intended for young children. Despite the restrictions implemented by these countries, developing countries like India, with a large number of plastic-users, do not have any policies for regulating BPA usage. The authorities should investigate and take action based on available information, and bring regulatory policies on the use of BPA in food contact plastics, especially intended for population under developmental stage and pregnant women.

Keywords: BPA policy, endocrine disruptor, low-dose effects, toxicity, tolerable daily intake.

ENDOCRINE disorders like infertility, obesity, thyroid disorders, male and female reproductive abnormalities have been increasing in the recent past. These disorders have been identified as significant public health burdens affecting more than 5% of the US population. Disorders like diabetes mellitus, obesity, metabolic disorders, osteoporosis, osteopenia, erectile dysfunction in male and thyroiditis are found to be more prevalent among the US population[1]. A five-fold increase of endocrine disorders like infertility, polycystic ovary syndrome (PCOS), thyroid, amenorrhea, hyperprolactinemia, menopause and hormonal contraception in Indian women was reported[2]. Besides other causes, exposure to synthetic chemicals like agrochemicals, industrial chemicals including solvents, plastics and plasticizers is one of the reasons for such endocrine disruptions[3]. These chemical compounds potentially disrupt hormonal functions and are collectively called as endocrine disrupting compounds (EDCs). These chemicals enter human body through oral ingestion, respiratory and/or dermal exposure. Through different mechanisms, EDCs bind to the hormonal receptors and affect the usual hormone actions. Bisphenol A (BPA) is one such synthetic chemical used largely in the manufacturing of polycarbonate (PC) plastics and epoxy resins. These PC plastics are widely used in various home appliances, such as kitchen wares, storage containers, etc.; thus exposure to humans is apparently high. BPA is leached into food substances under various circumstances via elevated temperature, longer storage or shelf-life, acidic pH, high pressure, etc.[3–7]. The repeated use of containers is also attributed to the high migration of this compound[8]. The potential endocrine-disrupting effects of this compound have been studied widely. Though many scientific evidences have been produced, the results vary on the level of toxicity of BPA on animal and human model systems. The governments, international monitoring agencies and various national level federal agencies are not certain about whether or not to restrict the use of this compound in food-contact materials. The dose responses showed that discrepancies lie across species level as the human testis model is more sensitive than that of rat and other animal model studies[9]. These discrepancies lead to a critical status quo where most experiments are conducted in rat and other animal models. To restrict the use of BPA in food-contact materials, we need conclusive evidence suggesting significant toxicity over hormone systems. This article intends to examine the position of developing countries especially India at present on the regulation of BPA.

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History of BPA

The first synthesis of BPA was achieved in 1891 by Dianin[10]. The unpublished report of BPA synthesis was studied later and synthesis of BPA and related compounds was published in 1905. Bayer Plastics of Germany and General Electric of USA utilized BPA in manufacturing polycarbonate plastic. Both companies patented the use of BPA in manufacture of PC plastics in 1955 (refs 11, 12). Since then, BPA is being used as a monomer in the making of PC plastics and widely used in electrical appliances, food storage containers, packaging materials, medical devices, etc. The manufacturing of epoxy resins using BPA was started since 1936, by CIBA Ltd, USA and is used as lining material in food containers, water pipelines and in dental sealants. The estrogenic nature of BPA was recognized by Dodds and Lawson[13,14]. Even though it has estrogenic properties, there were no evidences available for the use of BPA as therapeutic drug for humans.

Use of PC plastics as food containers for storage or food processing increases the exposure of BPA to humans. BPA migrated to food substances from PC plastic containers enters human system through oral ingestion. The potential endocrine disrupting effects of BPA was first recognized in 1997 (refs 15–17). Thereafter, several studies also provided evidence on the endocrine disrupting action of BPA[18–28]. BPA is similar in function to the natural hormone 17β-estradiol and binds mainly to the estrogen receptor (ER) to exhibit estrogenic activities[29,30]. Some of the chemicals such as bisphenol F (BPF) and bisphenol S (BPS) are generally used as alternatives in consumer products and labelled as 'BPA-free'. Rochester and Bolden[31] reviewed the toxicity of about 20 chemicals that are suggested as BPA-alternatives in 2015. They concluded that these compounds are also equally potent as BPA and exhibit endocrine disrupting effects.

Perspectives of international organizations on BPA regulation

The World Health Organization (WHO) and the Food and Agriculture Organization (FAO) jointly framed the International Food Safety Authorities Network (INFOSAN) in 2009. A report from this network expressed its uncertainty over the risks posed by BPA with the available scientific evidences[32]. The network adopted the overall no-observed-adverse-effect level (NOAEL) set by USFDA as a baseline for this assessment. In 2010, an expert panel of WHO recommended for public health officials to hold-off the restrictions on BPA suggested previously as studies were not conclusive of adverse effects. This recommendation was referenced by the EFSA's review on BPA toxicity which concludes no risks by low-doses of BPA[33]. An inter-organization programme for sound management of chemicals (IOMC) was framed by WHO and UNEP to review BPA toxicity in 2013. The expert panel of IOMC reported that the effects across model species are not similar and effects of BPA with the human testis model are more sensitive than that of the rat model[9]. This opinion has to be taken seriously and studied further to evaluate the effects of BPA across the species. It could help to have a solid conclusion on the toxicity posed to humans by this compound. In general, WHO is uncertain about the toxicity posed by BPA and holds no ground against BPA.

In 2008, USFDA reviewed the rodent studies and determined NOAEL for BPA as 5 mg/kg bw/day for human. This was set to 500-fold above the conservatory measures of human exposure including infants. This NOAEL measure was set based on uncertainty factors like intra-species variability, inter-species variability in reversible effects, irreversible reproductive or developmental effects and systemic toxicity from less-than-chronic exposure[34]. The FDA's 'Bisphenol A Joint Emerging Science Working Group' released an updated review of literature and data on bisphenol A in 2014. It summarized over 300 publications and concluded that current studies are leading to high uncertainty in addressing the dose-effects, estrogenicity and inadvertent exposure of BPA. FDA declared in its official website that BPA is safe for use in food-contact plastics, as it is migrated only in less quantity based on the review of scientific evidences[35]. This statement may encourage the manufacture of plastics and challenge against the restriction of BPA and further cause hesitation among other governments and agencies to implement stringent activities.

USEPA is a federal agency for monitoring, setting standards and enforcing activities for environmental protection. It initiated a rule-making process under Section 5 (b) (4) of the Toxic Substances Control Act (TSCA) intended to identify whether BPA is a compound of concern. The agency is setting up this rule based on long-term adverse effects of BPA on growth, reproduction and development of aquatic species at concentrations similar to those found in the environment. This proposal is under inter-agency review in the Office of Management and Budget. The agency has also proposed another regulation under section 4(a) of TSCA, especially to monitor BPA leaching into the environment around the landfills and manufacturing facilities for environmental degradation[36]. This rule would also enable EPA to monitor human exposure particularly in pregnant women and children. As of now, the agency is not yet decided if the toxicity of BPA over human exposure is at the level of concern or not. Even though the agency is not sure about the toxicity of BPA, design for the environment (DfE) a collaborative body of EPA encourages the public to reduce the BPA-exposure through alternative use of BPA-free consumer products. It made an attempt to screen 19 BPA-alternatives and found no safer alternative and most alternatives have high or moderate health risks, both to humans as well aquatic organisms[37].

In 2002, EFSA set a temporary Tolerable Daily Intake (t-TDI) of BPA as 10 μg/kg bw later in 2006, raised the t-TDI to 50 μg/kg bw after reviewing available evidences. With updated scientific outcomes, in 2014, EFSA reduced the TDI level to 5 μg/kg bw[38] and in 2015, further reduced it to 4 μg/kg bw[39]. A report by EFSA was released in 2015 on re-evaluation of the safety of BPA-containing food-contact plastics. The report concluded that there was no considerable adverse effects at the present level of exposure, but cannot be ignored completely with scientific information available currently[39,40]. Again in 2016, new evidences of BPA toxicity were evaluated by EFSA over immune systems, but the results were not conclusive[41]. Interestingly, in the re-evaluation report, it was referred as 'no concern' on BPA toxicity. In response to a claim by the ChemTrust, EFSA stated that the term 'no concern' was placed instead of 'low concern' to simplify the language for easy accessibility[42]. So it can be considered that BPA has some health concerns when used in the food-contact plastics.

The European Union Commission's implementing regulation amended the directive no. 321/2011, which enabled the restriction of BPA usage in the manufacture of baby feeding bottles. This restriction came to effect in the countries under EU from May 2011 (ref. 43). Among these discrepancies in toxicity of BPA, supply chain of European companies like Food Drink Europe, Empac and Plastics Europe jointly petitioned to challenge the French ban legislated in January 2015 (ref. 44). The Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) released an opinion in 2015, on the safety of the use of BPA. It suggested that use in medical devices poses risks to human health. It concluded that risks exist in systemic exposure to BPA by use in medical devices. Thus care must be taken to use devices which are not leaching this compound, especially devices being used in intensive care units for neonates, infants and dialysis procedures. It also suggested that alternatives can be used after reviewing their toxic profile[45]. Similarly we must ensure safer toxicity profile for compounds that can be used as alternatives in food-contact plastics. However, the European Union has implemented some restrictions on BPA even though EFSA is not conclusive on BPA toxicity over human health.

Countries' perspectives on BPA regulation

Only few countries are aware of the potential effects of BPA on human endocrine system and have adopted some restrictive measures on the use of BPA in food-contact plastics. Some developed countries like Japan and major developing countries like India, Nigeria, Indonesia, Bangladesh, Pakistan, Egypt, Mexico, etc. currently do not have any restrictions on use of bisphenol A in the manufacture of food-contact plastics. In total about 40 countries restricted manufacturing or at least restricted the use of BPA in food-contact plastics (Figure 1). African and Asian countries except China have neither scientific awareness on BPA-related health concerns nor legal restrictions on the use of BPA in consumer products.

Besides the countries discussed above, all countries under the European Union, Argentina, Brazil, Ecuador and Turkey have also banned or restricted the use of BPA especially in the articles that come in contact with infants and children under three years of age[46].

Forerunning health concerned actions by the developed countries

In 2009, the Canadian Health Ministry proposed a regulation to prohibit the use of BPA in plastic baby bottles[47]. In 2010, a final screening assessment by an expert committee formed by the Canadian Ministry recommended that the compound could be added to Schedule 1 Toxic Substance of the Canadian Environmental Protection Act, 1999. It was stated in the assessment that BPA entering into the environment may cause danger to human life or health[48]. The addition of BPA under this section would enable the ministry to manage risk on human health and environment. Considering the proposition and assessment report, the Government of Canada added BPA to Schedule 1 toxic substance list. Canada is the first country that implemented a regulation to restrict the use of bisphenol A[49,50]. This regulatory action by the Canadian Government has led other countries to be concerned for the public with reference to BPA.

In United States, the state of Massachusetts passed a bill intended to ban the use of BPA in food containers, and for other purposes considering the evidences of adverse effects named 'Ban Poisonous Additives Act of 2009' (ref. 51). Out of 50 states, 13 states and Washington DC (federal district) had restricted the use of BPA in consumer products. Other than these, Chicago city also banned the use of BPA-containing baby bottles in 2009. In 2014, the US Department of Health and Human Services directed the USFDA to implement strict criteria for hazard identification and risk assessment for building the weight-of-evidence evaluations including BPA[52]. The department also provided interim recommendations to the public to reduce exposure to BPA. It suggested and encouraged public to use 'BPA-free' plastic products. The US congress passed a bill to ban the use of BPA in food containers in September 2016. This is cited as section 2 under 'Ban Poisonous Additives Act of 2016' (ref. 53).

Besides the restriction on BPA by the European Union, France, in 2014 announced a ban on the use of BPA in plastics which have direct contact with babies and young children, which included baby feeding bottles. The Government of France is planning to introduce complete restriction of BPA in all kinds of food packaging[54]. In

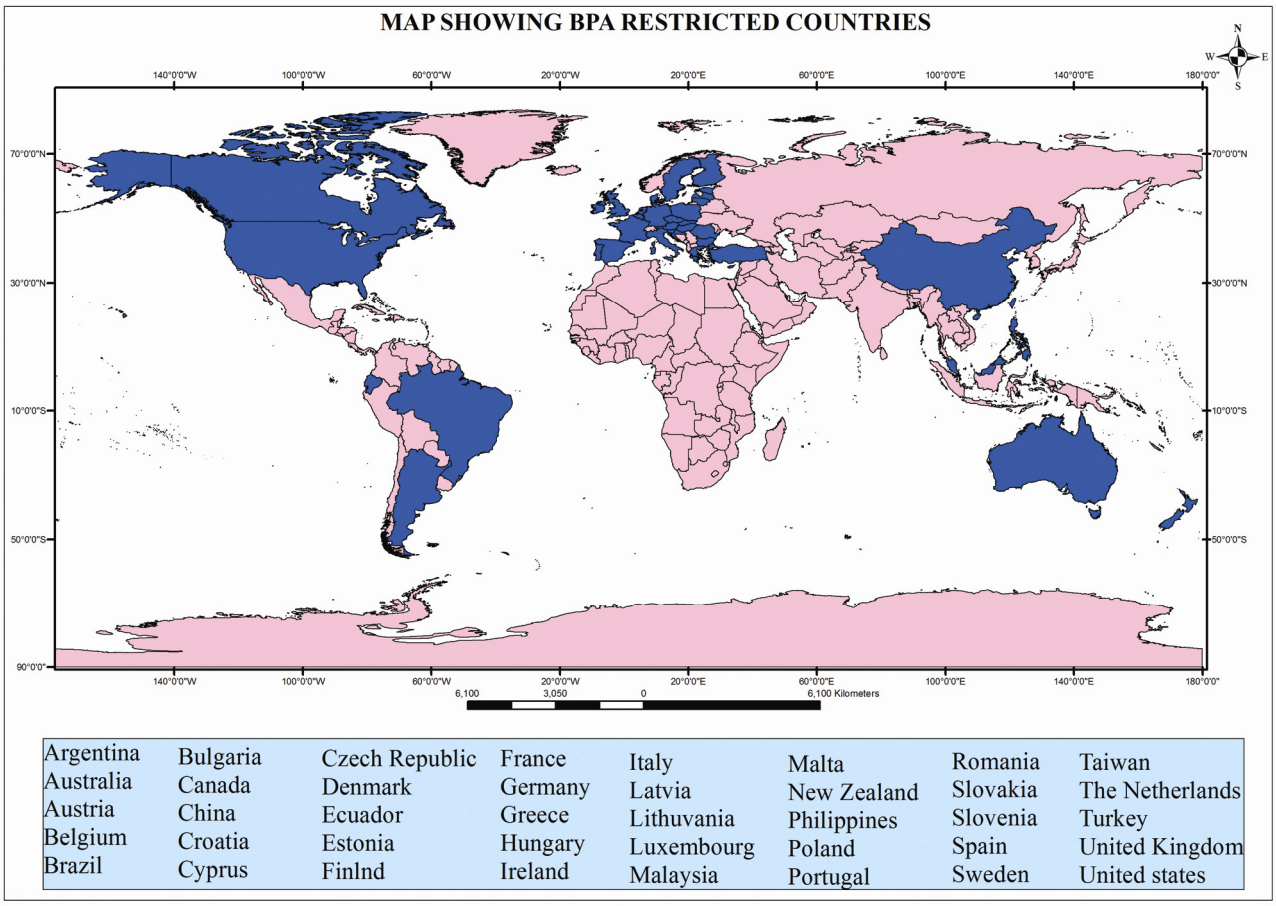

Figure 1. Countries which adopted BPA restrictive policies at least intended for the infants and children.

addition to restriction on the use of BPA in plastics and food containers, France also proposed that the European Union to prohibit the use of BPA in thermal papers used in labels and food packaging which are also thought to have health concerns[55,56]. The European Chemical Agency (ECHA) very recently included BPA in the candidate list of substances of very high concern and the reason for inclusion has been mentioned as 'toxic for reproduction'[57]. The legistation has been successfully implemented on the ban of BPA-containing materials of any sort which come in direct contact with food and pose threat to infants, children and pregnant and nursing mothers[58]. It was also noted that alternatives like BPS and other bisphenols are already in use which still pose similar health risks. However, the French government decided that they cannot restrict other BPA-alternatives owing to lack of insufficient toxicological data[56].

The Swedish Chemical agency, the nodal agency for Swedish Government, had proposed a thorough investigation in 2012 on the use of BPA in thermal papers. The agency is working in cooperation with the Swedish National Board of Housing, Building and Planning and also the National Food Agency to investigate the extent of BPA migration by the use of epoxy lining in water pipelines, toys and articles used by children[59]. In 2015, The Government of Sweden declared a ban on the use of BPA in food packaging materials for children under the age of three. Concerning the risks of negative effects on infants exposed to BPA in tap water, the Swedish government proposed to the European Union to restrict BPA in relining of pipelines[56].

Similar to France, a national level ban was announced in 2015 by Denmark on the use of BPA in food containers in addition to restrictions by EU. This was mainly intended for food containers in use by young children especially under three years of age. This ban was implemented temporarily and as a precautionary action against concerns raised by food safety experts that the compound affects children's learning ability[60].

The Government of Australia has not imposed any regulatory actions yet, concerned about BPA-related health risks. It has called for voluntary phase out of BPA from the public use in baby feeding bottles[61]. In Australia, the safety of food packaged in plastic containers is monitored by Food Standards Australia New Zealand (FSANZ). The safety of plastic containers is monitored by Australian Competition and Consumer Commission (ACCC). These organizations jointly work towards food safety in Australia

and New Zealand. The Australian Food and Grocery Council also extended support towards reduction of BPA usage and availability of BPA alternatives[62].

As in Australia, New Zealand also called for a voluntary phase-out of BPA intended towards consumer preference and not against any safety issues over BPA exposure[63]. The New Zealand government advised public to take BPA alternatives until conclusive evidence against safety of PC baby feeding bottles is ensured[64]. In addition, the New Zealand Food and Grocery Council also voluntarily involved itself in phasing-out of BPA used in polycarbonate baby feeding bottles[62].

Inconsistent health concerns by the developing countries on the use of BPA

The use of BPA in baby feeding bottles was banned in Malaysia effective from March 2012. The Ministry of Health of Malaysia saw a significant increase in migration from PC bottles owing to this regulatory action[65]. Still it should be noted that this is only a precautionary action and not based on any solid scientific evidence.

Recently in 2015, EcoWaste Coalition, an ecological group in the Philippines appealed to the Department of Health to restrict the use of BPA in baby feeding bottles[66]. The appeal stated that the country lacked technical facilities to analyse BPA leaching and toxicity which should not be a hindrance to announcing a precautionary ban on BPA concerned with children's health. This effort is appreciable and calls for generation of scientific evidences prior to any regulatory actions.

With high population and larger plastic users, developing countries like India and China should show serious concern on this issue. Previously, there was hesitation from the Chinese government in taking a decision on BPA ban. This hesitation was deliberately expressed by the Chinese government and they demanded that the Canadian federal regulators not to restrict the compound[50]. But later, five ministries including Health Ministry called for a ban on production followed by import and sale of BPA-containing baby feeding bottles in China[67]. In addition, the Supreme People's Court of China recommended maximum punishment for those who violated the food quality standards including BPA levels[28]. This recommendation ensured proper implementation of quality and safety regulations in China, and this must be taken to other countries.

The Indian context is still different in the sense that there is no concrete stance on the use of BPA in food-contact plastics. Some research studies are available in India stating the high incidence of endocrine disorders[2], increased rate of thyroid-related disorders[68]; presence of BPA in food and environmental samples[7,69–76]. These studies provide substantial evidence of the presence of BPA in articles, leaching into food substances and causing endocrine disruption in humans. Earlier, the standards of baby feeding bottles in India were brought under Section 11(2) of Infant Milk Substitutes, Feeding Bottle and Infant Foods (Regulation of Production, Supply and Distribution) Act, 1992 later amended in 2003 as The Infant Milk Substitute, Feeding Bottles and Infant Foods (Regulation of Production, Supply and Distribution) Amendment Act, 2003 [Section 2(c)]. No standards on amounts of BPA have been stated in these amendments. As a growing concern, based on several publications from various countries, there was a draft designed by Bureau of Indian Standards (BIS) to restrict the use of BPA in baby feeding bottles in 2013 (ref. 77). Neither has the draft been published nor any legal action proposed or imposed by the Indian Government.

Summary

Though a number of researchers have worked on the endocrine disrupting effects of BPA, they are unable to conclude whether this compound is likely to affect health or not. Initiatives have been taken by key organizations like WHO, EFSA, UFDA and USEPA, in monitoring research outcomes, formulating regulatory policies on the use of BPA in food-contact plastics. The USFDA is the only organization convinced that the compound is safe to use in plastic containers while others are still uncertain. The USFDA observed that the level of migration is very minimal to cause any adverse effects. Interestingly in contrast to this opinion, EFSA had reduced the tolerable daily intake (TDI) to 4 μg/kg bw from a previously set value of 50 μg/kg bw in 2006 and later revised as 5 μg/kg bw in 2014. This signifies that BPA is a compound of concern with health risks even at lower concentrations as evidenced by available research outcomes.

It is essential that extensive studies are conducted to clarify discrepancies on the low-dose effects and toxic effects across the species level. Further, the exposure risks to pregnant women also needs to be evaluated, because this compound can have effects on the developing foetus too. It is also important to note that no safer BPA-alternatives have been identified. The chief alternatives like BPF and BPS are also found to cause endocrine disrupting effects similar to that of BPA. Hence, it is not wise to use alternatives without knowing their adverse effects. So far, about 40 countries have restricted the use of BPA in food-contact plastics, especially intended for young children. Considering the potential endocrine disrupting effects, the government and regulatory agencies of developing countries like India – with high population and large plastic consumers – may come forward to restrict the use of BPA and related compounds in the manufacture of food-contact plastics and packaging materials. This could minimize health risks posed by BPA. Nevertheless, directions on the use of plastics, awareness on its

negative impacts and interim guidelines on the use of safe alternatives must be provided, with an intention to ensures the safety of vulnerable populations such as infants, children and pregnant women in specific.

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