Breast Cancer UK
Prevent the preventable

BCUK Background Briefing | BPA

What is Bisphenol A?

Bisphenol A (BPA) is a synthetic chemical first synthesised in 1891. The chemical structure of BPA shows similarity to that of Diethylstilboestrol (DES) (1), formerly used as a drug to treat women with gynaecological problems and to help prevent miscarriage. DES is now classified as a group I carcinogen by the International Association for Research on Cancer (IARC).

BPA was identified as being an artificial oestrogen as early as 1930 (2). Use of BPA for plastics production was not identified until after World War One, when it was found to react with phosgene and yield a clear, hard plastic polycarbonate.

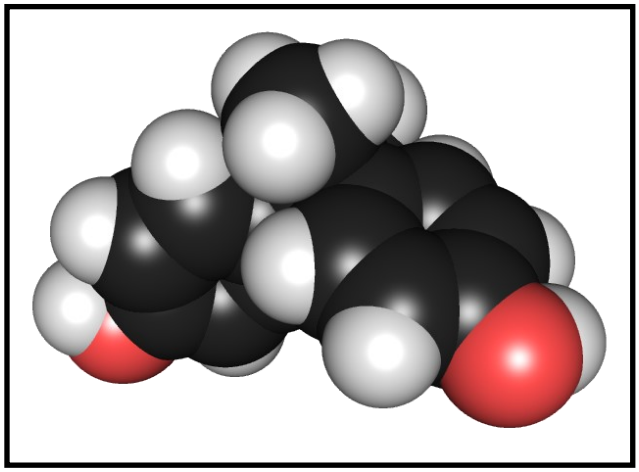
Over 3 billion kilograms of BPA are produced each year and it is estimated to be worth nearly £340,000 an hour to the global economy (3). The production of BPA has increased by 500% in the last three decades and continues to rise.

Where is it found?

BPA is used in polycarbonate plastic food and drink packaging and in epoxy resins that line some metal cans of food and drink. BPA is also used as an additive in polyvinyl chloride (PVC) plastics. It is found in CDs, mobile phone and computer casings, glasses, dental sealants, medical devices (4) and thermal till receipts.

Why should we be concerned?

BPA is able to migrate. It can rub off onto hands,



3D Chemical Structure of BPA

leach into food and drink contents (5) and is absorbed through the skin. This is because the chemical bonds between the monomers, or individual chemicals within articles or products in which BPA is used, are not stable.

Exposure to ultra-violet light, high temperatures (such as those used in sterilisation processes), or to acidic conditions (for example, in a can of tinned tomatoes), will increase leaching.

BPA is ubiquitous. It is found all over the planet in ecosystems and wildlife (6). It is estimated to be present in more than 93% of the adult population (7) and has been found in human urine samples (8), human serum (9), sweat (10), placental tissue (11), ovarian follicular fluid. Furthermore, evidence suggests it accumulates over time in human amniotic fluid (12). It has also been found in human breast milk (13), which confirms its presence in the breast, and at even higher levels in liver, brain and human adipose (fat) tissue (14).

Breast Cancer UK
Prevent the preventable

BCUK Background Briefing | BPA

There is sufficient evidence to suggest that dietary exposure is the main route of human exposure to BPA, along with regular contact with thermal receipt paper (15).

Whilst proponents of BPA claim that it is safe to use because human levels of exposure are low, evidence suggests that BPA is harmful even at very low levels of exposure (16, 17). BPA gives rise to 'non monotonic' dose responses, which means that it has varying effects at different doses, and so a low dose may be more harmful than a higher one. Therefore, the application of so-called Tolerable Daily Intakes (TDIs) (18) of BPA, which have been predicted from higher doses to permit its continued use in everyday products may well be unsafe for the consumer.

How is BPA linked with breast cancer?

There is a significant amount of scientific evidence that shows even low level exposure BPA has an adverse effect on the development of breast tissue. Laboratory experiments show that BPA has the ability to transform normal breast cells into cells of a more cancerous or overall malignant nature (19, 20, 21). Animal studies show that exposure to BPA in the womb, or during early life, can increase breast density, cell growth and increase susceptibility to tumours (22, 23, 24, 25, 26, 27). BPA has also been found to trigger DNA strand breaks, to interfere with cell division (28, 29) and with chemotherapy, making it less effective against breast cancers (30).

Plastic feeding utensils may contain BPA

Like DES, BPA is a synthetic oestrogen and is able to bind to oestrogen receptors both within and on the cell surface. BPA is therefore able to influence how genes and cells behave. Mammary tissues are primed to respond to the presence of oestrogen in order to develop and grow and, therefore, bind easily to BPA.

Links to other diseases

As well as being linked to breast cancer, BPA is also linked to a range of other conditions including obesity (31), heart disease and cardiovascular problems (32, 33), infertility (34), diabetes (35) and recurrent miscarriage (36).

What is the current regulatory position on BPA?

The European Commission decided to ban the use of BPA in baby bottles in March 2011 (37), because of concerns about the adverse effect of BPA on human health. It continues to be used,

BCUK Background Briefing | BPA

France took unilateral action in December 2012 to ban the use of BPA in food and drinks packaging and in thermal receipt paper (38). The ban which came into force in January 2015 has since been partially overturned by the country's courts (39). Sweden, Denmark and Belgium have all taken measures to reduce the use of BPA in products marketed at children under three years old. The European Commission member state REACH Committee is due to consider a proposed restriction on the placing on the market of thermal paper containing BPA. The EC is currently considering whether BPA should be permitted in food packaging.

The European Food Safety Authority's (EFSA) most recent review of BPA exposure and toxicity concluded that "BPA poses no health risk to consumers of any age group (including unborn children, infants and adolescents) at current exposure levels", but acknowledged that high levels of exposure may adversely affect the kidney, liver and mammary gland, and recommended the TDI be reduced from 50 µg/kg of bw/day to 4 µg/kg of bw/day (40). They also stated that there are "remaining uncertainties about BPA's toxic effects" and a further re-evaluation will be carried out when the results of long-term research by the US National Toxicology Program are available for evaluation in one or two years.

In February 2016, the European Commission and member states agreed to classify BPA as a category 1B presumed reproductive toxicant (41), meaning it is a substance which can adversely affect the human reproductive system. The EC Committee's decision follows that of the state of California, which last year added BPA to its proposition 65 list of chemicals that are known to cause cancer, birth defects or other reproductive harm (42). The new EU classification is important as it supports a proposal by the French REACH authority to classify BPA as a substance of very high concern (SVHC), according to REACH Article 57(a) (43). Listing of a substance as an SVHC is the first step in the procedure for restriction of its use and results in more stringent regulatory measures. There would also be an obligation to implement stronger preventative measures for professional use, principally by using substitutes.

What is Breast Cancer UK's position?

Breast Cancer UK submitted evidence to EFSA's consultations on BPA, expressing concern that studies relating to low dose exposures had been dismissed (Read Breast Cancer UK's submission to Part 1 and submission to Part 2); to the European Commission's roadmap on new measures for use of BPA in food packaging material (link to submission); and to the draft opinion of the Committee for Socio-economic Analysis proposing restrictions on the use of BPA in thermal paper (link to submission); and to the proposal to identify BPA as an SVHC owing to its classification in the hazard class reproductive toxicant (category 1B) (link to submission).

Breast Cancer UK
Prevent the preventable

BCUK Background Briefing | BPA

Breast Cancer UK position

What is Breast Cancer UK's position?

- Breast Cancer UK submitted evidence to both of EFSA's consultations on BPA, expressing concern that studies relating to low dose exposures had been dismissed (Read Breast Cancer UK's submission to Part 1 and submission to Part 2);
- Breast Cancer UK continue to call for a ban on the use of BPA in food and drinks packaging on the basis that studies show that low dose exposures to BPA have been shown to have an adverse effect on the developing mammary gland;
- Breast Cancer UK believe that BPA should be prohibited from use in all articles intended to come in to contact with food and drink, and that it should be replaced with safer alternatives;
- Breast Cancer UK believe that BPA should also be prohibited from use in till and other printed receipt papers;
- Breast Cancer UK believe that the use of BPA should be prohibited in any products intended for children under three years old and should be replaced with safer alternatives.

Information last reviewed: October 21, 2016

References

1. Rubin., B.A. & Soto., A. (2009) 'Bisphenol A: Perinatal exposure and body weight' Mol Cell Endocrinol. 2009 May 25; 304(1-2): 55. Published online 2009 Mar 9. doi: 10.1016/j.mce.2009.02.023
2. Dodds E. C. Lawson W. Synthetic estrogenic agents without the phenanthrene nucleus. Nature. 1936;137:996.
3. Melzer, D. a. G., T. (2010). 'Bisphenol A is everywhere – is it safe?' New Scientist 2783: 26-27.(Link to extract)
4. For example: auto-transfusion; apparatus; filters; bypasses; tubing; pumps; instruments; surgical equipment; blood pathway circuits; and, respiratory tubing circuits. These products are used on all types of patients e.g. adults, children etc.
5. Brotons, J. A., M. F. Olea-Serrano, et al. (1995). 'Xenoestrogens released from lacquer coatings in food cans.' Environ Health Perspect 103(6): 608-612.
6. Corrales, J. et al. (2015). Global Assessment of Bisphenol A in the Environment: Review and Analysis of Its Occurrence and Bioaccumulation. Dose-Response An International Journal 13(3): 1-29.
7. Shankar, A., and Teppala, Srinivas (2012). 'Urinary Bisphenol A and Hypertension in a Multiethnic sample of US Adults.' Journal of Environmental and Public Health 2012: 5; Shankar, A., S. Teppala, et al. (2012). 'Bisphenol A and Peripheral Arterial Disease: Results from the NHANES.' Environ Health Perspect; Shankar, A., S. Teppala, et al. (2012). 'Urinary Bisphenol A Levels and Measures of Obesity: Results from the National Health and Nutrition Examination Survey 2003-2008.' ISRN Endocrinol 2012: 965243;Shankar, A. Teppala, S. (2011). 'Relationship between urinary bisphenol A levels and diabetes mellitus.' J Clin Endocrinol Metab 96(12): 3822-3826.
8. Calafat, A. M., Zsuzsanna Kuklenyik, et al. (2005). 'Urinary Concentrations of Bisphenol A and 4-Nonylphenol in a Human Reference Population.' Environmental Health Perspectives 113: 391-395.
9. Takeuchi, T. and O. Tsutsumi (2002). 'Serum Bisphenol A concentrations showed gender differences, possibly linked to androgen levels.' Biochem. Biophys. Res. Commun. 291: 76-78. (Link to Abstract)
10. Genuis, S. J., S. Beesoon, et al. (2012). 'Human excretion of bisphenol A: blood, urine, and sweat (BUS) study.' J Environ Public Health2012: 185731.
11. Schonfelder, G., B. Flick, et al. (2002). 'In Utero exposure to low doses of bisphenol A lead to long term deleterious effects in the vagina.' Neoplasia 4: 98-102.
12. Ikezuki, Y., T. Osamu, et al. (2002). 'Determination of bisphenol A concentrations in human biological fluids reveals significant early prenatal exposure.' Human Reproduction 17(11): 2839-2841. (Link to Abstract)
13. Sun, Y., M. Irie, et al. (2004). 'Determination of bisphenol A in human breast milk by HPLC with column-switching and fluorescence detection.' Biomedical Chromatography 18(8): 501-507. (Link to Abstract)
14. Fernandez, M. F., J. P. Arrebola, et al. (2007). 'Bisphenol-A and chlorinated derivatives in adipose tissue of women.' Reprod Toxicol 24(2): 259-264. (Link to Abstract)
15. European Food Safety Authority (2013). DRAFT Scientific Opinion on the risks to public health related to the presence of bisphenol A (BPA) in foodstuffs – Part: exposure assessment 1: http://www.efsa.europa.eu/en/consultations/call/130725.htm.
16. Vandenberg, L. N., T. Colborn, et al. (2012). 'Hormones and endocrine-disrupting chemicals: low-dose effects and nonmonotonic dose responses.' Endocr Rev 33(3): 378-455.(Link to Abstract).
17. Jenkins, S., J. Wang, et al. (2011). 'Chronic oral exposure to bisphenol A results in a nonmonotonic dose response in mammary carcinogenesis and metastasis in MMTV-erbB2 mice.' Environ Health Perspect 119(11): 1604-1609.
18. TDI is an estimate of the amount of a substance expressed on a body weight basis, which can be ingested daily over a lifetime without appreciable risk.
19. Fernandez, M. F., J. P. Arrebola, et al. (2007). 'Bisphenol-A and chlorinated derivatives in adipose tissue of women.' Reprod Toxicol 24(2): 259-264. (Link to Abstract)
20. Fernandez, S, V et al. (2012). 'Expression and DNA methylation changes in human breast epithelial cells after bisphenol A (BPA) exposure. Int J Oncol. 2012 July; 41(1): 369–377. Published online 2012 April 20. doi:10.3892/ijo.2012.1444

References

.

21. Goodson, W. H., 3rd, M. G. Luciani, et al. (2011). 'Activation of the mTOR pathway by low levels of xenoestrogens in breast epithelial cells from high-risk women.' Carcinogenesis 32(11): 1724-1733.
22. Tharp, A. P., M. V. Maffini, et al. (2012). 'Bisphenol A alters the development of the rhesus monkey mammary gland.' Proc Natl Acad Sci U S A 109(21): 8190-8195.
23. Jenkins, et al. (2012). 'Endocrine-active chemicals in mammary cancer causation and prevention.' Steroid Biochem Mol Biol.
24. Durando et al. (2011). 'Prenatal exposure to bisphenol A promotes angiogenesis and alters steroid-mediated responses in the mammary glands of cycling rats.' J Steroid Biochem Mol Biol. 2011 Oct; 127(1-2):35-43. Epub 2011 Apr 14. (Link to Abstract)
25. Markey, C. M., E. H. Luque, et al. (2001). 'In Utero Exposure to Bisphenol A Alters the Development and Tissue Organization of the Mouse Mammary Gland.' Biology of Reproduction 65: 1215-1223.
26. Soto, A. M., Vandenberg, L.N., Maffini, M.V., Sonnenschein, C. (2008). 'Does breast cancer start in the womb?' Basic Clin Pharmacol Toxicol 102(2): 125-133. (Link to Abstract)
27. Jenkins, S., J. Wang, et al. (2011). 'Chronic oral exposure to bisphenol A results in a nonmonotonic dose response in mammary carcinogenesis and metastasis in MMTV-erbB2 mice.' Environ Health Perspect 119(11): 1604-1609; Jenkins, et al. (2012). 'Endocrine-active chemicals in mammary cancer causation and prevention.' Steroid Biochem Mol Biol.)129(3-5):191-200.
28. Iso, T. T. Watanabe, et al. (2006). 'DNA damage caused by bisphenol A and estradiol through estrogenic activity.' Biol Pharm Bull 29(2): 206-210. (Link to Abstract)
29. George, O., B. K. Bryant, et al. (2008). 'Bisphenol A directly targets tubulin to disrupt spindle organisation in embryonic and somatic cells.' ASC Chemical Biology.
30. LaPensee, E. W., C. R. LaPensee, et al. (2010). 'Bisphenol A and estradiol are equipotent in antagonizing cisplatin-induced cytotoxicity in breast cancer cells.' Cancer Lett 290(2): 167-173.
31. Shankar, A. and Teppala, Srinivas. (2012). 'Urinary Bisphenol A and Hypertension in a Multiethnic sample of US Adults.' Journal of Environmental and Public Health 2012: 5.
32. Melzer, D., N. J. Osborne, et al. (2012). 'Urinary bisphenol A concentration and risk of future coronary artery disease in apparently healthy men and women.' Circulation 125(12): 1482-1490.
33. Shankar, A., S. Teppala, et al. (2012). 'Bisphenol A and Peripheral Arterial Disease: Results from the NHANES.' Environ Health Perspect.120(9): 1297–1300
34. Salian, S., Doshi, T. and Vanage G. (2011). 'Perinatal exposure of rats to Bisphenol A affects fertility of male offspring--an overview.' Reprod Toxicol 3: 359-362.(Link to Abstract)
35. Shankar, A. a. T., S. (2011). 'Relationship between urinary bisphenol A levels and diabetes mellitus.' J Clin Endocrinol Metab 96(12): 3822-3826.
36. Mayumi, S.-O., Yasuhiko, Ozaki., Shin-ichi, Sonta., Tsunehisa, Makino., and Kaoru, Suzumori. (2005). 'Exposure to bisphenol A is associated with recurrent miscarriage.' Human Reproduction 20(8): 2325-232. https://www.scribd.com/document/43416742/Exposure-to-Bisphenol-a-is-Associated-With-Recurrent-Miscarriage
37. European Commission (2011) 'Ban of Bisphenol A in baby bottle' Health & Consumer Voice - March - 2011 Edition. http://ec.europa.eu/dgs/health_consumer/dyna/consumervoice/create_cv.cfm?cv_id=716.
38. The French law can be read here
39. Robert, A. (2015). France overturns ban on BPA in export products. EurActive France; published September 30, 2015. https://www.euractiv.com/section/science-policymaking/news/france-overturns-ban-on-bpa-in-export-products/ (accessed March 29, 2016).
40. EFSA (2015). European Food Safety Authority. No consumer health risk from bisphenol A exposure' exposure January 21 press release. http://www.efsa.europa.eu/en/press/news/150121 (accessed March 29, 2016)
41. ENDs Europe (2016). BPA toxicity classification strengthened. http://www.endseurope.com/search?tag=112,41&type=1,3,4,5&start=31 (accessed March 29, 2016).
42. OEHHA (2015). Changes to Proposition 65 list. Bisphenol A listed as known to the State of California to cause Reproductive toxicity, Effective May 11, 2015. http://oehha.ca.gov/prop65/CRNR_notices/list_changes/051115listBPA.html (accessed March 29, 2016).
43. ECHA (2016). European Chemicals Agency. Current SVHC intentions. http://echa.europa.eu/web/guest/registry-of-current-svhc-intentions (accessed March 29, 2016).