

## Ministerial Briefing: Flame Retardants in the UK

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### Conventional or typical BFRs

In the United Kingdom, until recently, the most commonly used brominated flame retardants (BFRs) were polybrominated diphenyl ethers (PBDEs), hexabromocyclododecanes (HBCD) and tetrabromobisphenol A (TBBPA)<sup>i</sup>. These “typical BFRs” are **persistent, bioaccumulating and toxic**<sup>ii</sup>. They are widespread in human and wild-life populations. Concentrations are generally **higher in children** (likely due to intake from breastfeeding and dust), where adverse effects are more pronounced (e.g. reference <sup>iii</sup>). Dietary intake and to a lesser extent house dust are the main sources of adult exposure to PBDEs. Due to **neurotoxic and endocrine disrupting effects**, the manufacture of PBDEs was banned or phased out in Europe and the US, between 2002-2013. This has reduced levels of PBDEs in European populations<sup>iv</sup>. Use of HBCD in the UK now requires authorisation<sup>v</sup>.

PBDEs and HBCD are **endocrine disruptors** which mainly **affect thyroid hormones** and may be associated with thyroid disorders<sup>vi</sup>. PBDE exposure has been linked to **autistic behaviour**<sup>vii</sup> in children. Prenatal exposure to PBDEs may result in **neuro-developmental problems**<sup>viii</sup>. Animal studies have shown PBDEs increase thyroid stimulating hormone levels in offspring. *in utero* exposure to an environmentally relevant mixture of HBCD and PBDEs may cause **developmental abnormalities** in offspring (e.g. abnormal number of digits)<sup>ix</sup>. PBDEs also disrupt androgens, progestins and oestrogens.

TBBPA [currently, the most widely used flame retardant]<sup>x</sup> and tetrachlorobisphenol A (TCBPA), are endocrine disruptors and act as thyroid hormone antagonists<sup>xi</sup>. TBBPA can **cause cancers** of the uterus in female rats and of the liver in male mice<sup>xii</sup>.

### Novel BFRs, emerging BFRs and other replacement FRs

Replacement or “novel BFRs” and “emerging BFRs” are likely to be as harmful as conventional ones. Novel BFRs have not yet been identified in food or animals, whereas emerging ones have. In Europe, replacement flame retardants widely used include organophosphate flame retardants, such as tris (1,3-dichloroisopropyl) phosphate (TDCPP) [used e.g. in polyurethane foams for furniture], triphenyl phosphate (TPP) [used, e.g. in synthetic resins] and the BFR, 2,2-Bis(bromomethyl)-1,3-propanediol (BBMP) [used e.g. in resins, plastic polymers, and rigid polyurethane foams]. TDCPP can **accumulate in human tissues and fluids** (e.g. adipose, breast milk) and its metabolite has been detected in urine<sup>xiii</sup>. TDCPP caused an **increased incidence of tumours in liver, kidney and testes** in rodents<sup>xiv</sup>. is genotoxic, and listed as a **human carcinogen** under California’s Proposition 65. *in vitro* and animal data have linked TDCPP to neurotoxicity and endocrine disruption<sup>xv</sup>. BBMP is also **carcinogenic** in rodent studies and **anticipated to be a human carcinogen**<sup>xvi</sup>. The chlorinated flame retardant, tris(2-chloroethyl) phosphate (TCEP) induces **kidney tumours** in rats and mice and is also listed under Proposition 65. TCEP and TPP induce oxidative stress and endocrine disruption in mice, which affects male reproductive development<sup>xvii</sup>.

## Flame Retardants and Breast Cancers

There is no direct evidence flame retardants increase breast cancer risk in humans, although many are **Endocrine Disrupting Chemicals** (EDCs), some act as **oestrogen mimics** or affect oestrogen metabolism and some have been shown to increase incidence of **mammary tumours** in rodents.

Tissue culture studies have shown PBDEs increase (normal) breast cell proliferation and induce **anti-apoptotic effects** (prevent programmed cell death) in the presence of oestrogen<sup>xviii</sup>. PBDEs have also been shown to increase proliferation and induce anti-apoptotic effects in breast cancer cells<sup>xix</sup>. The same study showed that PBDE-209 was able to **counteract the anti-cancer effects of tamoxifen**. HBCD, but not TBBPA, was found to be oestrogenic in E-Screen assays<sup>xx</sup>. Although TBBPA doesn't bind to oestrogen receptors, it can bind and inhibit a key oestrogen-metabolising enzyme (oestrogen sulfotransferase). Inhibiting this enzyme would cause an increase in levels of circulating oestrogens (as oestrogen sulfotransferase results in loss of binding of oestrogen to its receptor as well as increased oestrogen renal excretion)<sup>xxi</sup> potentially causing endocrine disruption which **may lead to increased breast cancer risk**.

There is limited data on breast cancer risk or oestrogenicity of replacement BFRs. However, some data based on animal and in vitro studies suggest some replacement BFRs or their metabolites may increase breast cancer risk. BBMP and a TDBPP metabolite, 2,3-dibromo-1-propanol (1,3-DCP), have been shown to increase mammary gland (and other) tumours in rodents<sup>xxii</sup>. 3-MCPD (a metabolite of 1,3-DCP, and so TDCPP), was also found to induce tumours in rat mammary glands. 3-MCPD is genotoxic in in vitro assays<sup>xxiii</sup>.

<sup>i</sup> Brinbaum L. S. and Staskal D. F. (2004) *Environmental Health Perspectives* 112: 9-17

<sup>ii</sup> Law et al. (2014) *Environmental International* 65: 147-158

<sup>iii</sup> Kim et al. (2014) *Chemosphere* 106: 1-19

<sup>iv</sup> Law et al. (2014) *op cit*

<sup>v</sup> Note: an exemption is for use in expanded and extruded polystyrene

<sup>vi</sup> Lyche et al. (2015) *Environment International* 74: 170-180

<sup>vii</sup> Braun et al. (2014) *Environmental Health Perspectives* 122: 513-520

<sup>viii</sup> Ding et al. (2015) *Environmental Research* 142: 104-111

<sup>ix</sup> Berger et al. (2014) *Toxicology*, 320: 56-66

<sup>x</sup> Lyche et al. (2015) *op cit*

<sup>xi</sup> Sun et al. (2009) *Toxicology in Vitro* 23(5): 950-954

<sup>xii</sup> National Toxicology Program (2014) Technical report on the Toxicology studies of Tetrabromobisphenol A CAS NO. 79-94-7

<sup>xiii</sup> Rudel et al. (2014) *Environmental Health Perspectives* 122 (9) 881-895

<sup>xiv</sup> Faust, J. B. and August, L. M. (2011) Evidence on the Carcinogenicity of Tris(1,3-Dichloro-2-Propyl) Phosphate. Sacramento, CA: Reproductive and Cancer Hazard Assessment Branch, Office of Environmental Health Hazard Assessment, California Environmental Protection Agency.

<sup>xv</sup> Betts, K. S. (2015) *Environmental Health Perspectives* 123(2): A44

<sup>xvi</sup> National Toxicology Program (2014). Report on Carcinogens, Thirteenth Edition. Research Triangle Park, NC: U.S. Department of Health and Human Services, Public Health Service: 2,2-Bis(bromomethyl)-1,3-propanediol, CAS No. 3296-90-0

<sup>xvii</sup> Chen et al. (2015) *Environmental Toxicology and Pharmacology* 40(1): 310-318

<sup>xviii</sup> Kwiecińska et al. (2011) *Pharmacological Reports* 63(1): 189-9

<sup>xix</sup> Li et al. (2012) *Environmental Health Perspectives* 120(4): 541-546

<sup>xx</sup> Dorosh et al. (2011) *Folia Biologica* 57: 35-39

<sup>xxi</sup> Gosavi et al. (2013) *Environmental Health Perspectives* 121: 1194-1199

<sup>xxii</sup> National Toxicology Program (2014) *op cit*

<sup>xxiii</sup> Faust, J. B. and August, L. M. (2011) *op cit*