EVALUATION OF NEW SCIENTIFIC EVIDENCE CONCERNING THE RESTRICTIONS CONTAINED IN ANNEX XVII TO REGULATION (EC) NO 1907/2006 (REACH)

REVIEW OF NEW AVAILABLE INFORMATION FOR

benzyl butyl phthalate (BBP)

CAS No 85-68-7
EINECS No 201-622-7

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REVIEW REPORT

JULY 2010

1. Introduction

Entries 51 and 52 of Annex XVII to REACH include the restrictions on the placing on the market and use of certain phthalates in toys and childcare articles, as initially introduced by Directive 2005/84/EC of the European Parliament and of the Council of 14 December 2005. As explained in the recitals of this Directive, the six restricted phthalates were sorted into two groups associated with a different scope for the restriction. For BBP and the two other phthalates which are classified as reprotoxic, category 2 according to Council Directive 67/548/EEC[1] (i.e. DEHP[2] and DBP[3]) the restriction covers the placing on the market and use in any type of toys and childcare articles. For the three non-classified phthalates (i.e. DINP[4], DIDP[5] and DNOP[6]) the restriction covers the placing on the market and use in toys and childcare articles which can be placed in the mouth by children. In addition, and as explicitly mentioned in entries 51 and 52 of Annex XVII, the Commission was to evaluate the restrictions concerning these six phthalates in the light of new scientific information by 16 January 2010, and if justified, these restrictions shall be modified accordingly.
The European Commission requested ECHA to review the available new scientific information for these phthalates and to evaluate whether there is evidence that would justify a re-examination of the existing restrictions.
According to the work plan agreed between ECHA and the European Commission, this document provides ECHA's report on its review of the new available information related to BBP.

The new available information related to BBP is rather limited, in particular if compared to other restricted phthalates like DEHP or DINP. Within the information submitted by stakeholders to the European Commission or ECHA, there is only few information available on the possible current uses of BBP in EU, and no study specifically dedicated to the exposure to BBP and potential related risks. It is nevertheless worth noticing that new biomonitoring studies on phthalates in human body fluids as proxy to overall exposure are also reported, with a main focus on the presence of BBP and/or its metabolites in pregnant women or breast milk. The exposure at pre-natal stage appears indeed to be a potential human health concern. However, most of these reports do not bring enough conclusive information, in particular detailed exposure estimations, that could readily be used for updating the previous exposure and risk assessments. It has to be noted that, according to the agreed work plan, the information on hazard properties of BBP has not been reviewed at this stage.

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[1] Council Directive 67/548/EEC of 27 June 1967 on the approximation of laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances. According to the CLP Regulation (Regulation (EC) No 1272/2008 on the classification, labelling and packaging of substances and mixtures) these three phthalates are classified as Toxic to Reproduction, category 1B.

[2] bis (2-ethylhexyl) phthalate; CAS No 117-81-7 / Einecs No 204-211-0

[3] dibutyl phthalate; CAS No 84-74-2 / Einecs No 201-557-4

[4] di-'isononyl' phthalate; CAS No 28553-12-0 and 68515-48-0 / Einecs No 249-079-5 and 271-090-9

[5] di-'isodecyl' phthalate; CAS No 26761-40-0 and 68515-49-1 / Einecs No 247-977-1 and 271-091-4

[6] di-n-octyl phthalate; CAS No 117-84-0 / Einecs No 204-214-7

2. Information on uses of the substance

Note: BBP is a phase-in substance according to the definition 3(20) of the REACH Regulation. BBP being classified as category 1B reproductive toxicant according to Regulation (EC) 1272/2008 (CLP), it can reasonably be expected that one or more registration dossiers for BBP will be submitted to ECHA by 30 November 2010. These registration dossier(s) will include information of the uses of BBP, as well as most probably a Chemical Safety Report with information on the volumes relevant for each use.
To date, no registration dossier has been submitted to ECHA.

Total use of BBP:

After manufacturing, BBP is either processed, mainly as plasticiser in polymers and in particular in PVC for floorings, or formulated as component in preparations (e.g. printing inks, adhesives and sealants, paints). More than 70%[7] of BBP is used as a plasticiser in polymer products, mainly PVC for flooring applications; other uses in polymers are in coating of leather and textiles, in calendering of films (ECHA, 2009b) or for primary/immediate packaging of medicinal products and active substances (RCOM, 2009). Plasticisers have the function of improving the polymer material's flexibility and workability. BBP is one of a number of substances used as plasticiser in PVC and other polymer materials; according to Industry, BBP is however an unusual plasticiser because of its chemical asymmetry which results in unique performance properties (ECHA, 2009b). In particular, it is used by the flooring industry because it adds surface properties to flooring materials that minimise maintenance and give them a prolonged life (www.bbp-facts.com). It is worthwhile noticing that BBP when used as a plasticiser is not chemically bound in the matrix. When used in preparations, sealants, adhesives, paints, coatings and inks are the main products in which BBP is found (ECHA, 2009b). BBP is also used as analytical standard for test and measurement instruments (RCOM, 2009).

A recent publication by the Danish Environmental Protection Agency (Danish EPA) (Danish EPA, 2009) gives an overview of several previous surveys aiming at analysing the presence of BBP in different consumer products to which 2 year-old children may in particular be exposed. It confirms that, in 2002, and in addition to the specific uses which are further described in the following sections of this document (i.e. toys and childcare articles, school supplies, other articles for/in contact with children, medical devices, cosmetics), BBP was reported to be found in vinyl floorings, in concentrations up to 2%.

However, as a consequence of the harmonised classification and labelling of BBP (category 1B reproductive toxicant according to new CLP Regulation[8]) companies have moved to the use of alternatives (ECHA, 2009b). This can be illustrated by the fact that the total manufacturing of BBP at EU level decreased from 45,000

[7] Industry even indicates that more than 90% of BBP is used for plasticising PVC or other polymers (www.bbp-facts.com)

[8] Regulation (EC) No 1272/2008 on the classification, labelling and packaging of substances and mixtures

tonnes/year in EU-15 in 1994-1997 to less than ca. 20,000 in EU-25 in 2007. With EU exports counting for ca. 12,000 tonnes/year, the net use of BBP in EU was estimated at ca. 8,000 tonnes/year in 2007 (ECHA, 2009b).
Furthermore, as BBP is on the Candidate List and it may be included in Annex XIV of REACH, the overall trend of decreasing use of BBP which has been observed in the last years in EU will probably continue in the next years.

Use in toys and childcare articles:
The restrictions on the use of BBP in toys and childcare articles as introduced in REACH Annex XVII entry 51 should have led in EU to a halt in the selling of such BBP-containing articles as of 16 January 2007. However, there is no further available information on the compliance of producers and importers with this restriction and whether BBP is present in these categories of products as a result of non-compliance with the existing restriction.

The already mentioned survey and health assessment of the exposure of 2-year old children to chemical substances in consumer products (Danish EPA, 2009) indicates that BBP was reported to be found in plasticine in year 2002 at concentration of 3.7%, and in 2005 in the surface of a wooden toy (wooden fishing boat; no concentration available). However, it has to be noted that these observations were made before the entry into force of the obligation in the current restriction. In other words if concentrations of greater than 0.1 % by mass of the plasticised material are today found on the market it is a question of non-compliance and would require enforcement action.
In addition to a detailed screening of existing surveys, the study reports on analyses performed on a series of products to which children are highly susceptible to be exposed[9]; among these products were some childcare articles like pacifiers (including their coverage), non-slip figures and (bath/shower) mats, diapers and bed linen, and soft toys[10]. It appears that BBP was not found in any of the tested products which could be categorised as toys or childcare articles (Danish EPA, 2009).

Use in school supplies:
In the framework of this review, no new information on the possible use of BBP in school supplies was made available by stakeholders. In particular, the dedicated survey conducted for the Danish EPA on the presence of chemicals substances in school bags, toy bags, pencil cases and erasers (Force Technology, 2007) does not specifically address and report on the presence of BBP in these categories of products. However, it states that among all the school supplies which were analysed, mainly DEHP and DINP were found but no attempt was made to quantify the small content in other phthalates, such as BBP[11], which were detected.

[9] for each category of product (i.e. jackets, mittens, rubber clogs, rubber boots, pacifiers (including their coverage), soap packaging, non slip figures and (bath/shower) mats, soft toys, diapers, bed linen) five (5) products were analysed

[10] note that the toys and childcare articles listed here are covered by the current restriction

[11] note that BBP is not specifically mentioned in the report as another phthalate which could be one of the other phthalates that were identified in a preliminary screening

Use in articles for/in contact with children:
It is reported in the above mentioned Danish study that BBP was only found in some (children) clothes, in concentrations up to 2.2% (Source: Greenpeace – Toxic textiles by Disney, 2003), and on printings on shirts, in concentrations up to 0.15% (Danish EPA, 2009).
As already mentioned previously in this document, other products than toys and childcare articles to which children are nevertheless highly susceptible to be exposed, such as outdoor clothes (jackets and mittens), footwear (rubber clogs and rubber boots) and bath soap packaging, were specifically analysed. It appears that BBP was found in none of the tested products.

Use in medical devices:
In the framework of this review, no new information on the possible use of BBP in medical devices was made available by stakeholders.

Use in cosmetic products:
In the framework of this review, no information on the possible use of BBP in cosmetics products was made available by stakeholders.
However, it has to be noted that since 22 November 2006 cosmetic products containing BBP shall not be supplied to consumers in the EU, in accordance with Commission Directive 2005/80/EC of 21 November 2005 amending Council Directive 76/768/EEC concerning cosmetic products.

3. Information on exposure and related risk

3.1. General population - Overall exposure

Several recent studies based on new biomonitoring data confirm the exposure of the general population to BBP, covering several countries all over the world, including the EU. In these studies primary and secondary metabolites of BBP were indeed measured in several body fluids (urine, breast milk, saliva and serum) of different samples of the general population. Metabolites of BBP were for instance found in 43.5% of the breast milk samples from a total of 62 women in southern Italy (Latini G *et al*., 2009), as well as in Finnish and Danish cohorts' breast milk (Main KM *et al*, 2006). BBP metabolites were also reported in urinary samples of pregnant women in Israel (Berman T *et al*, 2008) and Mexico (Meeker JD *et al*, 2008). In Germany, the regular measurement of the concentration of BBP metabolites in urinary samples from adult subjects allowed to estimate the median daily intake of BBP of the general population at ca. 0.2 µg/kg bw/day as of 1998 (Wittassek M *et al*, 2007). If compared to the lowest NOAEL of 50 mg/kg bw/day selected in the EU Risk Assessment Report (EU RAR)[12], this estimation would lead to a sufficient margin of safety (250,000, i.e. well above 100) and would not indicate health concerns, even though it appears that 2% of the subjects were still presenting in 2003. Furthermore, on the basis of the results of a study led in 2005 in the United States in which the level of phthalates' metabolites in urinary samples of pregnant women were measured, it was estimated (modelling calculations) that the daily exposure to BBP of this sample of the general population was 2.47 µg/kg bw/day (95^{th} percentile), with peak values up to 15.53 µg/kg bw/day (Marsee K. *et al*, 2006). Compared to the above mentioned NOAEL, this would lead to a sufficient margin of safety (> 500). It was not possible to conclude in the framework of this review if these findings would still be applicable to the current situation within EU countries.

3.2. Occupational exposure

In the framework of this review, no information on occupational exposure to and related risks for workers from BBP was made available.

3.3. Children's exposure

In the following sections, an overview of the new available information, as well as a comparative analysis with the information contained in the EU RAR (where possible) are given for each of the main categories of known contributors to the exposure of children to BBP. Finally, available estimations of the overall exposure and related risks are discussed.

[12] for developmental toxicity in offspring (in rats); note that the EU RAR also selected a NOAEL of 100 mg/kg bw/day for fertility (in rats) and a NOAEL of 151 mg/kg bw/day for repeated dose toxicity

a) Exposure and risks from toys and childcare articles

As already mentioned above, although restrictions on the use of BBP in toys and childcare articles as introduced in REACH, Annex XVII, entry 51 should have led in the EU to a halt in the selling of these BBP-containing articles as of 16 January 2007, there is no further information available on the compliance of producers and importers with this restriction, and whether BBP is still present in these categories of products as a result of non-compliance with the existing restriction.
From the available information, there is no new data and/or estimation of the potential exposure and risks from toys and childcare articles which would be applicable to the sub-population of children as a whole. However, in their survey and health assessment of the exposure of the particular sub-group of 2-year old children (Danish EPA, 2009), the Danish authorities made an estimation of the possible exposures and risks from toys[13]. The calculations did not include the potential contribution of plasticine since the only migration values available for this product were for release to the indoor air, and not to sweat (or saliva) as usually considered for toys and childcare articles as the main vector of human exposure. Therefore, taking into account exposure through both the oral (3 h/day) and dermal (9 h/day) routes and a migration value of 1.3 mg/kg (over a period of 1 hour) for the only remaining toy product in which BBP was detected in an earlier survey (wooden toys), the daily exposure is estimated to be 4.17 µg/kg bw/day, leading to a margin of safety of ca. 12,000 if compared to the NOAEL of 50 mg/kg bw/day used in the EU RAR.

b) Exposure and risks from the use in school supplies

As already mentioned under a previous section of this document (see "*2. Information on uses of the substance / Use in school supplies*") the only available information submitted in the framework of this review (Force Technology, 2007) does not provide any values for the potential concentration in BBP of these categories of products. However, it states that among all the school supplies which were analysed the content in other phthalates than DEHP and DINP was low. Therefore, it can reasonably be expected that the likelihood to find BBP in school supplies at concentration levels which could lead to substantial exposures and raise human health concerns is low. In their updated health assessment of the exposure of the particular sub-group of 2-year old children to DBP (Danish EPA, 2009), the Danish authorities did not include the potential contribution of these products in their calculation of the overall exposure to DBP and related risks.

c) Exposure and risks from other sources

There appears to be no new available information related to exposures and risks from other sources of BBP, and more generally to overall exposures and risks, which would be applicable to the sub-population of children as a whole. However, in their new health risk assessment for the particular sub-group of 2-year old children (Danish EPA, 2009), the Danish authorities developed an updated estimation of the overall exposure to BBP, but also included updated estimations for the specific contributions of indoor climate (dust and air), food, toys, and other consumer products such as

[13] no updated estimations were conducted for childcare articles since the presence of BBP in this sub-category of products was reported in none of the studies used in the framework of the Danish report

clothes. This section presents the results and conclusions of this study with regard to all the potential sources which have not been discussed otherwise in the previous specific sections of this document (i.e. toys and childcare articles, and school supplies). The estimation of the total combined exposure will then be discussed in the next section.

With regard to indoor climate (air and dust), the updated risk assessment estimates the daily ingestion of DBP (95th percentile) to be between 5.23 µg/kg bw/day[14] and 10.36 µg/kg bw/day[15], depending on whether a summer (50 mg of dust ingested on a daily basis) or a winter (100 mg of dust ingested on a daily basis) scenario is used. Although it was not explicitly mentioned in the report, it is assumed that exposure to BBP from vinyl floorings is already included in these estimations, as it was the case for updated calculations for DBP. If compared to the NOAEL of 50 mg/kg bw/day used in the EU RAR, the associated margin of safety is ca. 4,800 or more. Therefore, it can be concluded that the exposure to DBP from indoor climate does not as such constitute a health risk for 2-year old children.

For exposure to BBP from food, the updated exposure estimations suggest to use a worst-case value of 9 µg/kg bw/day (from EFSA (2005a) as cited in Danish EPA, 2009). It can be concluded that this updated estimation is higher but still in the same order of magnitude as the estimated average intake of 0.02 mg BBP/day via diet for general population, leading to an intake of 1.3 µg/kg bw/day for a 15.2-kg[16] child, as was estimated in the EU RAR (EU RAR, 2007). These figures confirm that food is (one of) the major contributor(s) to the overall exposure of children to DBP. All these estimations would nevertheless lead to a margin of safety of ca. 5,500 if compared to the NOAEL of 50 mg/kg bw/day used in the EU RAR, and therefore to the confirmation that exposure to BBP from food does not raise health concerns as such.

As far as the other articles which were investigated in the framework of the Danish study are concerned, it appeared from the screening of previous studies that no migration estimations were available for (children) clothes and printings on shirts, which were the only items reported to contain BBP. Therefore, no exposure and related risks estimations were performed and the potential contribution of these (categories of) products could not be included in the updated health risk assessment.

d) Overall exposure and risks

There is no new estimation of the overall exposure to BBP and related risks available which would be applicable to the sub-population of children as a whole. The survey and health assessment of the exposure of 2 year-old children to chemical substances in consumer products (Danish EPA, 2009) gives nevertheless an updated estimation of the combined exposure to BBP of this particular sub-group of the general population which can be expected to give a general trend for children in general. On the basis of the specific exposure estimations as described in the previous paragraphs of this document, the maximum daily intake - including contributions from food, indoor

[14] 50th percentile: 1.18 µg/kg bw/day

[15] 50th percentile: 2.27 µg/kg bw/day

[16] average weight used for a 2-year old child in the Danish study (Danish EPA, 2009)

climate and toys - for 2-year old children in BBP is estimated at 18.4 µg/kg bw/day in summer and 23.21 µg/kg bw/day in winter. If compared to a NOAEL of 50 mg/kg bw/day[17], these total exposure estimations would lead to margins of safety of ca. 2,700 and 2,150 for summer and winter scenarios respectively, and to the general conclusion that the actual total exposure of 2-year old children to BBP should not raise any human health concerns. Moreover, it has to be noted that these updated combined exposure estimations have been calculated by adding all the available worst-case scenario values, and in particular for the two main contributors which are food and indoor climate (95th percentile). In the EU RAR for DEHP[18], it is stated that "*it is generally difficult to quantitatively assess combined exposure, as addition of several reasonable worst-case values (e.g. 95th percentile exposure values) could lead to a rather unrealistic sum, because it is perhaps not that likely that an individual belongs to the 5% most highly exposed individuals for all different exposure routes/sources*".

Furthermore, in addition to updated substance-specific risk assessments for individual chemicals, the Danish report proposes cumulative Risk Characterisation Ratios for several substances which have been grouped as anti-androgenic substances by the Danish authorities, oestrogen like substances and substances that may have both effects. Different ratios have been calculated for winter and summer scenarios, taking into account the total chemical burden via the following routes[19]:

- ingestion of food,
- ingestion of dust (50 mg in summer / 100 mg in winter),
- dermal contact with toys (9 hours in summer / 6 hours in winter),
- contact with other objects than toys, i.e. moisturising cream, bath articles and other textiles than winter clothing,
- contact with sunscreen lotion (summer only),
- contact with rubber clogs (summer only),
- contact with jackets/mittens (winter only).

As already mentioned in this document, BBP has been considered by the Danish authorities as an anti-androgenic substance with a proposed NOAEL of 50 mg/kg bw/day, on the basis of the same study as was used in the EU RAR to determine a NOAEL of 50 mg/kg bw/day for development toxicity in offspring in rats.

Moreover, it has to be mentioned that over the last years particular attention has been paid to prenatal exposure of foetuses and on exposure of neonates/infants, in particular via breast feeding, and certain recent studies which were submitted in the framework of this review mention that foetal exposure may be a route of exposure of higher concern than post-natal exposure (Wittassek M *et al*, 2009; Meeker JD *et al*, 2008). In particular, an abstract of a pilot study was submitted in the framework of

[17] note that in their updated risk assessment for 2-year old children (Danish EPA, 2009) the Danish authorities also use a NOAEL of 50 mg/kg bw/day for antiandrogenic effects, based on the same study on reduced anogenital distance (AGD) in rat offspring exposed during pregnancy, as used in the EU RAR

[18] it is assumed here that this general statement also applies to BBP

[19] same as those considered in the substance specific assessments, e.g. for BBP

this review, indicating that metabolites of BBP were detected in 11 pairs of amniotic fluid and suggesting that BBP and its metabolites can reach the human foetus. No conclusions in terms of exposure and potential health effects and risks were nevertheless made available (Wittassek M *et al*, 2009).

4. Conclusions and suggestions for further action

In conclusion, BBP appears to be used in lower total volumes than those reported when the EU RAR was agreed. Moreover, from the available information, there is no evidence of any new significant uses of BBP if compared to those already identified in the EU RAR. The available information also appears to confirm that the major remaining contributors of children's exposure to BBP are food and indoor climate (air and dust). The abstract of a study which was made available in the framework of this review also confirms that the use of consumer products and different indoor sources dominate the exposure to BBP of the general population, including children (Wormuth M *et al*, 2006).

From a risk assessment developed by the Danish authorities for the specific sub-group of 2-year old children it appears that the current total exposure of 2-year old children to BBP should not raise any human health concerns. In particular, it appears that the exposure from toys and childcare articles is limited and therefore does not raise any concerns for human health; it can be assumed that the limitation of the occurrence of BBP in these categories of products has been achieved and maintained by the current restriction on the use of BBP in toys and childcare articles.

The available new information with regard to uses of and exposure to BBP is rather limited and does not bring a new perspective to the assessments which were carried out in the past and used as a basis for the current restrictions on BBP; no new risk assessment was submitted in the framework of this review which covers all potentially sensitive sub-populations (e.g. children) which were addressed in the EU RAR. Even though further information would be needed to confirm some assumptions made in the present review report and the conclusions on exposure levels arising from certain uses of BBP, ECHA considers that the new information which was made available in the framework of this review does not indicate the need for an urgent re-examination of the existing restriction on BBP.
Therefore, ECHA suggests to wait for the submission of the registration dossier(s) for BBP after which the Commission may decide whether specific aspects of these registration dossier(s) should be assessed to confirm or contest the conclusion of this review that there is no need to re-examine the current restriction. Furthermore, as BBP is already included in the Candidate List in accordance with Article 59 of the REACH Regulation, the notifications under Article 7(2) may bring further information on the presence of BBP in articles after June 2011. Moreover, in case BBP will be included in Annex XIV of REACH, the potential future applications for authorisation may further clarify the uses of BBP and possibilities to control their related risks.

It has also to be noted that the general topic of cumulative and/or synergistic effects of exposure to several chemicals, and in particular to several phthalates or other substances suspected to have endocrine disrupting effects, regularly appears through the documents which were under the scope of this review (e.g. in Borch *et al*, 2004; AFSSET, 2009; National Research Council, 2008, as cited in AFSSET, 2009; Ghisari & Bonefeld-Jorgensen, 2009; Tanida *et al*, 2009; Lottrup *et al*, 2006; Sharpe, 2008). It is suggested in some of these studies that, even though the exposure to individual phthalates may be not of concern for human health, except maybe for certain specific

sub-populations, it cannot be excluded that the total exposure to all phthalates or to a phthalate together with other chemicals could raise health concerns, and this issue should therefore be further investigated. Furthermore, in its opinion of 6 February 2008 (SCENIHR, 2008), SCENIHR states that "*Combined exposure of different population and subpopulation is possible and may occur at different times or together. Due to the wide use of DEHP in society humans may be exposed from many different sources and exposed to other phthalates as well. It is obvious that combined exposure to DEHP, DBP, BBP, DIBP, and DINP having the same mechanism of action may potentially cause at least an additive effect. Combined exposure to DEHP and DINP had showed an additive effect (Borch* et al. *2004)*". The survey and health assessment of the exposure of 2 year-olds children to chemical substances in consumer products which was recently published by the Danish authorities (Danish EPA, 2009) also considers a cumulative risk assessment of potential endocrine-like substances, including BBP (as well as other phthalates DEHP, DBP, DINP and DiBP). The assessment of the potential combined effect of exposure to different phthalates goes beyond the scope of this evaluation of new scientific evidence concerning the current restrictions on BBP. Moreover, in the context of the Council discussion on this subject[20] the Commission has indicated that it will review the existing legislation in terms of its suitability to assess the effects of combined exposure.

[20] information from the Danish delegation on "*Combination Effects of Chemicals – children exposed to multiple endocrine disrupters*" dealt under "other business" at the meeting of the Council (Environment) on 21 October 2009 (Doc. ref. 14420/09 ENV 674 CHIMIE 79)

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