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

bis (2-ethylhexyl) phthalate (DEHP)

CAS No 117-81-7
EINECS No 204-211-0

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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 DEHP and the two other phthalates which are classified as reprotoxic, category 2 according to Council Directive 67/548/EEC[1] (i.e. DBP[2] and BBP[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 DEHP.

Recent scientific studies related to (classified[7]) phthalates seem to have given main focus on DEHP.
Most of the new available information consists in report studies on the hazard properties of the substance; some of the available articles also report on concerns about potential long term health effects on children due to their exposure at foetal and/or neonatal stages. It has to be noted that, according to the agreed work plan, the information on hazard properties of DEHP has however not been reviewed at this stage.

Many 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 DEHP or its

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

[3] benzyl butyl phthalate; CAS No 85-68-7 / Einecs No 201-622-7

[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

[7] as category 1B reproductive toxicant according to Regulation (EC) 1272/2008 (CLP)

metabolites in pregnant women or breast milk. However, most of these reports do not bring enough conclusive information, in particular detailed exposure estimations, that could be readily used for updating the previous exposure and risk assessments. In many cases, the need for further studies is claimed in order to confirm the preliminary findings and get (better) estimations of the actual exposures and related level of risks.

Furthermore, the use of DEHP in specific applications has been further investigated over the last years, in particular with respect to exposure of specific sub-populations such as exposure of children to school supplies or other products such as clothes or shoes, and patients under medical treatment involving PVC-containing medical devices.

2. Information on uses of the substance

Note: DEHP is a phase-in substance according to the definition 3(20) of the REACH Regulation. DEHP 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 DEHP will be submitted to ECHA by 30 November 2010. These registration dossiers will include information on the uses of DEHP, as well as most probably a Chemical Safety Report with information on the volumes relevant for each use.
To date, only registration dossiers as part of a joint submission for transported isolated intermediates have been submitted to ECHA.

Total use of DEHP:
DEHP has been the main "*general purpose*" phthalate used over the last 50 years. It has had applications in a wide range of soft-PVC and non-PVC polymer materials, these being further processed in the production of a range of indoor and outdoor products, both for industrial/professional and consumer uses. In addition to polymer applications DEHP has also been used in adhesives, sealants (which are often applied to windows and doors for improved insulation), rubber, lacquers, paints and printing inks. Therefore, DEHP can be found in building and construction materials (e.g. in flooring, roofing, industrial doors, wires, cables, hoses and profiles), in coated fabrics (such as artificial leather for bags and automotive applications, book covers and bindings, maps and folders), in medical devices (e.g. blood bags, dialysis equipment) as well as in a multitude of other products such as traffic cones, buoys, curtains for lorries and train compartments, tarpaulins, signs, flexible containers, disposable gloves or dipped tool handles, sports mats, swimming pool covers, shower curtains, napkins, stationery films, water beds, furniture, luggage or shoe soles. It has also been reported to be used in primary packaging of medicinal products and active pharmaceutical substances (EU, 2008; ECHA, 2009; www.dehp-facts.com).

A recent publication of the Danish Environmental Protection Agency (Danish EPA) (Danish EPA, 2009) gives an overview of several previous surveys aiming at analysing the presence of DEHP in different consumer products to which 2 year-old children may in particular be exposed. It confirms that, in years 2002-2008, and in addition to the specific uses which are further described in the following sections of this document, DEHP was reported to be found in vinyl floorings and in vinyl wallpaper (in concentrations up to 16% and 10% w/w respectively) and in lamination materials (no concentration estimations available). In addition, it indicates that DEHP was also detected in other household equipments and products like carpets (in concentrations up to 9.2%), shower curtains[8] (in concentrations up to 9.2%) and wrapping paper ("*Christmas paper*", in concentrations below 0.1%).

However, a consequence of the harmonised classification and labelling of "*Low Molecular Weight (LMW)*" phthalates such as DEHP, DBP and BBP (category 1B reproductive toxicant according to new CLP Regulation[9]) and the overall conclusions

[8] including in decorative fluids that they may contain

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

of the EU Risk Assessment Reports (EU RAR) prepared in the context of Council Regulation (EEC) No. 793/93 on the evaluation and control of existing substances was that companies moved to the use of general purpose non-classified "*High Molecular Weight (HMW)*" phthalates, and in particular to DINP (ECPI workshop, 2009). In the case of DEHP, this transfer can be illustrated by the following figures and facts:

- in Western Europe, DEHP represents nowadays (2008 figures) only ca. 18% of the overall consumption of plasticisers, when DINP, DIDP and DPHP[10] represent together ca. 65% (ECPI workshop, 2009; CEFIC, 2010); in comparison, at global level DEHP represents 50% of the total use of plasticisers, compared to ca. 30% for DINP and DIDP together (ECPI workshop, 2009);

- in 1999, DEHP was representing 42% of the consumption of phthalates in Western Europe, compared to only 35% for DINP and DIDP; however, the use of other phthalates, and in particular DINP has constantly increased since 1994, whilst the manufacture of DEHP has decreased from 595,000 tonnes/year in EU-15 in 1997 to 340,000 tonnes/year in 2007 (ECHA, 2009a), for a total use of DEHP of only 221,000 tonnes/year in 2004 (EU, 2008), and ca. 210,000 tonnes/year in the last 2 to 3 years (ECPI workshop, 2009); Industry confirmed that the current trend is the replacement of DEHP (and other LMW phthalates) by HMW phthalates (DINP, DIDP[11], DPHP[12]) (CEFIC, 2010a).

Furthermore, as DEHP is on the Candidate List and it may be included in Annex XIV of REACH, the overall trend of decreasing use of DEHP 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 DEHP 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 these DEHP-containing articles as of 16 January 2007. However, there is no further information available on the compliance of producers and importers with this restriction, and on whether and to what extend DEHP is still present in these categories of products.

The already mentioned survey and health assessment of the exposure of 2 year-old children to chemical substances in consumer products (Danish EPA, 2009) shows that, over the period 2002-2007, DEHP was found in plasticine (in 2002, in concentrations lower than 0.1%) and in several categories of toys (toys made of

[10] di-propylheptyl phthalate; CAS No 53306-54-0 / Einecs No 258-469-4 (CEFIC, 2010)

[11] according to Industry, the current EU consumption for DIDP is approximately the same as was reported in the EU RAR for this substance for the year 1994 (CEFIC, 2010; CEFIC, 2010a)

[12] di-propylheptyl phthalate; CAS No 53306-54-0 / Einecs No 258-469-4; DPHP is a new substance developed during the last 5 years which has now become available on the EU market and is produced nowadays in significant quantities (CEFIC, 2010; CEFIC, 2010a)

plastic foam like books, balls, masks, jigsaws or swords; dolls and "Disney/cartoons" characters; inflatable feeding bottles; stickers for bath tubs; wooden toys; play bags; so called "*mucous toys*"), in some cases in concentrations over 0.1% and up to 19.1%. In addition to a detailed screening of the existing surveys, a series of products to which children are highly susceptible to be exposed were also specifically analysed[13], including some childcare articles like pacifiers (including their coverage), non-slip figures and (bath/shower) mats, diapers and bed linen, and soft toys[14]. Among all these categories of products, it appears that DEHP was only found in pacifiers' coverage in very low concentrations, i.e. below 0.1%, and in shower mats in concentrations up to 12.9%. 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.

It has also to be noted that the presence of DEHP in erasers which can be categorised as toys rather than school supplies was confirmed by a survey conducted in the United Kingdom, and in particular for those erasers which do not present the CE mark, at concentrations up to 29.82 % (Phthalates in PVC erasers, LGC Ltd, UK). DEHP was also indirectly detected in the component of a toy bag[15] from which DEHP had migrated to artificial sweat, but without any further investigations about the actual concentration in DEHP in the product. Similarly, phthalate-containing PVC was found in components of two[16] (2) other children bags which can be categorised as toys rather than school supplies, without however any further investigations on which specific phthalate(s) was(were) concerned (Force Technology, 2007).

Use in school supplies:

It appears from the available information that DEHP is used as plasticiser in some PVC-containing school supplies, and in particular in non-toy erasers. A survey conducted for the Danish EPA (Force Technology, 2007) showed that 10 out of 26 (38.5%) tested erasers were containing phthalates; among the nine (9) erasers which were further analysed, three (3) were containing DEHP (33%), in concentrations up to 44% w/w. The results and conclusions of a new survey and health assessment of the exposure of 2 year-old children to chemical substances in consumer products (Danish EPA, 2009) confirms that such erasers, and in particular erasers containing

[13] 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

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

[15] note that this product was labelled with the following remark « *This bag is not toy keep away from babies* »

[16] out of 6 products analysed for this category of toys

aromas/fragrance (categorised as "*scented toy/eraser*"), could theoretically[17] be found in day-care centres.
DEHP was also found in the PVC-made component of one pencil case[18]; the concentration of DEHP in that component was 17% w/w (Force Technology, 2007).
It has to be mentioned that some phthalate-containing PVC was also found in all of the four (4) school bags analysed in the framework of this study, without further investigations on which particular phthalate was concerned (Force Technology, 2007).

Use in articles for/in contact with children:
It is reported in the already mentioned recent Danish study that DEHP was found in some (children) clothes in concentrations up to 17%, in body stockings in concentrations up to 1.8%, and on printings on shirts in concentrations up to 1.1%; it was also detected in lunch boxes and swimming boards, both in concentrations lower than 0.1% (Danish EPA, 2009).
As already mentioned in a previous section, in addition to a detailed screening of the existing surveys, a series of non-toy products 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 also specifically analysed[19]. It appears that DEHP was found in several articles like jackets[20] (in loose reflector pieces, in concentrations up to 21.3%), in mittens (in labels and outer material, in concentrations up to 14.7% and below 0.1% respectively), in rubber clogs (in concentrations up to 1.6%), and in PVC-containing soap packaging (in concentrations up to 8%) (Danish EPA, 2009).

Use in medical devices and medicinal products:
According to Industry, DEHP remains the main phthalate used in medical devices (ECPI, 2007). DEHP is included in the European Pharmacopeia for these applications, which is not the case of other general purpose phthalates such as DINP or DIDP. In its opinion "*The safety of medical devices containing DEHP-plasticized PVC or other plasticizers on neonates and other groups at risk*" of 6 February 2008 (SCENIHR, 2008), the Scientific Committee on Emerging and Newly-Identified Health Risks (SCENIHR) confirms that "*DEHP is currently the primary plasticizer used in PVC-containing medical devices such as containers for blood or nutrients, tubings and catheters*", and also indicates that "*DEHP has beneficial properties in stabilising the membranes of red blood cells enabling blood storage for several weeks*", without however giving further details on whether alternatives to DEHP can offer similar properties. On the other hand, SCENIHR indicates that, even though "*the use of*

[17] note that there is no clear indication in the above mentioned reports whether these products have actually been found in day-care centres, or if it is just considered as a reasonable assumption that they can be used in such places

[18] out of seven products analysed for this category of school supplies

[19] 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

[20] it has to be noted that no quantitative analysis of the concentration of DEHP in zipper straps was performed in the framework of this survey

plastics in medical application is increasing and the medical plastics market was anticipated to grow by more than 3% annually in 2005 [, there is also] *a considerable interest from medical plastic producers in developing alternative materials to plasticised PVC*".

As far as the devices in which DEHP can be found, Industry indicates that DEHP is used in almost all PVC healthcare applications (www.dehp-facts.com), and SCENIHR gives in its above mentioned opinion a list of procedures in which medical devices made of DEHP-containing soft PVC can be found, and from which a potential for high exposure to DEHP was identified (SCENIHR, 2008):

- Exchange transfusion in **neonates**,
- Extracorporeal membrane oxygenation (ECMO) in **neonates**,
- Total Parenteral Nutrition (TPN) in **neonates**,
- Multiple procedures in sick **neonates**,
- Enteral nutrition in **neonates** and **adults**,
- Transfusion in **adult** undergoing ECMO,
- Haemodialysis in **peripubertal males**,
- Haemodialysis in **pregnant or lactating women**,
- Hearth transplantation or coronary artery bypass graft surgery,
- Massive infusion of blood into trauma patient.

Furthermore, the available information also mentions the use of phthalates in the coating of commonly used pharmaceuticals such as antibiotics, antihistamines, and laxatives; herbal preparations and nutritional supplements may also contain phthalates (J.L. Lyche et al, 2009). However, there are no further details about which phthalates are specifically concerned by these applications.

Use in cosmetic products:
It appears from the available information that the level of metabolites of DEHP that were found in urine samples of pregnant women who participated in a biomonitoring study in Israel could be related to the number of personal care products used, and therefore that DEHP was actually present in some cosmetic products, at least in certain countries. However, the small size of the sample (19) and the exposure estimates based on a single urine sample, did not allow the authors of this study to draw firm conclusions (Berman T. *et al*, 2008).
However, it has to be noted that since 1 April 2005 cosmetic products containing DEHP shall not be supplied to consumers in the EU, in accordance with Commission Directive 2004/93/EC of 21 September 2004 amending Council Directive 76/768/EEC concerning cosmetic products.

Use in packaging, including food contact materials:
Firstly, from the available information, it appears that DEHP was found in the packaging of cosmetic products (body shampoo/bath gel) specifically intended for children use, but in concentrations lower than 0.1% w/w (Danish EPA, 2009).

As far as food packaging is concerned, the use of DEHP in food contact materials is already restricted under Commission Directive 2007/19/EC of 30 March 2007

amending Directive 2002/72/EC relating to plastic materials and articles intended to come into contact with food and Council Directive 85/572/EEC laying down the list of simulants to be used for testing migration of constituents of plastic materials and articles intended to come into contact with foodstuffs.

Nevertheless, it has to be noted that food is still considered as one of the major contributors to the overall exposure of humans, and in particular of children, to DEHP (J.L. Lyche *et al*, 2009). SCENIHR indicates that "*diet has been determined as the main source of DEHP exposure for the general population with fatty foods […]*" (based on Clark *et al* 2003, ECB 2004, Meek and Chan 1994, Peterson and Breindahl 2000, Wormuth *et al* 2006, as cited in SCENIHR, 2008). According to the available information, the presence of DEHP in food results not only from the migration from materials in contact with food during production, processing and via packaging, but also from dispersion of DEHP in the environment (J.L. Lyche et al, 2009; Danish EPA, 2009).

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 DEHP, covering several countries all over the world, including the EU. In these studies primary and secondary metabolites of DEHP were indeed measured in several body fluids (e.g. urine, breast milk, saliva, serum) of different samples of the general population. Metabolites of DEHP were for instance found in 100% 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 samples (Main KM *et al*, 2006). DEHP 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 DEHP metabolites in urinary samples from adult subjects allowed to estimate the median daily intake of DEHP of the general population at 4 µg/kg bw/day over the years 1988-1993, followed by a continuous decrease to 2.4 µg/kg bw/day in 2003 (Wittassek M *et al*, 2007). If compared to the oral NOAEL of 4.8 mg/kg bw/day (total daily intake) for development and testicular toxicity as selected in the framework of the EU RAR, theses estimations would lead to sufficient margins of safety (> 800, i.e. well above 100) and would not indicate health concerns. 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 DEHP of this sample of the general population was 9.32 µg/kg bw/day (95^{th} percentile), with peak values up to 41.1 µg/kg bw/day (Marsee K. *et al*, 2006). Compared to the above mentioned NOAEL this would lead to a sufficient margin of safety (> 100), except in very specific cases where peak values would be reached. It was not possible to conclude in the framework of this review if these findings would be applicable to the current situation within EU countries.

SCENIHR also states that "*there are indications that exposure to DEHP in the general population has decreased during the last years*" (SCENIHR, 2008). This appears to be consistent with the indication that DEHP has already been progressively replaced in most of its applications by general purpose non-classified "*High Molecular Weight Phthalates (HMWP)*", and in particular DINP (see paragraph "*2. Information on uses of the substance*").
Finally, Industry (ECPI workshop, 2009) indicated that phthalates-containing PVC has now been replaced in all food-packaging applications (e.g. from printing inks). If this was confirmed, the contribution of this potential source may need to be updated compared to the assumptions made in the framework of the EU RAR. It was not possible, on the basis of the available information, to come to any conclusions on this issue in the framework of the present review.

3.2. Occupational exposure

In the framework of this review, no new information on occupational exposure and related risks for workers was made available by stakeholders.

3.3. Children's exposure

For children, the use of toys and childcare articles (ca. 200 µg/kg bw/day, and in particular the mouthing of their soft plastic components – see further details under paragraph "*a) Exposure and risks from toys and childcare articles*"), indoor air (22 µg/kg bw/day) and food (same order of magnitude than indoor air) were identified in the EU RAR as the main sources of exposure to DEHP (EU, 2008).

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 DEHP. Finally, available estimations of the overall exposure and related risks are discussed.

a) Exposure and risks from toys and childcare articles

As already mentioned above, although restrictions on the use of DEHP 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 DEHP-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 DEHP is still present in these categories of products as a result of non-compliance with the existing restriction.
It appears from the available information that a remaining exposure cannot be excluded from the use of consumers articles which can be categorised as toys but are not necessarily identified as such (e.g. toy erasers, toy bags, etc.). As further detailed under paragraph "*b) Exposure and risks from the use in school supplies*", some of these articles may lead to health concerns, and in particular (toy) erasers, if used under certain specific conditions. Moreover, toys which were bought before the entry into force of the current restriction and are still in use can also contribute to the overall exposure of children to DEHP.

From the available information, there is no new estimation of the exposure and risks from toys and childcare articles which would be applicable either to the sub-population of children as a whole, or to the same sub-categories as those specifically identified in certain parts of the EU RAR. However, in a survey and health assessment of the exposure of the particular sub-group of 2-year old children which was recently published (Danish EPA, 2009), the Danish authorities tackled this issue by proposing estimations of possible remaining exposures and risks from certain articles.
As far as toys are concerned, the updated estimation for the daily ingestion of DEHP was built on the case of a play bag for which the Danish EPA indicates that it was presenting the highest migration value[21] (2.4 mg/kg over a period of 4 hours) among

[21] a higher migration (to the air) value was measured for plasticine (23 mg material released/kg, when heated at 200°C), but this value was assumed to be included in the exposure estimations for indoor climate; a value of 5,1 µg/g was also reported for wooden toys, but not selected due to uncertainties on the toys from where it was measured, and in particular whether that part was accessible to children's mouth or not

all the toys for which data was available (from a previous study)[22]. Taking into account exposure through both the oral (3 h/day) and dermal (9 h/day) routes, the daily exposure is estimated to be 0.38 µg/kg bw/day, leading to a margin of safety of ca. 12,000 if compared to the NOAEL of 4.8 mg/kg bw/day as used in the EU RAR.
As for childcare articles, it appears from the recent Danish study (Danish EPA, 2009) that, DEHP can migrate from shower mats (25 mg/kg) while no migration seems to occur beyond the detection threshold (2 mg/kg) from the tested pacifiers. The related daily exposure (on the basis of *inter alia* a contact period of 30 min/day) is estimated at 0.042 µg/kg bw/day, leading to a specific margin of safety higher than 100,000 for a NOAEL of 4.8 mg/kg bw/day.

Therefore, in the framework of this study, the contribution of toys and childcare articles (shower mat) to the overall exposure of 2-year old children to DEHP is estimated to be 0.42 µg/kg bw/day leading to a margin of safety greater than 11,000. If compared to the exposure estimations made in the EU RAR (200 µg/kg/day via oral route + 9 µg /kg/day via dermal route), this appears to be very low, leading to the conclusion that toys and childcare articles are not a significant exposure route, and should not raise concern anymore. However, even though it can be reasonably expected that the exposure of children to DEHP via toys and childcare articles has indeed dramatically decreased since the entry into force of the current restrictions, the differences in the scopes[23] and assumptions on the basis of which these two estimations were developed do not allow drawing firm conclusions in terms of the actual decrease of exposure from toys and childcare articles in general, and the remaining total exposure and level of risk.

b) Exposure and risks from the use in school supplies

In 2007, a study was conducted for the Danish EPA in order to evaluate the potential risks from exposure of children to school bags, toys bags, pencil cases and erasers. According to the available information, the only potentially significant source of exposure of children to DEHP from these categories of products are erasers where the major route of exposure would be via ingestion (sucking and/or swallowing) under specific conditions (daily intake of a significant amount of product, during a long period of time). In particular, it was concluded that the risks via dermal exposure (skin absorption) to a school bag, a toy bag and/or a pencil case (dermal exposure to erasers not investigated) was not significant: the potential combined exposure via both a school bag, a toy bag and a pencil case was indeed estimated at 0.04 µg/kg bw/day[24], to be compared to the NOAEL of 4.8 mg/kg bw/day and leading to a margin of safety of 120,000 (Force Technology, 2007; EU RAR, 2008).
Regarding exposure to DEHP from erasers, a maximum possible daily intake of DEHP for a 20 kg-child (i.e. approx. 6 year old) of 0.19 mg/kg bw/day (through sucking) and 3.67 mg/kg bw/day (through ingestion) was estimated, leading to

[22] within this category of products, migration rates where available only for play bags Bratz doll, plasticine and wooden toys

[23] the exposure from only 1 toy bag - which is not necessarily the product reflecting the actual exposure of children to toys - and 1 shower mat were taken into account in the updated assessment from Danish authorities

[24] on the basis of the assumption that the duration of dermal contact with the product is 1 hour/day

margins of safety[25] of respectively 25.2 and 1.3 which is lower than the value of 100 which is usually considered as an acceptable cut-off limit for the considered end-points (EU RAR, 2008)[26]. On the basis of these estimations, it was concluded that the ingestion and/or sucking/chewing of erasers could constitute a risk for a certain sub-population of children and under certain conditions (i.e. one hour daily exposure or a long period of time). However, it is worth noting that, as explicitly stated in the study report (Danish EPA, 2007), the above estimations contain many uncertainties. In particular, the measured concentrations of DEHP in artificial saliva that are used as a basis for the health risk assessment in connection with sucking of an eraser are "*probably overestimated by a factor of six*"; a correction of the estimated daily intake of DEHP by the same factor would lead to an updated margin of safety of ca. 150, and an acceptable level of risk. Similarly, the authors admit themselves that swallowing large pieces of erasers, which appears as the potential main contribution to daily intake of DEHP, is not expected to be recurrent over a long period of time, but rather a one-time event. In its "*Opinion on phthalates in school supplies"* of 17 October 2008, the Scientific Committee on Health and Environmental Risks (SCHER) (SCHER, 2008), SCHER also pointed out all the above mentioned limitations of the study and concluded that the "*phthalates* [including DEHP] *in the articles tested do not significantly contribute to the body burden of phthalates of children"*. In particular, SCHER estimated that even in the specific scenario consisting in swallowing particles bitten off an eraser "*it is unlikely that this exposure leads to health consequences*". Furthermore, SCHER considered that clarifications and/or further studies would be needed, and in particular a new migration study should be conducted. It has not been possible to conclude in the framework of the present review whether new migration studies conducted meanwhile could contribute to such clarifications.

In the context of their assessment of the exposure of 2-year old children the Danish authorities estimated the potential contribution of erasers to the total burden of 2-year old children in DEHP at 7.90 µg/kg bw/day (Danish EPA, 2009). This estimation appears to be much lower than the calculation made in the framework of the above mentioned previous study (Force Technology, 2007). From the available information, it seems that this major difference comes from the fact that, even though the same migration was used in both studies, it was also assumed that 2-year old children are in contact with erasers only 1 minute a day, when any other siblings are doing their homework, and can only suck 50% of the eraser. Therefore, even if this new estimation appears to be more realistic with regard to the estimation of the actual exposure of children to DEHP via erasers over a long period of time, it can nevertheless not be concluded that it represents correctly the exposure of other sub-groups of the children's sub-population of consumers, and in particular the approximately 6-year old children sub-group.

[25] for a NOAEL of 4.8 mg/kg bw/day (development and testicular toxicity) as selected in the EU RAR and also used in this study

[26] it has to be noted that EU RAR however recommends a cut-off limit higher than 100-200 (depending on age; 200 for infants, 100 for children) for effects on the testes and fertility; EU RAR even recommends for babies (0-3 months) a margin of safety of around 250 for testicular effects and fertility, in particular when combined exposures are estimated. Note: according to our understanding of assumptions made in the EU RAR, infants are 0 to ca. 1 year-old (and include 0-3 months babies)

c) Exposure and risks from other sources

There appears to be no new available information related to exposures and risks from other sources, and more generally to overall exposures and risks, which would be applicable to sub-population of children as a whole. However, in their new health risk assessment for the particular sub-population of 2-year old children (Danish EPA, 2009), the Danish authorities propose an updated estimation of the overall exposure to DEHP, but also include updated estimations of contributions from indoor climate (air and dust), food, toys, and other consumer products such as erasers, baby changing mats/cushions, as well as newly investigated items like mittens, pacifiers, bath/shower mats and soap packaging. 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. The estimation of the combined exposure will then be discussed in the next section.

With regard to indoor climate (air and dust), the risk assessment developed by the Danish authorities estimates the daily ingestion of DEHP (95th percentile, which is considered in the EU RAR as a worst-case value) between 23.41 µg/kg bw/day[27] and 46.65 µg/kg bw/day[28], depending on whether a summer (50 mg of dust ingested on a daily basis) or a winter scenario (100 mg of dust ingested on a daily basis) is used. These updated estimations appear to be slightly higher but still comparable to those used in the EU RAR (22 µg/kg bw/day as a worst-case estimate), and confirm that, if not constituting a health risk as such, indoor climate is a major contributor to the overall exposure of children to DEHP. However, it has to be noted that for a daily ingestion of 46.65 µg/kg bw/day, the margin of safety is of 103, which is at the limit of acceptability (in particular for infants), and the Danish report indicates that even higher levels of DEHP in indoor climate have already been measured, without giving further details and taking them into account in their exposure calculations. Another available piece of information mentions that DEHP was measured at concentrations of 1.24 mg/g of dust in certain houses in Bulgaria (B. Kolarik *et al*, 2008, referenced by Agence française de sécurité sanitaire de l'environnement et du travail (AFSSET), AFSSET, 2009). Using the assumption of an ingestion of 50 mg (summer scenario) to 100 mg (winter scenario) of dust per day, this would lead to a daily intake of 62 to 124 µg of DEHP per day for 15.2 kg-children, indicating a daily exposure of 4.1 to 8.2 µg/kg bw/day from indoor dust route only.

For exposure from food, the updated exposure estimations suggest a worst-case value of 44 µg/kg bw/day (from Wormuth *et al*, 2006 as cited in Danish EPA, 2009), which is in the same order of magnitude as the contribution of the regional exposure (19 µg/kg bw/day) and specific exposure from infant formulae or breast milk feeding (maximum of 13 µg/kg bw/day and maximum of 6 µg/kg bw/day respectively) as were estimated in the EU RAR. In this new study, there are no further details about the potential additional local exposures from industrial sites. Therefore, as it was concluded for exposure from indoor climate, it is confirmed that exposure from food, if not constituting a health risk as such, can still be considered as a major contributor to the overall exposure of children to DEHP. In worst-case scenarios, such a level of exposure could even lead to margins of safety close to 100 if compared to the NOAEL

[27] 50th percentile: 2.89 µg/kg bw/day

[28] 50th percentile: 5.71 µg/kg bw/day

of 4.8 mg/kg bw/day, which is the acceptable cut-off limit for children used in the EU RAR[29].
As far as the other articles which were investigated in the framework of the Danish study are concerned, it first of all appears that migration studies showed that in rubber clogs no migration occurs beyond the detection threshold (2 mg/kg). Therefore, the potential contribution of this category of products was not taken into account in the risk assessment developed by the Danish authorities. For jackets and mittens, on the basis of the highest measured migration rate of 0.68 µg/g (over a period of 3 hours) from the label with the product name[30] and a 3-hour daily sucking period, the total exposure is estimated at 0.197 µg/kg bw/day, leading to a specific margin of safety of more than 24,000. Finally, the potential contribution of a PVC-containing soap packaging was estimated at 0.01 µg/kg bw/day[31], leading to a margin of safety of 480,000, which represents the smallest contribution of DEHP from consumer products included in the scope of the study. It has to be noted that the Danish authorities considered this soap-packaging as a toy, which should then respect the current restrictions on toys and childcare articles.

d) Overall exposure and risks

There is no new estimation of the overall exposure to DEHP and related risks which would be applicable to the sub-population of children as a whole, or to the same sub-categories as those specifically identified in certain parts of the EU RAR.

The survey and health assessment of the exposure of 2 year-old children to chemical substances in consumer products (Danish EPA, 2009) gives however an updated estimation of the combined exposure to DEHP of this particular sub-group of the general population, which can be expected to give a general trend for the other sub-groups of the children's specific population. On the basis of the specific exposure estimations as described in the previous paragraphs of this document, the maximum daily intake[32] for 2-year old children in DEHP is estimated at 99.15 µg/kg bw/day in winter and 75.74 µg/kg bw/day in summer, leading to margins of safety lower than 100 (48.4 and 63.4 respectively). This would lead to the conclusion that, in addition to newborns which were identified in the EU RAR as under risks with regard to the total combined exposure, 2-year old children is also a sub-group of the consumers population for which there are potentially health risks from the exposure to DEHP-containing articles. However, it has to be noted that these updated combined exposure

[29] it has to be noted that EU RAR however recommends a cut-off limit higher than 100-200 (depending on age; 200 for infants, 100 for children) for effects on the testes and fertility; EU RAR even recommends for babies (0-3 months) a margin of safety of around 250 for testicular effects and fertility, in particular when combined exposures are estimated. Note: according to our understanding of assumptions made in the EU RAR, infants are 0 to ca. 1 year-old (and include 0-3 months babies)

[30] from the label with the product name; it has to be noted that DEHP was also found in the outer material of the mitten, with a migration rate of 0.27 µg/g

[31] assumptions : DEHP concentration : 8% / contact time : 30 min/day / migration rate : 2 µg/g over a period of 30 min / contact with 75% of the bath packaging

[32] including contributions from food, indoor climate, toys and childcare articles (play bag and shower mat here), erasers and other investigated consumer products (jacket and mittens here, only taken into account in the winter scenario)

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, 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*". In the present case, if only 50th percentile values are taken into account for these contributors, the total daily intakes would lead to margins of safety of 200 or more, for both summer and winter scenarios. It has however to be noted that the worst-case estimations for food (both in summer and winter scenarios) or for indoor climate (in the winter scenario only) may already indicate concerns for human health, with margins of safety around 100 if compared to a NOAEL of 4.8 mg/kg bw/day.

Whatever the conclusions in terms of total combined exposure and related risks may be, the Danish report tends to confirm that the two main contributors appear to remain food, with a contribution of 44% (winter scenario) to 58% (summer scenario) of the total daily intake, and indoor climate, contributing to 30% (summer scenario) up to 47% (winter scenario). This conclusion appears to be also valid for the general population as a whole (J.L. Lyche *et al*, 2009). Toys and childcare articles appear to represent nowadays a very small proportion of the total intake of DEHP of children. As already mentioned under paragraph a) above the differences in the scopes[33] and assumptions on the basis of which the estimations in the EU RAR and in this new study were developed do not allow drawing firm conclusions in terms of the actual exposure from toys and childcare articles in general. However, it can be reasonably expected that the exposure of children to DEHP via toys and childcare articles has substantially decreased since the entry into force of the current restrictions, and will keep on decreasing with the progressive replacement of articles which were put on the market before the restrictions entered into force and are still in use. Therefore the contribution of these articles in the total daily intake of children will remain very limited if compared to other 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, 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[34]:

- 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),

[33] the exposure from only 1 toy bag - which is not necessarily the product reflecting the actual exposure of children to toys - and 1 shower mat were taken into account in the updated assessment from Danish authorities

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

– contact with jackets/mittens (winter only).

In that report, DEHP has been considered by the Danish authorities as an anti-androgenic substance.

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 this review, indicating that metabolites of DEHP were detected in 11 pairs of amniotic fluid and suggesting that DEHP 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).

4.3. Exposure of neonates and patients from medical devices

According to SCENIHR (SCENIHR, 2008), medical procedures involving PVC-containing medical devices "*can lead to DEHP exposures much higher than the background levels*" for the general population, which is exposed mainly via food and indoor air. SCENIHR indicates that "*for some treatments the mg/kg bw/day range may easily be reached*" and further specifies that "*for blood transfusion procedures peak values up to 22 mg/kg bw/day have been estimated"*. SCENIHR also stated that "*premature neonates in intensive care units, being dependent on multiple medical procedures, can receive even higher DEHP exposures than adults relative to their body weight (up to 35 mg/kg bw over 10 day period). This exposure may be even higher than the doses observed to induce reproductive toxicity in animals*". In the EU RAR, it is also indicated that the exposure scenarios for medical equipment causing high exposure are long-term haemodialysis in adults (3.1 mg/kg bw/day), long-term blood transfusion in children (0.075 mg/kg bw/day), transfusions in neonates (1.7 mg/kg bw/day), and extra corporal oxygenation in children (based on a qualitative assessment). Taking into account an estimated total combined exposure (general population) in the order of 20-30 µg/kg bw/day for adults and ca. 250 µg/kg bw/day for children, and if compared to a NOAEL of 4.8 mg/kg bw/day selected in the framework of the EU RAR, it can be concluded that there is no margin of safety for the use of certain medical procedures, in certain conditions.

However, SCENIHR also stressed the facts that "*the extent of exposure largely depends upon the medical treatment given and the duration of the treatment*" and the absence of margin of safety "*is justified by the beneficial effects of these* [medical] *procedures*" requesting the use of medical devices made of DEHP-containing plastic (components), making the use of Tolerable Daily Intake[35] "*not appropriate in these procedures*", especially in the light of the "*very special group of patients involved*". SCENIHR also mentioned in its conclusions that for many of the procedures which have been identified as major contributors to the exposure of patients (see paragraph

[35] 48 µg/kg bw/day here, based on a No Observed Adverse Effect Level for reproductive effects in rats of 4.8 mg/kg bw/day

"*2. Information on uses of the substance*"), the actual extent of exposure is still unknown or spans several orders of magnitude", leading SCENIHR to propose that "*Research is needed to determine (i) the multiple sources and pathways of human exposure to phthalates; (ii) whether exposure to phthalates at the levels found in the general population is a cause for health concern; and (iii) to what extent human exposure to phthalates may impair human health*". It has been neither foreseen nor possible to conclude in the framework of the present review whether the studies which were conducted meanwhile could contribute to such clarifications and lead to major changes in the exposure and risk assessments made in the framework of the EU RAR (EU RAR, 2008).

Finally, it should be underlined that, in its opinion, SCENIHR indicated that also "*voluntary medical treatments such as apheresis procedure to donate blood products can cause significant exposure to DEHP"*, meaning that this other sub-population should be considered if further investigations are initiated in the field of health effects, exposure and risk assessments from the use of DEHP-containing (soft) plastics in medical devices.

4. Conclusions and suggestions for further action

In conclusion, even though new reports on biomonitoring studies tend to confirm the exposure of all groups of the population, overall DEHP appears to be used in lower total volumes than those reported when the conclusions of the EU RAR were agreed in the past.

The available information does not show that the current uses of DEHP would lead to major health concerns, including those which were not already identified in the EU RAR. The new available information only shows that, in addition to the categories of products which had already been investigated in the past, DEHP-containing PVC is also used in some limited categories of school supplies (erasers, bags, pencil cases), as well as in some other specific consumer products to which children may be exposed (soap packaging, bath/shower mats, pacifiers coverages, some (children) clothes and winter equipments like mittens or jackets). However, this information is based on a relatively limited number of products tested and, therefore, there is a need to be cautious in drawing definitive conclusions in terms of the significance of the additional/new exposure. It has also to be noted that some of these products are childcare articles and should no longer be found on the market with a DEHP content of more than 0.1% w/w. Moreover, it appears from a risk assessment developed by the Danish authorities for the specific sub-group of 2-year old children that the exposure to DEHP via these items remains very limited and does not constitute as such a health risk. In the framework of this study, erasers were the only category of products identified as of potential concern. However, it appears that the level of exposure to DEHP leading to health risks can be reached only in very specific and unlikely conditions of use. Therefore, the available information appears to confirm that the two major remaining contributors of children's exposure to DEHP are food and indoor climate (air and dust), whereas the contribution from toys and childcare articles seems to have substantially decreased following the entry into force of the current restrictions[36]. It has to be noted that the abstract of another study which was made available in the framework of this review also confirms that food has a major influence on the total exposure to DEHP of the general population, including children (Wormuth M *et al*, 2006).
For the specific sub-group of 2-year old children (Danish EPA, 2009), it was estimated that the exposure to DEHP via food[37] could already be at the level of the DNEL, the same applying to exposure via indoor climate in winter. These sources would lead to unacceptable levels of risks when estimated combined exposures are taken into account[38]. However, it has to be noted that these estimations were obtained

[36] according to an updated health assessment of the exposure of the particular sub-group of 2-year old children which was recently developed by the Danish authorities, the current exposure of this particular sub-group to DEHP via toys and childcare articles can be estimated at 0,42 µg/kg bw/day (Danish EPA, 2009); if compared to the exposure estimations made in the EU RAR (200 µg/kg/day via oral route + 9 µg/kg/day via dermal route), this would lead, if applicable to the whole group of children, to a decrease of 99.8% of the exposure of children to DEHP via these categories of products

[37] as a result of dispersion in the environment and as a consequence of migration from materials in contact with food (Danish EPA, 2009)

[38] if worst case scenarios for potential contributions from indoor climate and food are used (46.65 µg/kg bw/day and 44 µg/kg bw/day respectively), the combined exposure would be estimated at 90.65

on the basis of worst-case scenarios and, even though flooring and wallpaper have already been identified in the past as potential major contributors to the exposure to DEHP via indoor climate, it is not precisely indicated what the actual sources are and what their respective share is in the intake in DEHP. Therefore, in order to conclude whether there is actually a need for addressing these potential risks via new regulatory measures, further in-depth assessment would be needed, in particular to get clarity on the actual contributors to the contamination of indoor climate by DEHP. Furthermore, it is not clear either whether these conclusions can also be applied to other sub-groups of the children population. It is expected that the registration dossiers for DEHP under the REACH regulation, which should be submitted this year to ECHA, will already bring useful information in that respect.

ECHA considers that the available new information with regard to uses of and exposure to DEHP 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 DEHP; 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 DEHP, 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 DEHP.
Therefore, ECHA suggests to wait for the submission of the registration dossier(s) for DEHP 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 DEHP 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 DEHP in articles after June 2011. Moreover, in case DEHP will be included in Annex XIV of REACH, the potential future applications for authorisation may further clarify the uses of DEHP and possibilities to control their related risks. In particular, the exposure to DEHP from indoor sources (e.g. flooring and wallpaper) may need to be further investigated in order to more precisely identify the main potential contributors to children's exposure to DEHP via this route.

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

µg/kg bw/day, leading to a margin of safety of ca. 53 if compared to the NOAEL of 4.8 mg/kg bw/day selected in the EU RAR

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-old 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 DEHP (as well as other phthalates DBP, BBP, DiBP and DINP). 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 DEHP. Moreover, in the context of the Council discussion on this subject[39] the Commission has indicated that it will review the existing legislation in terms of its suitability to assess the effects of combined exposure.

[39] 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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