Committee for Risk Assessment (RAC)

Opinion

on an Annex XV dossier proposing restrictions on
four phthalates

ECHA/RAC/RES-O-0000001412-86-07/F

Adopted

15 June 2012

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Opinion of the Committee for Risk Assessment
on an Annex XV dossier proposing restrictions of the manufacture, placing on the market or use of a substance within the Community

Having regard to Regulation (EC) No 1907/2006 of the European Parliament and of the Council 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (the REACH Regulation), and in particular the definition of a restriction in Article 3(31) and Title VIII thereof, the Committee for Risk Assessment (RAC) has adopted an opinion in accordance with Article 70 of the REACH Regulation on the proposal for restriction of

Chemical name(s):	***Bis(2-ethylhexyl) phthalate***
EC No.:	***204-211-0***
CAS No.:	***117-81-7***
Chemical name(s):	***Benzyl butyl phthalate***
EC No.:	***201-622-7***
CAS No.:	***85-68-7***
Chemical name(s):	***Dibutyl phthalate***
EC No.:	***201-557-4***
CAS No.:	***84-74-2***
Chemical name(s):	***Disobutyl phthalate***
EC No.:	***201-553-2***
CAS No.:	***84-69-5***

This document presents the opinion adopted by RAC. The Background Document (BD), as a supportive document to both RAC and SEAC opinions, gives the detailed ground for the opinions of RAC and SEAC.

PROCESS FOR ADOPTION OF THE OPINION

Denmark has submitted a proposal for a restriction together with the justification and background information documented in an Annex XV dossier. The dossier conforming to the requirements of Annex XV of the REACH Regulation was made publicly available at ***http://echa.europa.eu/web/guest/restrictions-under-consideration*** on ***16/09/2011.***
Interested parties were invited to submit comments and contributions by ***16/03/2012.***

ADOPTION OF THE OPINION OF RAC

Rapporteur, appointed by RAC: ***Marja Pronk***
Co-rapporteur, appointed by RAC: ***Agnes Schulte***

The RAC opinion as to whether the suggested restrictions are appropriate in reducing the risk to human health and/or the environment has been reached in accordance with Article 70 of the REACH Regulation on ***15 June 2012***.

The opinion takes into account the comments of interested parties provided in accordance with Article 69(6) of the REACH Regulation.

The RAC opinion was adopted ***by consensus.***

OPINION

RAC has formulated its opinion on the proposed restriction based on information related to the identified risk and to the identified options to reduce the risk as documented in the Annex XV report and submitted by interested parties as well as other available information as recorded in the Background Document.

RAC considers that the proposed restriction is not justified because the available data do not indicate that currently (2012) there is a risk from combined exposure to the four phthalates. The regulatory requirements and consequent reduction in use are further reducing the risk, as will the authorisation requirements imposed on these phthalates in the next few years.

JUSTIFICATION FOR THE OPINION OF RAC

Identified hazard and risk

The restriction proposal is targeted at four phthalates that:

- have in common that they adversely affect the male reproductive organs and sexual differentiation during foetal development, due to their anti-androgenic effects, and for which all four are classified as reproductive toxicants category 1B;
- are present in a great variety of consumer articles, due to their widespread and dispersive use (in particular in plastics like PVC).

As a consequence, there is concern for reproductive and developmental disorders in the general population, because of combined exposure to these phthalates during the whole lifetime, both in a cumulative way (exposure to several phthalates with the same mode of action) and an aggregated way (per phthalate exposure to a broad range of articles via various sources like direct contact and indoor emissions).

Hazard

The toxicity of three of the four phthalates (DEHP, DBP and BBP) has extensively been reviewed in the recent past, i.a. in the EU by the European Chemicals Bureau (within the framework of the Existing Substances Regulation (EEC) 793/93, resulting in EU-Risk Assessment Reports (RARs)) and by the European Food Safety Authority (EFSA). The European Chemicals Agency (ECHA) identified all four phthalates as Substances of Very High Concern (SVHC), based on their classification as reproductive toxicants category 1B.

The EU-RARs form the main information source in the Background Document (BD), supplemented with recent literature not yet addressed in the EU-RARs.

Toxicokinetics - absorption

Following oral administration, phthalates are generally rapidly absorbed from the gastrointestinal tract (probably in monoform). Phthalates can also be absorbed through the lungs, whereas absorption through the skin appears to be limited.

For DEHP, the extent of oral absorption in rats is estimated to be around 60-70%. For adult humans, information from two recent studies indicates a similar percentage. There are no data on oral absorption in children, and the few data available on oral absorption in young animals do not allow a conclusion on possible age differences. For children therefore, a default of 100% for oral absorption is assumed appropriate.

For all other absorption fractions for DEHP, BBP and DBP, the values established in the EU-RARs are considered appropriate. For DIBP it is assumed that it has the same absorption fractions as DBP, given the similarities between these two phthalates. An overview of the absorption percentages used in the risk assessment of the four phthalates is given in Table 1.

Table 1. Absorption percentages used in the risk assessment

	Oral absorption	Dermal absorption	Inhalatory absorption
DEHP	70% adult, 100% child	5%	75% adult, 100% child
DBP/DIBP	100%	10%	100%
BBP	100%	5%	100%

Toxicity other than reproductive toxicity

Available data on the four phthalates DEHP, DBP, DIBP and BBP indicate that all four are of low acute toxicity and induce no skin and eye irritation or skin sensitisation. In repeated dose toxicity studies, the main organs affected besides reproductive organs (testis, in particular) are the liver (lowest NOAELs for non-peroxisome related effects for DEHP, DBP and BBP 28.9, 152 and 151 mg/kg bw/day, respectively) and the kidneys (lowest NOAELs for DEHP, DBP and BBP 28.9, 152, and 151 mg/kg bw/day, respectively). For DIBP, only few and rather old repeated dose toxicity studies are available. Available data on mutagenicity results in the conclusion that the four phthalates are not mutagenic. In rodent carcinogenicity studies, DEHP induced liver tumours in both rats and mice, but as phthalates are known to cause peroxisome proliferation, these tumours are not considered relevant for humans. The finding of Leydig cell tumours in one study in rats was not confirmed in four other lifetime studies or in multigeneration studies with DEHP. BBP tested negative for carcinogenicity in mice; in rats findings of mononuclear cell leukaemia, benign pancreas tumours and urinary bladder tumours were of doubtful significance. For DBP and DIBP, no carcinogenicity data are available. DEHP, DBP, DIBP and BBP are not classified for any other human health endpoint than for reproductive toxicity (see below), indicative of the latter endpoint being the most sensitive endpoint for the four phthalates under consideration.

<u>Reproductive toxicity</u>

Human data

The anti-androgenic related effects that are suspected to be relevant in humans in relation to the four phthalates are congenital malformations of the male reproductive organs, reduced semen quality, reduced male reproductive hormone levels, and changes in pubertal timing including changes in breast development. It has been hypothesised that these disorders may comprise a testicular dysgenesis syndrome with a common origin in foetal life. Testicular cancer may also be part of this syndrome, and it has been speculated whether prenatal exposure to phthalates may play a role in the increasing incidence levels of this and other hormone dependent cancers like breast cancer.

Unfortunately, the available epidemiology studies are associated with such uncertainties that the studies do not allow to conclude on a direct causal relationship between the effects investigated (congenital malformation of the male genitalia, semen quality, pubertal timing and testicular cancer) and phthalate exposure. Besides, anti-androgenic effects are not unique to the phthalates; numerous other chemicals show these effects as well. It is therefore, impossible to give a qualitative or quantitative indication of the contribution of the phthalates to the infertility problems and increases in hormone dependent cancers observed in humans.

Animal data

The four phthalates DEHP, DBP, DIBP and BBP are classified as toxic to reproduction on the evidence of adverse effects on the reproductive organs in rats and mice, which are attributed to an anti-androgenic mode of action. Indeed, when looking into all the available relevant reproductive toxicity studies, RAC recognised that multiple mechanisms may have occurred at the same time, leading to several effects that however all seem to follow from an anti-androgenic mode of action. The effects include early marker effects (e.g. on anogenital distance (AGD) and nipple retention), morphological and functional effects (e.g. on testes, epididymes etc.). Although early marker effects may not be adverse *per se*, RAC concluded that in the case of the four phthalates all effects attributable to an anti-androgenic mode of action (be it functional or an early marker) are relevant endpoints, since they are so consistently observed in connection with each other in the available studies. Therefore, the most sensitive of these effects, resulting in the lowest No (or

Lowest)-Observed-Adverse-Effect Level (N(L)OAEL), was selected for each of the four phthalates for use in the establishment of Derived No-Effect Levels (DNELs).

For DEHP, a NOAEL of 4.8 mg/kg bw/day found in a three-generation study with dietary exposure of rats (Wolfe & Layton, 2003) served as a starting point. In this study, testicular toxicity (small testes/epididymes/seminal vesicles and minimal testis atrophy) was observed in offspring exposed to 14 mg DEHP/kg bw/day and above as the most sensitive effect attributable to an anti-androgenic mode of action. RAC noted that the same NOAEL was selected in the EU-RAR on DEHP and by EFSA when establishing a Tolerable Daily Intake (TDI) of 0.05 mg/kg bw for DEHP. RAC considers the NOAEL of 4.8 mg/kg bw/day to be "conservative", given the low incidences at the LOAEL.

The selected key study for DBP revealed as the most sensitive effect delayed germ cell development in prepubertal rats and mammary gland changes (vacuolar degeneration and alveolar atrophy) in adult male rats exposed perinatally (from gestation day 15 to post-natal day 21) to ≥ 20 mg DBP/kg feed (corresponding to 1.5-3 mg/kg bw/day; Lee et al., 2004). RAC noted that EFSA took the same study as the basis for the TDI of 0.01 mg/kg bw for DBP, by converting the LOAEL of 20 mg/kg feed into 2 mg/kg bw and making use of an uncertainty factor of 200.

For DIBP, the LOAEL of 125 mg/kg bw/day from the study of Saillenfait et al. (2008) was taken as the starting value for DNEL derivation. Histopathological effects in testes (degeneration of seminiferous tubules) and oligo-/azospermia in epididymes were observed in male rats perinatally (from gestation day 12 to 21) exposed by gavage to dosages ranging from 125 to 625 mg DIBP/kg bw/day. Given the low incidences found at the LOAEL, the LOAEL can be considered "conservative". On the other hand, RAC noted the steep dose-response in this study.

For BBP, reduced AGD in male rats was the most sensitive endpoint. It was found at LOAELs of 500, 250 and 100 mg/kg bw/day in two-generation studies by Nagao et al. (2000), Tyl et al. (2004) and Aso et al. (2005), respectively. The overall NOAEL for this effect was 50 mg/kg bw/day from the Tyl et al. study. RAC noted that this NOAEL was also selected in the EU-RAR on BBP and by EFSA when establishing a TDI of 0.5 mg/kg bw for BBP.

DNEL derivation

In deriving DNELs for the four phthalates, assessment factors need to be applied for intra- and interspecies differences and, where necessary, for LOAEL-NOAEL extrapolation. RAC concluded that other assessment factors are not necessary.

For intraspecies differences, a factor of 10 (default) is suggested. The same factor of 10 (= 4*2.5) is suggested for interspecies differences. RAC discussed lowering this latter default factor based on information on toxicokinetics (metabolism, distribution) and toxicodynamic data from studies in marmosets. This information possibly points to interspecies differences in sensitivity to the reproductive toxic effects of phthalates. From the toxicokinetic data available it seems that there are differences in metabolism and distribution between rats and primates, including humans. Whereas all species hydrolyse the phthalates into the monoform, which is subsequently further metabolised into oxidative metabolites, in contrast to primates, in rats there is no appreciable glucuronidation of the oxidative metabolites. It further appears that, whereas the distribution pattern is the same, rats show higher levels than marmosets of phthalate metabolites in tissues, including testes. In toxicity studies, marmosets appear less sensitive than rats for phthalate toxicity. These differences are believed by some to indicate that marmosets are a more appropriate model species than rats to study the reproductive toxic effects of phthalates, and have for instance resulted in the use of an interspecies factor of 3 in the risk assessment of DEHP by the FDA, Health Canada and in Japan. RAC however considered the toxicokinetic differences to be quantitative rather than qualitative, and judged the information on quantitative differences insufficient for providing convincing evidence for a reduced hazard. This is because of the

complexity of the (multiple) mechanisms in play for the phthalates toxicity, not all of which may relate to reduced testosterone levels and/or steroidogenesis, and for which the ultimate toxic metabolites are unknown. One of the toxic metabolites is thought to be the mono-form, formed after enzymatic hydrolysis by e.g. lipase. Whereas some studies seem to indicate that lipase activity is higher in rats than in marmosets, resulting in more toxic metabolites, other studies indicate the opposite or even that lipase activity in humans may be higher than in marmosets and rats. Moreover, studies in rats have shown variable sensitivity to phthalate toxicity depending on the life stage, with rats exposed prenatally and during suckling being much more vulnerable than e.g. sexually mature rats. For marmosets, however, limited data are available for in utero, peri- and neonatal exposure. There is no study with exposure during the entire life cycle such as the multigeneration studies in rats. In fact, there is only one developmental toxicity study (using a single high dose of MBP) with a period of exposure that covers the sensitive window for the programming of the male reproductive system, demonstrating some effects on the testes of neonatal marmosets of which the toxicological significance is unclear. This, combined with the relatively low number of (non-inbred) animals tested in the marmoset studies, makes it difficult to compare the results with those found in (inbred) rats.

All in all, RAC concluded that there is too much uncertainty in the data available to allow a conclusion on humans being less, equally or more sensitive than rats, and thus suggested not to deviate from the default interspecies factor of 10.

For LOAEL-predicted NOAEL extrapolation, RAC suggested an assessment factor of 3 for both DBP and DIBP, in line with the REACH Guidance (Guidance on information requirements and chemical safety assessment, Chapter R.8). It was noted that for DIBP the "conservative" LOAEL would possibly allow a factor smaller than 3; yet, a factor of 3 was considered more appropriate, to compensate for the steep dose-response observed and for the small database available on DIBP. For DBP, RAC considered a factor of 3 more appropriate than a factor 2, which was the factor applied by EFSA in deriving a TDI for DBP. EFSA judged this factor to be sufficient, given the reversibility of the effects at all dose levels and especially at the LOAEL in the Lee et al. (2004) study, and acknowledging that in several reproductive toxicity studies with longer exposure periods approximately 30-fold higher NOAELs or LOAELs had been determined. Following a review of the Lee et al. (2004) study, however, RAC considered the data on reversibility of the effects on germ cell development unconvincing. Besides, RAC noted differences in sensitivity between animals in that same study, as well as a delayed onset of other (mammary gland) effects and a recovery time of unusual duration.

In Table 2, the DNELs derived for DEHP, DBP, DIBP and BBP are presented.

Table 2. Overview of selected overall N(L)OAELs for DNEL derivation

	NOAEL in mg/kg bw/d	**LOAEL in mg/kg bw/d**	**Endpoint**	**AFs**	**DNEL external in mg/kg bw/d**	**DNEL internal [#] in mg/kg bw/d**
DEHP	**4.8**	14	Small male reproductive organs (testes/epididymes/ seminal vesicles) and minimal testis atrophy	4*2.5*10 = 100	0.05	0.035
DBP	–	**2**	Reduced spermatocyte development at postnatal day 21, and mammary gland changes (vacuolar degeneration and alveolar atrophy) in adult male offspring	4*2.5*10*3 = 300	0.0067	0.0067
DIBP	**-**	**125**	Degeneration of seminiferous tubules and oligo-/azospermia in epididymides	4*2.5*10*3 = 300	0.42	0.42

	NOAEL in mg/kg bw/d	LOAEL in mg/kg bw/d	Endpoint	AFs	DNEL external in mg/kg bw/d	DNEL internal # in mg/kg bw/d
BBP	**50**	100	Reduced anogenital distance	4*2.5*10 = 100	0.5	0.5

for calculation of the internal DNEL, the external DNEL is corrected for oral absorption (70% for DEHP, 100% for DBP, DIBP and BBP)

Since the derived DNELs are based on N(L)OAELs for developmental reproductive effects in multigeneration and developmental toxicity studies, they are most relevant to assess the risk for pregnant women. RAC acknowledged that these DNELs may not be relevant for assessing the risks for children, as the critical period of exposure in the studies is prenatally and early postnatally (although that is more difficult to determine in a multigeneration study than in a developmental toxicity study), which does not mimic direct exposure of children. Given however that phthalates exert the most effect during the developmental phase, and pregnant women (and thus foetuses) and very small children are the main target groups to protect, it was concluded that the derived DNELs could also be used for evaluating risks to toddlers (recognising though that even toddlers are not completely comparable to very small children). Using the derived DNELs to assess the risks for older children and for non-pregnant adults was considered less appropriate. Being however not the main target groups to protect, it was not considered necessary to derive separate DNELs for them but to apply the same DNELs, bearing in mind the conservatism in using DNELs based on N(L)OAELs in dams also for older children and for non-pregnant adults.

Dose addition

In order to get more insight into the risks associated with combined exposure to four phthalates that are all classified as toxic to reproduction and act via an anti-androgen mode of action, dose addition (DA) is used in the BD as method to predict the combination effects. DA describes the additive effects mathematically by summing up the doses of the individual chemicals in a mixture[1] adjusted for their differences in potencies. The BD applies the Hazard Index method for DA, i.e. correction for differences in potency takes place at the DNEL- and subsequent risk characterisation ratio (RCR) level, with the total risk being the sum of the RCRs of the individual phthalates.

In the past five years, a number of reports and studies have been published that address the combined toxic effects of mixtures of chemicals. In several of those that investigated the mixture effects of anti-androgenic substances (including phthalates) it was found that combined exposure to these substances results in cumulative effects consistent with DA. DA occurs when chemicals in a mixture act in the same way, by the same mode of action, and differ only in their potencies; it implies that the effects of exposure to a mixture of such compounds are equivalent to the effects of the sum of the potency-corrected doses of each compound. DA predicts that no-effect doses of individual chemicals will produce an increased response when combined, in contrast to the independent action (IA) model for combined exposure that predicts that such a combination will produce no effect. This is because in IA, one chemical does not influence the toxicity of another, and the effects of exposure to such a mixture are the combination of the effects of each compound. Based on the results of the mixture studies, the use of DA in the cumulative risk assessment of phthalates and other anti-androgens producing common adverse outcomes is recommended by some experts/expert groups (e.g. NRC, 2008, Kortenkamp et al., 2009, Kortenkamp & Faust, 2010), to be applied over the whole dose range, and even when the mode of action is dissimilar. Others however (e.g. Borgert et al., 2012) have criticised the assumption that DA is valid over the whole dose range, and consider the extrapolation to far lower doses than have been tested (and which are more representative of human exposure) to be highly

[1] Mixture has not been used here as defined in CLP, but in a general way.

uncertain and overly conservative, all the more since in Hazard Index-based DA the default assumption is that the developing male reproductive tract of humans responds to chemicals at doses, two orders of magnitude (i.e. at least a factor of 100, the standard factor applied to N(L)OAELs) lower than those required to affect rats. In their opinion, the DA approach can only be used for a rough screening assessment; when a risk is identified, a more biologically based approach is warranted, for instance the Human Relevant Potency Threshold (HRPT) approach. This approach would apply DA to combined human phthalate exposures that are within a factor five-fold lower than rat N(L)OAELs for effects on the male reproductive tract, but would apply IA to lower exposure levels, i.e. for cumulative risk assessment at current levels of human exposure to phthalates.

Taking into account the above, RAC judged the proposed DA for the four phthalates to be appropriate for first tier risk assessment, with due consideration of the uncertainties and conservativeness involved when interpreting the RCRs. RAC further judged the use of the proposed Hazard Index method appropriate in the case of the four phthalates, because it allows for individual substances to have different endpoints (as long as the mode of action is similar) and different designs of key studies and even LOAELs instead of NOAELs (as both aspects can be addressed by applying assessment factors). RAC also noted that the Hazard Index method is in line with recent recommendations of three EU Scientific Committees (on Consumer Safety (SCCS), on Emerging and Newly Identified Health Risks (SCENIHR), and on Health and Environmental Risks (SCHER)), who mention in their opinion on "Toxicity and Assessment of Chemical Mixtures" (2011) that the Hazard Index is the preferred approach when extensive mechanistic information is not available, which is the case for the phthalates.

In the BD, the Hazard Index method is applied on an internal level, i.e. one internal DNEL per phthalate (corrected for oral absorption; see last column in Table 2) was compared with internal exposure estimates, to allow summation via different routes of exposure to the phthalates (oral, dermal, inhalation). Although this is not in line with the REACH Guidance on combined exposure, which advocates the comparison of route-specific external DNELs with external exposure estimates and subsequent summation of the route-specific RCRs, RAC noted that both ways result in the same outcome.

Use and exposure

Use

In 2009-2010, the use of the four phthalates in articles in the EU was reduced by 35% in comparison to the use in 2007 (see Table 3), indicating that substitution has already started.

Table 3. Estimated tonnages of the four phthalates in articles marketed in the EU in 2007 and 2009-2010

	2007			**2009-10**		
	EU production for EU market*	Import	Total for EU market	EU production for EU market*	Import	Total for EU market
Articles within scope						
DEHP	200,100 (236,700 - 36,600)	40,000	240,100	120,000	35,000	155,000
DBP, DIBP, BBP	11,400 (15,400 - 4,000)	4,000	15,400	6,800	3,500	10,300
total	211,500	44,000	255,500	126,900	38,500	165,400
All articles						
DEHP	245,600 (282,200 - 36,600)	40,000 + n.d.	285,600 + n.d.	146,800	35,000	181,800

	2007			2009-10		
	EU production for EU market*	Import	Total for EU market	EU production for EU market*	Import	Total for EU market
DBP, DIBP, BBP	23,000 (27,000 - 4,000)	4,000 + n.d.	27,000 + n.d.	13,000	3,500	16,500
total	268,600 (309,200 - 40,600)	44,000 + n.d	312,600	159,800	38,500	198,300
Articles outside scope						
DEHP	45,500	n.d.	45,500 + n.d.	26,800	n.d.	26,800 + n.d.
DBP, DIBP, BBP	11,600	n.d.	11,600 + n.d.	6,200 - export	n.d	6,200 + n.d.
total	57,100	n.d.	57,100 + n.d.	33,000 (57,200 - 24,200)	n.d.	33,000 + n.d.

* = Total EU production minus export (calculation in brackets)

There is widespread use of the four phthalates in consumer articles made from PVC (representing 94% of the total use), but they can for instance also be found in other plastic materials, in mixtures such as dispersions, paints and varnishes, as emulsifiers, repellents and carrier fluids in biocides. The phthalates are used as softeners in PVC products, e.g. in flooring, wallpapers, wires and cables, water beds and air mattresses, tablecloths, curtains, bathing equipment, bags, brief-/suitcases, footwear, balls, stationery stuff like rubbers. Typical concentrations of the phthalates in articles are between 25 and 50%.

Exposure

Exposure may result from direct contact to articles and indirectly from dust and indoor air containing phthalates. Furthermore, exposure to phthalates may arise from food intake. So, exposure via inhalation, ingestion and dermal routes was estimated. This was done in the BD for three population groups (two years old, six/seven years old and adults) as representatives of the general population because of differences in their behaviour (e.g. mouthing behaviour for small children) and exposure patterns/characteristics. By correcting for absorption, the exposure estimates were converted into internal values, to allow summation via different routes of exposure.

The variability of exposure was presented in the BD in the form of an average (and range of) median value (where appropriate) and 95th percentile value, with the average median value representing a realistic scenario, and the average 95th percentile value a realistic worst case scenario.

In order to derive exposure estimates for total article exposure, for total indoor environment exposure and for food exposure, first per age-group and per phthalate the values representing the realistic scenario were summed, and likewise the values representing the realistic worst case scenario. In a second step, per age-group these sums per phthalate were summed to derive total phthalate exposure estimates for articles, indoor environment and food.

Exposure to articles

The main focus in the restriction proposal is on articles from which a high exposure of the four phthalates is expected due to a direct and repetitive/long contact and due to their phthalate emission to the indoor environment. In the BD, data from a number of recent Danish EPA surveys on a broad variety of plastic articles containing phthalates placed on the Danish market have been used to address exposure from direct contact. The articles for which analytical data are available for the migration to artificial sweat or saliva were selected for exposure assessment. These articles are seen by the dossier submitter as

representative for other articles found in the indoor environment or articles with direct skin contact as it is considered impossible to measure all articles (groups) in which the four phthalates can be found and as it is assumed that phthalates have exactly the same function and use in the plastic. The exposure to the four phthalates from these articles is calculated in the BD with first tier models for the dermal and oral route, using the migration rate data and exposure assumptions. The dermal and oral exposure estimates are given in Table 4. As no migration of BBP was measured for any of the selected articles, BBP is not included in this table.

Table 4. Dermal and oral exposure to phthalates (internal values in µg/kg bw/day) from articles

Product		**exposure DEHP**			**exposure DIBP**			**exposure DBP**		
		2-year	6/7year	adults	2-year	6/7year	adults	2-year	6/7year	adults
Plastic sandals (median)		0.8956	1.8715	0.7146	0	0	3.7601	0	0	0
Plastic sandals (wc) [#]		3.6175	0	1.4375	3.5615	0	2.6109	0	3.9107	5.4952
Bag		0.0600 *0.0088*	0.0550	0.0320	0	0	0	0	0	0
Shower curtain		0.0038 *0.0066*	0.0035	0	0	0	0	0	0	0
Oilcloth		0.1084 *0.0077*	0.1130	0.0646	0	0	0	0	0	0
Water wing		0.1013	0.1167	0	0	0	0	0	0	0
Swimming pool		0.3646 *0.0088*	0.3813	0	0	0	0	0	0	0
Balance ball		0.1148 *0.0263*	0.1288	0.0648	0	0	0	0	0	0
Training ball		0	0	0	1.1002 *0.4057*	1.0127	0.5897	0	0	0
Sex toy		0	0	0.001/ 0.9167 *	0	0	0	0	0	0
Eraser mouthing/ eating [$]			*15.8/ 176.0*							
Articles total	**median**	**1.71**	**18.46**	**0.88**	**1.51**	**1.01**	**4.35**	**0**	**0**	**0**
	wc	**4.43**	**176.80**	**2.52**	**5.07**	**1.01**	**3.20**	**0**	**3.91**	**5.50**

[#] The only difference with the "median" scenario is the use of a different migration rate for sandals. The worst case value is based on migration to artificial sweat + sunscreen (applied to upper part of foot).
* The first value is based on the migration to artificial sweat and the second value is based on the migration to artificial sweat + oil based lubricant (worst case scenario).
[$] The first value is based on mouthing erasers for 60 min/day, the second value on ingestion of 8 mg eraser/day (worst case scenario).

In the BD, it is acknowledged that exposure from articles is based on a few selected articles only, namely those for which migration data are available. The dossier submitter was not able to extend the list of articles for which migration data are available, as the Public Consultation did not result in data on more articles/article groups and their content and migration of phthalates. In order to attempt to estimate the exposure to several other phthalate containing articles covered by the restriction, an approach could have been made to try to find a correlation between the content and the migration of phthalates, and apply this to exemplary articles from the various article groups identified (so-called sentinel exposure estimation). The dossier submitter could not find such a correlation for articles in general, noting that the migration of phthalates from a material will depend on a lot of factors such as the material, the use of the article and the additives in the material. The dossier submitter chose not to use an overall migration rate for phthalates from articles in a sentinel exposure estimation, but to base the exposure assessment on the few articles where migration of phthalates has been measured.

RAC noted that not calculating the exposure from other articles containing the four phthalates would probably lead to an underestimation of the total exposure from articles, as the articles considered are only a few of several that the different age-groups can be exposed to. As is, for instance, the possible large contribution to dermal exposure from PVC flooring not taken into consideration for small children. Looking at the notifications that industry had to provide because DEHP, DBP, DIBP and BBP are included in the Candidate

List (in total 88, 16, 7 and 3 notifications, respectively, mentioning a large number of consumer articles containing the phthalates), it indeed appears that especially for DEHP 10 articles is only a small fraction of the articles in which it is present. On the other hand, however, the mere presence in an article does not automatically mean that under normal conditions of use there will be (high) migration, and thus (high) exposure upon direct contact.

A further cause for possible underestimation may be that the analytic methods for measurement of migration used static conditions (for all articles except sandals, for which dynamic (shaking) conditions were used), whereas migration is known to be higher under dynamic conditions. Within dynamic methods there is also a difference: the head over heel method (Simoneau & Rijk, 2001) to simulate dynamic agitation reveals even higher migration rates from sandals than dynamic shaking conditions.

It is noted that the exposure to sex toys was calculated using an absorption value of 5%. This probably presents an underestimation, as for instance the mucous membranes coming into contact with the sex toys are richly perfused tissues, enhancing absorption.

Migration data on other phthalates than DEHP are available for only one or two articles (DIBP to artificial saliva and sweat from training balls, DIBP and DBP to sweat from sandals). No migration data are available for BBP. With respect to the assessment of combined exposure to the four phthalates, these data gaps may lead to underestimation.

On the other hand, RAC considers the exposure estimates that have been generated for the articles presented in Table 4 to be very worst case, for several reasons:

- A first tier model was used to calculate the exposure (intrinsically worst case due to model assumptions).
- Input parameters are worst case for the fixed values (only migration data were variable), and are identical for the realistic scenario and the realistic worst case scenario. So the exposure assumptions (exposed surface, exposure duration) are the same for the two scenarios, and whereas they may be considered appropriate for the realistic worst case scenario, they result in overestimation for the realistic scenario.
- It is assumed that people are exposed to these articles *daily (throughout the year)*, whereas some of the articles considered for exposure assessment are seasonal products.
- It is also assumed that people are exposed to *all* selected articles on a daily basis, that all these articles contain phthalates, and that the migration rates for all articles are and remain over time as high as was found for two articles (sandals - based on a single pair of plastic sandals - and sex toys). It is unknown how representative these articles are for the article groups on the market. From the surveys it appears that in the majority of plastic articles analysed, the four phthalates were either not detectable or only present in insignificant (<1% w/w) amounts.
- The values presented for the realistic article exposure scenario are therefore already worst case exposure estimates for a high-end user, whereas for plastic sandals the value for the realistic worst case scenario is a "worst" worst case exposure estimate for a high-end user.
- Summation of the values representative for the realistic worst case scenario results in a percentile approximating 100, so the values taken forward to the risk characterisation are very worst case.

It is further remarkable that 7 out of 10 articles addressed hardly, if anything at all, contribute to the direct exposure from articles, despite assuming very worst case input parameters also for these articles. Hence, the exposure estimations for all age-groups only depend on one or two articles, for some of which it is not likely that they will be used every day by the whole age-group in the 'extreme variant' (such as 'eraser eating' for 6/7-year olds).

It is not known how the potential underestimation from not calculating exposure to other (possibly major) sources and from the analytical methods used compares to the

overestimation resulting from the worst case exposure assumptions. However, given the very worst case nature of the exposures calculated and the fact that despite very worst case input parameters 7 out of 10 articles hardly contribute to the direct exposure from articles, RAC considered the exposure estimates presented in the BD for total articles to be very conservative and dealt with them as such when interpreting the risks. Besides, taking into account the results of the surveys that indicate that certainly not all individual plastic articles belonging to an article category will contain the four phthalates in significant amounts, it is unlikely that each and every person will be in direct contact to plastic articles that all have the highest content and highest migration rate (continuously) of phthalates every day. So individuals may possibly have, every now and then, a high exposure (under rather extreme conditions) from direct contact but that will not be the case on a population level.

Exposure from indoor environment

In the BD, the exposure to phthalates from the indoor environment is based on measurements of concentrations in house dust in Europe (literature data) and measurements of indoor air concentrations (using simulation, calculation and literature data, for DEHP only). Exposure to house dust describes the ingestion of dust, assuming conservative dust intakes of 50 mg for adults and 6/7-year old children and 100 mg for 2-year olds. It is presented in Table 5 as the (weighted) average median and average 95th percentile of a number of median and 95th percentile values found in various studies. The simulation for indoor air is based on data from analysed articles, mainly with large surfaces such as PVC flooring, wall paper, mattresses and shower curtains.

Table 5. Internal exposure to phthalates (in µg/kg bw/day) from indoor environment

Internal exposure estimates, in µg/kg bw/day	**Age**	**Median, average "realistic case"**	**95th percentile, average$^{\$}$ "realistic worst case"**
Estimated exposure from indoor dust			
DEHP	2-year old 6/7-year old Adult	3.02 0.99 0.27	14.84 4.88 1.32
DBP	2-year old 6/7-year old Adult	0.28 0.09 0.04	1.92 0.63 0.24
DIBP	2-year old 6/7-year old Adult	0.21 0.07 0.03	2.05 0.67 0.26
BBP	2-year old 6/7-year old Adult	0.14 0.04 0.02	2.34 0.77 0.30
Simulated exposure from particles in air and air in indoor environment *			
DEHP, air	2-year old 6/7-year old Adult	0.07 0.08 0.03	0.34 0.42 0.15
DEHP, particles in air	2-year old 6/7-year old Adult	0.34 0.42 0.14	1.68 2.09 0.72
DEHP, indoor air total	2-year old 6/7-year old Adult	0.40 0.50 0.17	2.02 2.52 0.87

$^{\$}$ The average 95th percentile value gives the average variation in 95th percentile values over the various studies. It is not the 95th percentile of all individual data from all studies combined.
* Simulations revealed negligible concentrations in air for DIBP, DBP and BBP in comparison with DEHP.

The exposure estimates for indoor environment via dust have taken into account data from more than one study and more than one (Northern) European country. RAC noted that part of these data originate from before the restriction on three of the four phthalates in toys and childcare articles (temporary from 1999, made definitive in 2005), which could possibly

point to some values being overestimates. RAC further noted that no data for Southern and Eastern European countries are available. It is not known how these would affect the estimates generated above.

Exposure from food

Two sources may result in phthalate exposure via food: environmental pollution and food contact material (FCM) use. The BD presents estimates for this exposure based on data reported in literature. These estimates result from different methods, e.g. EUSES calculations using environmental data, 24 hour diet measurements, food concentrations calculated to exposure intakes using a food consumption survey. Some data are quite old, and even the most recent data are from before the current EU legislation on phthalates in FCM (concerning plastics only) came into force in 2008. Compared to the older data, the most recent data originating from 2007 (a Total Diet Study from the UK) are at the low end of the measured exposure estimates.

In the BD, it is acknowledged that the exposure of phthalates from food may be overestimated because of a lack of very recent data. It is expected that the exposure of phthalates in food is reduced due to the regulation of phthalates in plastic FCM. It is, however, expected that there still will be an exposure from food as:

- one of the sources of phthalates in food is phthalates from the environment. Phthalates in food from the environment will originate from the production of articles containing phthalates, from the use of articles and when the articles end up in the waste stream, but there is no information on the size of the source,
- some food contact materials will be able to migrate phthalates and,
- market surveillance has shown that the limits are still exceeded from time to time.

Given the wide range of methods used, the large time span as to the year of origin of the data in the different studies, and a possible decreasing trend in time in the estimates, RAC gave preference to the use of the Total Diet Study as a starting point for risk assessment. This study generated intake estimates based on phthalate measurements in food samples in the UK in 2007 in combination with corresponding consumption data from the National Diet and Nutrition Survey (NDNS). This study only presented 97.5th percentile values and that since they originate from 2007, the exposure estimates (see Table 6) might represent overestimations.

Table 6. Internal exposure to phthalates (in µg/kg bw/day) from food

Internal exposure estimates, in µg/kg bw/day	**Age**	**97.5th percentile** **Total Diet Study UK**
DEHP	2-year old 6/7-year old Adult	9.9 6.7 2.8
DBP	2-year old 6/7-year old Adult	1.0 0.7 0.3
DIBP	2-year old 6/7-year old Adult	2.7 1.8 0.9
BBP	2-year old 6/7-year old Adult	1.3 0.9 0.5

The uncertainties in the food estimates as to which part can be attributed to FCM use, and which to environmental pollution are difficult to solve, given the lack of very recent data. Very rough estimates indicate that 40% of food exposure may result from FCM use, leaving 60% for the environment. As the relative contribution of environmental pollution originates from all articles, including the ones exempted and derogated, it would also be important to

have for the environmental part a rough idea of the share of the exempted and derogated articles vs the share of the articles included in the scope.

Biomonitoring data

Biomonitoring data are expected to give a good representation of the total/combined levels of phthalates that the population has been exposed to. Biomonitoring data from literature were provided in the BD to contribute to the validation of the exposure estimates generated for articles, indoor environment and food. It is to be noted that none of the available studies relate to samples taken after 2008 when the ban on DEHP, DBP and BBP in toys and childcare articles and the legislation on phthalates in plastic FCM were in force.

Given the uncertainties in the exposure estimates for articles, food etc., RAC considers the the data from biomonitoring studies to be important as evidence for a possible risk from the phthalates, and regards them as higher tier exposure assessment. Three fairly recent, valid studies from Europe are available. These studies reported (external) exposure estimates for the four phthalates deduced from their metabolite levels in urine, samples of which were collected in 2007 (Frederiksen et al., 2011; Koch et al., 2011). A study by Wittassek et al. (2007b; with sample collection in 2001/2003) was used to fill the data gaps for adults in the Frederiksen study. RAC combined these estimates (after correcting them for absorption; see Table 7, presenting the (weighted) average median and average 95th percentile for the three studies) for use in risk assessment. RAC noted that there are other recent EU studies available (e.g. Göen et al., 2011, with sampling time from 2002-2008), but as these do not report intake levels, only urinary metabolite levels, they are of no direct use.

Table 7. Internal exposure to phthalates (in µg/kg bw/day), based on biomonitoring data

Internal exposure estimates, in µg/kg bw/day	**Age**	**Median "realistic case"**	**95th percentile "realistic worst case"**
DEHP	Child Adult	4.81 1.85	21.06 4.48
DBP	Child Adult	1.9 2.2	6.4 7.3
DIBP	Child Adult	2.1 1.5	11.0 4.2
BBP	Child Adult	0.51 0.24	3.35 0.75

There are, however, also some uncertainties with the biomonitoring data. It is possible that they are underestimations, because the data available are from a relatively small number of people (approximately 300 in total), not covering all age-groups, and probably not reflecting the situation in the whole of Europe (data available are from Germany and Denmark). Highly exposed individuals might be missed or be present in other European countries. For children, the data in Table 7 relates to ages between 5-10 years, so better reflects the situation for the 6/7-year olds than for the 2-year olds. For the latter age-group, the data may possibly be underestimated, as authors of earlier biomonitoring studies with sampling in 2001-2002 (Koch et al., 2007, Wittassek et al., 2007a) reported higher daily intakes for DEHP, DBP and BBP with decreasing age within the age-group 2-14 years. However, comparing the intake values for the age-group 2-4 with those of the next higher age-groups of 5-6 and 7-8 years, RAC found no consistent pattern for the three phthalates, especially not for DBP and BBP.

On the other side, the data taken are recent, but not recent enough to take into account the situation affected by implementing the measures on FCM (2008), cosmetics (2005), and maybe even toys and childcare articles (1999/2005). So, the data may represent an overestimation of the present exposure. Some authors have reported a downward trend in internal body burden for DEHP, DBP and BBP and an upward trend for DINP (for instance for young German adults in the years from 1988 to 2008 (Göen et al., 2011)), which seems to

reflect that substitution has already taken place in the last decades. Given the limited number of valid studies, it is not known whether this trend is seen more generally in Europe and, due to lack of studies with recent sampling times, what the trend is over the last five years. There was, however, a 35% reduction in phthalate use in Europe from 2007 to 2009/2010, and although that cannot be directly translated into a 35% reduction in phthalate body burden, it is not unreasonable to assume that the phthalate body burden will have decreased over the last five years in Europe. RAC is aware of some ongoing projects regarding biomonitoring of phthalates in Europe (e.g. the DEMOCOPHES project, and a Norwegian survey with sampling time 2008-2010); these may provide more accurate information on the current body burden once the results become available.

Risk

In the risk characterisation part of the BD, RCRs were calculated at an internal level, i.e. one internal DNEL per phthalate (corrected for oral absorption; see last column in Table 2) was compared with the internal exposure estimates for that particular phthalate. Subsequently, the RCRs per phthalate were summed into a total RCR.

Risk characterisation and exposure evaluation reflect that consumers are exposed to the four phthalates through several routes, from a great variety of consumer articles, and from other sources like food and environment.

In the BD, risk is estimated for exemplary articles that are assumed to be representative for the risk by combined exposure to numerous articles in the consumer's surrounding containing the four phthalates. It is recognised that incomplete sets of information on many articles are given due to the fact that information on the content and migration of the phthalates is not available for many articles. More of such information was specifically asked for during the Public Consultation of the Annex XV report, but hardly any was supplied by interested parties. The concept of combined exposure, however, relies on the fact that the phthalates are contained in many consumer articles. The large number of consumer articles presented in the notifications for DEHP, DBP, DIBP and BBP due to their inclusion in the Candidate List strengthens this.

In Table 8, the RCR values for the four phthalates combined are presented for the various exposure estimates. RCR values at or above 1 have been highlighted in grey.

Table 8. RCR values for all four phthalates combining exposure from indoor air, dust, food and consumer products

	Age	RCR for realistic scenario	RCR for realistic worst case scenario	RCRs for individual phthalates in realistic worst case scenario			
				DEHP	DBP	DIBP	BBP
RCR articles	**2-year old**	0.05	0.14	0.127	-	0.012	-
	6/7-year old	0.53	5.64	5.051	0.584	0.002	-
	Adult	0.04	0.90	0.072	0.821	0.008	-
RCR dust	**2-year old**	0.13	0.72	0.424	0.287	0.005	0.005
	6/7-year old	0.04	0.24	0.139	0.094	0.002	0.002
	Adult	0.01	0.07	0.038	0.036	0.001	0.001
RCR indoor air	**2-year old**	0.01	0.06	0.058		negligible	
	6/7-year old	0.01	0.07	0.072			
	Adult	0.005	0.02	0.025			
RCR indoor environment	**2-year old**	0.14	0.78				
	6/7-year old	0.06	0.31				
	Adult	0.02	0.10				
RCR articles and indoor environment	**2-year old**	0.19	0.92				
	6/7-year old	0.59	5.95				
	Adult	0.05	1.00				
RCR food	**2-year old**	(0.44)*	0.44	0.283	0.149	0.006	0.003
	6/7-year old	(0.30)	0.30	0.191	0.104	0.004	0.002
	Adult	(0.13)	0.13	0.080	0.045	0.002	0.001
RCR indoor environment and food	**2-year old**	(0.58)	1.22				
	6/7-year old	(0.36)	0.61				
	Adult	(0.15)	0.23				
RCR total (articles, indoor environment and food)	**2-year old**	**(0.63)**	**1.36**	**0.891**	**0.436**	**0.023**	**0.007**
	6/7-year old	**(0.89)**	**6.25**	**5.454**	**0.782**	**0.008**	**0.003**
	Adult	**(0.18)**	**1.13**	**0.215**	**0.901**	**0.010**	**0.005**

* In the Total Diet Study no median values were reported, only 97.5th percentiles. These values have also been taken forward for the realistic case (between brackets), only to give an indication of where the total risk for the realistic case would end up.

From the calculated RCRs, the following can be concluded:

- In the realistic worst case, the combined exposure identified from the few articles with high concentrations and migrations is likely to exceed levels that possibly pose health risks for 6/7-year olds. For adults, the RCR is close to 1, and when exposure from other sources (mainly from dust and food) is taken into account an RCR just above 1 is revealed. Taking into account other exposures (mainly dust) than direct, exposure to articles also reveals an RCR slightly above 1 for 2-year old children.

- On their own, the RCR values for indoor air, dust and for food are below 1 for all exposure groups.

- If the total RCR is measured alone from food and indoor environment because of the difficulties and uncertainties in estimating the exposure from articles, the RCR values are above 1 only for 2-year olds in the worst case scenario. For these RCR values there is no exposure from articles and this should be added, as there will be an exposure from the direct contact with articles containing phthalates.

Several RCRs >1 have been identified in the BD, some of which are only slightly above 1, but others quite a bit higher, indicating exposures likely to be exceeding levels that possibly pose a health risk. It is only the summed 95th percentiles (representing the realistic worst case) that show RCRs at or above 1. It is to be noted however, that the summation of (average) 95th percentiles of the separate exposure estimates for articles, indoor environment and food is rather worst case, as cumulation results in unknown, possibly unrealistically high, total exposure estimate percentiles.

The concept in the BD assuming phthalates in many more articles than identified is appreciated (and confirmed by the notifications provided by industry), but uncertainties

about the total sum of phthalate exposure and risks from direct contact remain. As to the presented exposure estimates there are also uncertainties. On the one hand, they may be underestimated (limited migration data on only a few articles are available), on the other hand they may be overestimated (given very worst case exposure assumptions). It is not known how the potential underestimation compares to the overestimation. Given however the very worst case nature of the exposures calculated, and the fact that even with very worst case input parameters most articles will probably hardly contribute to the direct exposure from articles as compared to the estimated contribution from plastic sandals, erasers and sex toys, RAC assumed that they outbalance the lacking information/calculations on exposure to other articles. All the more because not all articles will contain phthalates in significant amounts, and the presence of phthalates in articles does not automatically mean (high) migration, and thus (high) exposure upon direct contact under normal conditions of use.

For adults, the articles are the major contributor to the size of the total RCR, much more so than food and indoor environment. It is to be noted though that it is only a very small number of articles (plastic sandals and sex toys) that effectively contribute to this: plastic sandals with DBP (RCR 0.82) or DEHP (RCR 0.04) and sex toys with DEHP (RCR 0.03) are responsible for 91, 4.6 and 2.9% of the total article RCR respectively, and for 73, 3.6 and 2.3% of the total RCR respectively. Further, the assumption that the same person is daily exposed to plastic sandals with a continuous high phthalate concentration/migration and to sex toys with oil based lubricants (although exposure to the latter itself could possibly be even higher as absorption in richly perfused mucous membranes is likely to be higher than the assumed 5%). On a population level, that assumption does not seem to be realistic, as the results of the surveys indicate that certainly not all individual plastic articles belonging to an article category will contain the four phthalates in significant amounts. The resulting risk estimates are therefore likely to represent an overestimation of the risk for an unknown part of the population.

For 6/7-year olds, the articles contribute by far the most to the size of the total RCR. As with adults, it is only a very small number of articles (mainly erasers, containing DEHP) that significantly contribute to this (contributing an RCR of 5, which is 89% of the total article RCR and 80% of the total RCR), based on very conservative exposure estimates (daily intake of 8 mg eraser). Sandals with DBP further contribute with an RCR of 0.6.

RAC noted that in 2008 the EU Scientific Committee on Health and Environmental Risks (SCHER) reviewed the findings of the Danish EPA on phthalates in school supplies, in particular erasers. Of the 26 erasers studied, 9 were made of PVC, and only 3 of these had a measurable content of DEHP (up to 44%). Whereas the Danish EPA concluded that daily intake of a small amount of eraser with DEHP during a longer period (and likewise daily sucking on an eraser with a high content of DEHP) may represent a health risk, SCHER concluded that phthalates in school supplies do not significantly contribute to the body burden of phthalates in children. Although from a single available exploratory experiment SCHER estimated that biting off pieces of an eraser and swallowing them could exceed the TDI for DEHP, SCHER considered this behaviour to represent a short-time habit of children or even a one-time event, for which a comparison with a TDI derived for lifetime exposure is inappropriate. This exposure was concluded as unlikely to lead to health consequences.

For 2-year olds, articles do not contribute significantly to the size of the total RCR, but especially for this age-group it may be expected that other major contributors exist that have not been dealt with in the article exposure assessment. For this age group, the main source is the indoor environment, especially dust (containing mainly DEHP and DBP, and much less DIBP and BBP), for which a rather conservative daily consumption of 100 mg is assumed.

Food appears to be an important contributor to the total RCR, and again that is mainly due to the presence of DEHP and DBP, not to that of DIBP and BBP. Yet, there are uncertainties in these data, as all the available data are from before the most recent EU legislation on phthalates in FCM (concerning plastics only) was in force in 2008. There may be some

overestimation in the values presented. It is however, not clear how much the articles intended to be restricted contribute to the food exposure, and how much comes from food contact material use.

Although RCR values >1 have been identified in the BD, some of which are only slightly above 1, it is difficult to judge what the risks actually are, given the uncertainties and in some cases high degree of conservatism in the exposure estimates generated for articles, food and the indoor environment. Probabilistic risk assessment could possibly have provided more insight into that, but it is recognised that that would not have been an easy task for such a complex case. What can be seen from the part on the right in Table 8 is that in the realistic worst case the aggregate exposure per individual phthalate does not result in RCR values >1 for DBP, DIBP and BBP, whereas it does for DEHP for 6/7-year olds. But that is caused by one article only (erasers) through exposure in an unrealistic worst case scenario. Further, as already concluded above, it can be seen that the cumulative exposure to the four phthalates results in RCR values >1 for all age-groups. That, however, is attributable to two of the four phthalates only. DEHP contributes by far the most to this, especially for 2-year olds and 6/7-year olds. The large contribution of DEHP is not unexpected, given that more than 90% of the phthalates used in the EU in articles is DEHP, and is evident for the direct exposure to articles (obviously, because migration data were almost exclusively available for DEHP), indoor air, dust and food, with direct exposure being the most important one. But, as indicated before, the latter is mainly attributable to a few articles only (erasers, plastic sandals and sex toys). The other contributor is DBP, especially in adults, but in adults and 6/7-year olds that is mainly attributable to one article only (plastic sandals). In 2-year olds, it is mainly DBP in dust and food that contributes to the total RCR values calculated.

This brings into question the wide scope of the restriction proposal, as from the above it seems that only two of the four phthalates are responsible, and only a few articles. Given however the uncertainties in the generated exposure estimates, RAC considered it of most importance to look at the biomonitoring data, because these are expected to give a good representation of the total/combined levels of phthalates that the population has been exposed to and thus are more reliable. In Table 9, the RCR values for the biomonitoring data are presented, with values at or above 1 highlighted in grey.

Table 9. RCR values for biomonitoring data on the four phthalates (total + individual)

Age		**Total**	**DEHP**	**DBP**	**DIBP**	**BBP**
Child	**RCR for realistic scenario (median)**	**0.43**	**0.137**	**0.284**	**0.005**	**0.001**
	RCR for realistic worst case scenario (95th percentile)	**1.59**	**0.602**	**0.955**	**0.026**	**0.007**
Adult	**RCR for realistic scenario (median)**	**0.39**	**0.053**	**0.328**	**0.004**	**0.001**
	RCR for realistic worst case scenario (95th percentile)	**1.23**	**0.128**	**1.090**	**0.010**	**0.002**

When looking at the realistic worst case scenario (which covers the population as a whole better than the realistic scenario, which would only cover around 50% of the population), the most recent available biomonitoring data seem to support that there might be a risk from the phthalates, both for children and for adults, although the RCRs calculated are not much above 1. For both children and adults, DBP is the main contributor to the cumulative RCR values (60 and 89%, respectively). This is mainly caused by the low DNEL for DBP, as exposure is not or not much higher than for the other phthalates. DEHP is the second main contributor (38 and 10%, respectively), and forms the highest exposure source in children. When looking at the phthalates individually, the exposures to DEHP, DIBP and BBP in both the realistic and realistic worst case are well below their respective N(L)OAELs (margins of 230-2,600, 11,400-83,300 and 15,000-208,300, respectively) and thus their respective RCRs are well below 1. For DBP, the margins are smaller (275-1,050) in the realistic worst

case resulting in an RCR value just above 1. This mainly has to do with the fact that DBP has a much lower LOAEL than the other three phthalates.

There are, however, some uncertainties with the biomonitoring data as well, as indicated in the section on *Biomonitoring data*, so that it is not known what the current body burden for the four phthalates is and thus what the current RCRs would be as a result of combined exposure. Moreover, it should be realised that the biomonitoring RCRs in Table 9 do not only present the result of exposure to articles intended to be restricted, but to *all* sources of the four phthalates. Furthermore, the RCRs in the realistic worst case scenario are overestimates, as they are the result of a summation of 95th percentiles, i.e. meaning that an individual for each of the four phthalates is exposed to its 95th percentile exposure estimate, which may not likely be the case. The uncertainty herein is somewhat reduced by the fact that only two of the four phthalates significantly contribute.

As remarked in the section on *Use*, a decrease of 35% in the volume of the four phthalates placed on the EU market has been observed between 2007 and 2009/2010 (see Table 3). This decrease, plus the clear indications for a continuing decrease up to 2012, will have a considerable impact on the present day risk level. Many articles in the scope have a service-life of 10-30 years, therefore the decrease in volumes placed on the market will have a delayed effect on the reduction in exposure to the phthalates.

In an attempt to better describe the robustness of the RCRs presented in Table 9 (indicative for the risk around 2007) and for what could be the current RCRs, the uncertainties in the biomonitoring data as well as the identified uncertainties in the hazard assessment have been listed in Table 10, alongside their expected influence on the calculated RCRs.

Table 10. Overview of sources of uncertainty in the phthalate risk assessment based on biomonitoring data and influence on RCRs (↓ towards lower RCR, ↑ towards higher RCR)

Source	**Description**	**Effect on RCR**
HAZARD		
- NOAEL DEHP of 4.8 mg/kg bw/d from 3-gen study	"Conservative" as basis for DNEL for all age groups, given low incidences at LOAEL.	↓
- LOAEL DBP of 2 mg/kg bw/d from dev.tox study	"Conservative" as basis for DNEL for 6/7-yr olds and non-pregnant adults, as N(L)OAEL from dev.tox study is most valid for pregnant women (and very small children), and N(L)OAEL in two-gen study (including postnatal exposure) was considerably higher. It might also be conservative as basis for DNEL for 2-yr olds, although they are closer to 'very small children' than the above mentioned age groups.	↓ (↓)
- LOAEL DIBP of 125 mg/kg bw/d from dev.tox study	Could potentially be conservative as basis for DNEL for 6/7-yr olds and non-pregnant adults, and possibly also for 2-yr olds (see above for DBP), but no data with relevant (postnatal) exposure period available to compare with.	(↓)
- Interspecies factor of 10 applied in DNEL derivation	Set at default, but some indications that factor might be lower (humans seem not more sensitive than rats, but evidence was considered not (yet) conclusive).	(↓)
EXPOSURE – Biomonitoring		
- Sampling time of the data	Data are the most recent available, but not recent enough to take into account the effects of various legal measures and the substitution already taking place. These are expected to result in a continuation of the gradual decline observed over the last decades.	↓
- Representativeness of the data, European-wide	Data are from a relatively small number of people in a small number of European countries, and do not cover all age groups. It is unclear how well they reflect the situation in whole Europe; the effect on RCR could go either way.	↑ ↓
- Representativeness of the data for 2-yr olds	Data better reflect the situation for the 6/7-year olds than for the 2-year olds who, based on earlier biomonitoring studies, might have a different intake than the 6/7-year olds.	(↑)
- Summation of the 95th percentiles of the individual phthalates	Summation results in an unknown, but higher than 95th percentile total exposure estimate percentile.	↓

It was found to be very difficult to estimate the magnitude of each arrow in the table above. The RCRs calculated for the 2007 situation are 1.23 for adults and 1.59 for children, so that overall only a factor of approximately 2 is necessary to bring them below 1. The uncertainty analysis indicates that more uncertainties seem to point to lower RCRs than to higher RCRs. It therefore seems reasonable to assume that for the 2007 situation the cumulative RCRs could well be lower than the ones calculated in Table 9, so closer to or below 1.

It also seems reasonable to assume that for the present day situation, the RCRs will be even lower than the 2007 RCRs, given the steady decline observed over the last decades (for instance 35% over the period 2007-2009/2010) in tonnages of the four phthalates used in Europe. Although this cannot be directly translated into a similar decrease in exposure to the four phthalates, there will be a considerable downward effect on the body burden (as

e.g. demonstrated by Göen et al. (2011) over the period 1988-2008), and consequently the RCRs would be below 1. RAC concluded that the data available do not indicate that currently (2012) there is a risk from combined exposure to the four phthalates.

Existing legal requirements and risk management measures

Since 1999, DEHP, DBP and BBP have been subject to restrictions in toys and childcare articles. Currently, entry 51 in Annex XVII to REACH restricts these phthalates in toys and childcare articles in concentrations above 0.1% by weight of the plasticised material. Furthermore, as all four are classified as toxic to reproduction category 1B, from July 2013 DEHP, DBP, DIBP and BBP are restricted under the Toy Safety Directive (2009/48/EC) in concentrations above the specific limit for classification.

The use of DEHP, DBP and BBP in cosmetics is restricted under the Cosmetics Directive (76/768/EEC), and their use in plastic for food contact materials is regulated under Regulation (EC) No 1935/2004 and specific measures thereunder (e.g. Commission Regulation (EU) 10/2011). DEHP, DBP and BBP may be used in non-fatty foods provided the migration of the plasticiser does not exceed the Specific Migration Limit (SML) of 1.5, 0.3 and 30 mg/kg food, respectively. The use of DIBP is not allowed in plastic for food contact materials. Furthermore, a Total SML is set, i.e. 60 mg/kg expressed as the sum of the substances (DEHP, DBP, BBP, DINP, DIDP, and 15 other substances).

DEHP, DBP, DIBP and BBP have all been identified as Substances of Very High Concern (SVHC), and all four are already included in REACH Annex XIV and thus subject to the authorisation process (with sunset date 21 February 2015). The authorisation process, however, does not cover placing on the market of articles containing the phthalates and therefore does not cover imported articles. Numerous articles could therefore still contain the four phthalates. It is also noted that the authorisation process does not take into account combined exposure from both individual articles and individual substances.

The information collected in the BD shows that the four phthalates are still used in large quantities in articles for use indoors and/or with direct human contact. But for many fields of application, voluntary phasing out of the four phthalates and/or phthalates in general has already taken place, or is in the process. The substitution to other plasticisers than the four phthalates, i.e. started off by the ban on toys and childcare articles, has been going on for the last 10-15 years, which is reflected in the steady decline observed in tonnages of the four phthalates used in Europe over the last decades. Consequently, also the exposure of the public to the four phthalates has decreased. A further impact on the exposure can be expected from the authorisation process (see the section on *Effectiveness* below).

Justification that action is required on a Community-wide basis

In principle, action on a Community-wide basis for four phthalates that share the same reproductive toxic properties and are present in many articles that consumers throughout the EU are exposed to on a daily basis, would seem appropriate if the combined exposure is demonstrated to result in health risks. RAC however, considered that this is not the case, as indicated in the section *Justification that the suggested restriction is the most appropriate Community-wide measure.*

Justification that the suggested restriction is the most appropriate Community-wide measure

The proposed restriction aims for a ban on the placing on the market of all articles containing one or more of the four phthalates DEHP, DBP, BBP or DIBP in a concentration greater than 0.1% of each by weight of any plasticised material, with exemptions for articles that do not contribute to the direct exposure to humans. These are articles that are

solely used outdoors (including storage) and are used without prolonged contact to skin, or are used without contact with mucous membranes.

The other risk management options (RMO) presented in the BD are slightly different variations of the proposed restriction (= RMO1). RMO2 proposes a wider scope, i.e. a restriction on all articles, whereas RMO3 proposes a narrower scope, i.e. a restriction on identified groups of articles. RMO4 is a proposal for a restriction based on a migration limit instead of a concentration limit.

The reference point for comparing the effectiveness, practicality and monitorability of the proposed restriction and the other RMOs is the baseline. The baseline describes the risk to be addressed, taking into account future market trends and the effects of other Community legislation and risk management measures on exposure in the foreseeable future.

Effectiveness in reducing the identified risks, proportionality to the risks

Risk reduction capacity

RAC concluded that the data available do not indicate that currently (2012) there is a risk from combined exposure to the four phthalates. This section examines the effect of future trends on the risk.

Substitution to other plasticisers than the four phthalates has been going on for the last 10-15 years. The substitution process is expected to continue in the future, at least for uses where the costs are considered to be limited. It will be supported by the requirement in REACH for a supplier of an article containing an SVHC in a concentration of more than 0.1% to inform the customer (upon request) if the article contains such a substance. It is expected that this will further stimulate the movement away from the four phthalates (all identified as SVHCs), and that the amount of articles containing the four phthalates will decline. Consequently, the exposure of the public to the four phthalates will continue to decrease, further lowering the RCRs.

Another impact can be expected from the authorisation process. After 21 February 2015, the placing on the market and the use of the four phthalates is prohibited unless an authorisation is granted. Authorisation will affect the amount of the four phthalates in EU produced articles, because applications for authorisation will not be received or granted for all uses, as along with demonstration of adequate control applicants will also have to provide an analysis on alternatives and, when suitable alternatives are available, a substitution plan. The same kind of phthalate-containing articles can however still be imported, because import will not be covered by authorisation. So, on an individual level, people can still be exposed to articles with one or more of the four phthalates, but on a population level, the exposure is expected to decline.

SEAC has defined a baseline (see Appendix 1 to the BD). Taken as a given the volumes estimated in 2007 and 2009-2010 (see Table 3), the projected volumes in 2015 and 2020 would be 131,000 and 113,000 tonnes respectively, without taking into account authorisation and recycling. This means a decrease of 49 and 56% respectively as compared to the volume in 2007 (255,500 tonnes). The projected volumes in 2020 for the baseline (including effects of authorisation and recycling) would vary from 38,000 tonnes (low bound) to 79,000 tonnes (high bound). This would mean a decrease in volume by 69-85% as compared to the volume in 2007.

Despite the inherent uncertainties in the estimations of the future volumes, there are clear indications for a decrease in volume. As a consequence, the exposure to the four phthalates will also decrease, given also the delay in effect on exposure as a result of the past market trend. There is however no direct correlation between the two, i.e. for example a 70% decrease in volume does not mean a 70% decrease in exposure. In an attempt to better

describe the risk reduction capacity, break-even points have been calculated, based on the biomonitoring RCRs from Table 9. The result is presented in Table 11.

Table 11. Break-even calculation for the 2007 biomonitoring data

	RCR biomonitoring for realistic worst case	**decrease needed to reach RCR = 1**	**decrease needed to reach RCR = 0.8**
Children	1.59	37%	50%
Adult	1.23	19%	35%

Based on the RCRs, calculated using the latest available biomonitoring data from 2007, a decrease in exposure estimates of 19-37% is necessary to reach an RCR of 1. To reach an RCR at which there will likely be no risk (e.g. an RCR of 0.8), a decrease in exposure estimates of 35-50% is necessary. Comparing these percentages with those for the anticipated decrease in volume (49-56% without taking into account authorisation, 69-85% with authorisation), it would seem that the decrease in volume without taking into account authorisation will reduce the risk to a level below 1. A further decrease can be expected in the near future from authorisation. In conclusion, action on a Community-wide basis in the form of the proposed restriction (or any of the other proposed RMOs) is not considered to be justified.

Given the uncertainties identified, RAC recommends that the developments on the four phthalates (in market trends, uses, body burden based on biomonitoring, content in and migration from articles, etc.) should be monitored within an appropriate time period.

RAC further noted that REACH requires ECHA to consider whether the use of the four phthalates in articles (including ones imported into the EU) poses a risk to human health or the environment that is not adequately controlled, given that all four phthalates are listed in REACH Annex XIV. If the risk is not adequately controlled, according to Article 69(2)[2], ECHA shall prepare a restriction proposal.

Comparison to health risks from use of alternatives

The substitution to other plasticisers than the four phthalates, and to other materials, has been going on for the last 10-15 years. The movement to alternatives in fact resulted in a steady decline in tonnages of the four phthalates used in Europe over the last decades. According to the BD, for all applications alternatives exist. DINP and DIDP have become the dominant alternatives, especially to DEHP, due to their closeness in performance, their availability and their only moderately higher costs.

For DINP, it is concluded in the BD that it has similar toxic developmental effects as the phthalates proposed to be restricted, however at a higher dose (NOAEL for reproductive developmental effects is 300 mg/kg bw/day). A more sensitive effect of DINP is on the liver, with a NOAEL of 15 mg/kg bw/day for non-peroxisome proliferation related effects in chronic rodent studies.

Available data from two-generation studies with DIDP indicates developmental effects at high doses that were related to reduced body weight gain. Developmental landmarks (AGD, nipple retention and preputial separation) were not impaired, and no histopathological damages were observed in adult testes. The NOAEL based on decreased survival rates was 33 mg/kg bw/day DIDP. Like for DINP, liver toxicity appears to be the most sensitive effect (although both are not classified for liver or other chronic effects) and also a NOAEL of 15

[2] Article 69(2) of REACH Regulation: "After the date referred to in Article 58(1)(c)(i) for a substance listed in Annex XIV, the Agency shall consider whether the use of that substance in articles poses a risk to human health or the environment that is not adequately controlled. If the Agency considers that the risk is not adequately controlled, it shall prepare a dossier which conforms to the requirements of Annex XV."

mg/kg bw/day was derived from a 13-week study in dogs, which were not sensitive to peroxisome proliferation.

In the ECHA draft review report on DINP and DIDP (launched for Public Consultation from 7 May – 31 July 2012), a recent study by Clewell et al. (2011) seems to indicate that for DINP prenatal gavage exposure of 250 mg/kg bw on GD 19 reduced testis testosterone levels in rats (NOAEL 50 mg/kg bw/day) when measured 2 hours after dosing, while exposure from GD 12-19 did not affect AGD and testis histomorphology up to 250 mg/kg bw/day. So, there is some uncertainty as to the conclusion that DINP is less potent than DEHP, DBP, DIBP and BBP with regard to its anti-androgenic effects on reproductive development. Besides, DINP is a mixture of C-9 rich, di-C8-10 branched chain dialkylesters of ortho-phthalic acid. Different compositions are on the market and may have been used for testing. For DIDP, the draft review report refers to a recent two-year carcinogenicity study by Cho et al. (2008), for which the LOAEL was concluded to be 22 mg/kg bw/day, based on spongiosis hepatis.

The overall assessment of DINP and DIDP as major alternatives indicates that they may cause liver effects at lower doses than developmental reproductive effects.

As to the hazardous properties of the alternatives other than DINP and DIDP, their overall assessment indicates that they do not pose a comparable or additional risk compared to the four phthalates DEHP, DBP, BBP and DIBP. For some of the endpoints (other than reprotoxicity) some of the alternatives may also be harmful to health or the environment, but since none is classified and the effects of the most used phthalates are less significant compared to the four phthalates, it can be assumed that using the alternatives instead of the four phthalates in question will result in an overall benefit. Uncertainties remain, though, as the BD does not contain an in-depth assessment of all human health endpoints (e.g. carcinogenicity) for each of the substances.

Practicality, including enforceability

Given that RAC considered the proposed restriction (and the other RMOs presented in the BD) not justified, the practicality (including enforceability) of it is no longer relevant.

Monitorability

Given that RAC considered the proposed restriction (and the other RMOs presented in the BD) not justified, the monitorability of it is no longer relevant.

BASIS FOR THE OPINION

The Background Document, provided as a supportive document, gives the detailed grounds for the opinions.

Following combined exposure to the four phthalates from direct contact to articles and from indirect exposure to articles via indoor air and dust and food, RCR values >1 have been identified in the BD, some of which are only slightly above 1. It is difficult, however, to judge how high the risks actually are, given the uncertainties and degree of conservatism in the exposure estimates for articles, food and indoor environment. RAC therefore concluded that the biomonitoring data available on the four phthalates are more reliable for risk identification.

RAC acknowledged that based on biomonitoring data from before 2008 there could be a risk from the combined exposure to the four phthalates, both for children and for adults, although the RCRs calculated are not much above 1. More recent biomonitoring data are not available at the moment (RAC is aware of some ongoing biomonitoring studies), making it difficult for RAC to quantify the present day risk. But the steady decline observed over the last decades in both tonnages of the four phthalates used in Europe (for instance 35% over the period 2007-2009/2010) and their body burden, plus the clear indications for a continuation of this decline up to the 2012 situation, will result in considerably lower RCRs. RAC concluded that the data available do not indicate that currently (2012) there is a risk from combined exposure to the four phthalates, and therefore considered action on a Community-wide basis in the form of the proposed restriction (or any of the other proposed RMOs) not justified. The regulatory requirements and consequent reduction in use will further reduce the risk, as will the authorisation requirements imposed on these phthalates in the next few years.

Conclusion: The opinion of RAC does not support the restriction proposed in the Annex XV report submitted by Denmark.

RAC recommends that the developments on the four phthalates (in market trends, use, body burden based on biomonitoring, content in and migration from articles, etc.) should be monitored within an appropriate time period.