COMMITTEE ON TOXICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

COT STATEMENT ON DIETARY EXPOSURE TO PHTHALATES – DATA FROM THE TOTAL DIET STUDY (TDS)

Introduction

1. A recent study funded by the Food Standards Agency (FSA) has looked for the presence of phthalate diesters, a few phthalate monoesters and phthalic acid in Total Diet Study (TDS) samples from 2007. The results will be published in a Food Safety Information Sheet (FSIS) at: http://www.food.gov.uk/science/surveillance/.

2. The Committee was invited to consider the potential risk to consumers at the levels of dietary exposure estimated from this survey and to advise on whether the levels of phthalate esters in foods were a health concern. Potential health concerns are mainly based upon the endocrine effects of phthalates.

Phthalate esters

3. Phthalate esters (phthalates) are the dialkyl or monoalkyl esters of phthalic acid. Phthalates have a variety of industrial uses, including as plasticizers that impart flexibility and durability to polyvinyl chloride (PVC) products. Phthalates may be present in food due to their widespread presence as environmental contaminants or due to migration from food contact materials. They are found in a wide range of household and consumer goods - for example, lubricating oils, solvents, and personal care products. When incorporated into PVC, phthalates are not covalently bound and are therefore easily released into the environment, leading to animal and human exposure.

Use of phthalates in food contact materials

4. In Europe there has been a move away from use of phthalates in flexible packaging (e.g. cling film), but they are still used in plastic tubing and flexible hoses in food processing equipment. Historically, phthalates have been used to soften the

seals on food jars so that they repeatedly give a good seal between the glass jar and the lid for "twist-on, twist-off" type lids. However, such use has largely been replaced, particularly in containers for fatty types of food.

5. The use of certain phthalates is permitted by EU legislation on food contact plastics (Directive 2002/72/EC as amended). In the EU, restrictions have been imposed on 5 particular phthalates, by Commission Directive 2007/19/EC, amending Directive 2002/72/EC. The use of di-butylphthalate (DBP), di(2-ethylhexyl)phthalate (DEHP), butylbenzylphthalate (BBP), di-isononylphthalate (DINP) and di-isodecylphthalate (DIDP) are subject to restriction by that Directive. The restrictions specify the scope of use that is permitted and maximum permitted specific migration limit* (SML) for each compound. These restrictions have been fully implemented in UK law for the protection of UK consumers.

Previous COT evaluations

6. In 1996, the COT considered levels of phthalates in infant formulae that had been recorded in surveillance conducted by the Ministry of Agriculture, Fisheries and Food (MAFF). The Committee concluded that the levels of total phthalates found in the survey of infant formulae were unlikely to pose any risk to the health of infants, but that it would be wise to ensure adequate safety margins. Given the widespread distribution of phthalates and their occurrence in the ingredients of infant formulae, it was considered unlikely that it would be possible to eliminate phthalates from infant formulae altogether.

7. More recently (May 2010) the Committee considered information from a report by the Danish Environmental Protection Agency (EPA) on time trends in exposure to phthalates from a variety of sources, including diet, and potential risks to health. The Committee focused its discussions on the exposure estimates and toxicological endpoints used in the risk assessments for each substance.

8. In addition, at the COT meeting in June 2010, data were presented from Scandinavia on phthalate exposure from rubber clogs. The information provided to COT on this topic can be accessed at http://cot.food.gov.uk/pdfs/tox201016.pdf

Previous evaluations by other scientific committees

9. In 1995 the European Commission's Scientific Committee for Food (SCF, 2005) set temporary Tolerable Daily Intakes (t-TDIs) for DBP and BBP, a Tolerable

* A specific migration limits (SML) is defined as the maximum permitted amount of a given substance that can be released from a material or article into food or food simulant.

Daily Intake (TDI) for DEHP, and a group TDI for DINP with DIDP (see Table 1). A group TDI is used if exposure to more than one member of a structurally related family of chemicals is likely to occur frequently, and the chemicals have been demonstrated to have a common target organ and the same mode of action.

10. In 2005 the Scientific Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food (AFC) of the European Food Safety Authority (EFSA) was asked to re-evaluate DBP, BBP, DEHP, DINP and DIDP for use in the manufacture of food contact materials[1,2,3,4,5]. The AFC panel revised the previous t-TDIs and TDIs for the phthalates under consideration; furthermore the Panel concluded that a group TDI was inappropriate[5] (see Table 1 below).

11. A TDI for DEP has not been set by SCF or EFSA but DEP was reviewed by the World Health Organisation (WHO) in a Concise International Chemical Assessment Document (CICAD) in 2003, which proposed a TDI of 0.5 mg/kg bw/day[6].

12. TDIs are not available for the other phthalates measured in the FSA survey samples.

Table 1: Previously established Tolerable Daily intake levels for phthalates

Phthalate	Previous TDI (SCF, 1995) mg/kg bw/day	Current TDI, EFSA 2005 mg/kg bw/day	Current TDI, CICAD 2003 mg/kg bw/day
DBP	0.05 (t-TDI)	0.01	
DEHP	0.05	0.05	
BBP	0.01(t-TDI)	0.50	
DINP	0.15 (group-TDI with DIDP)	0.15	
DIDP	0.15 (group-TDI with DINP)	0.15	
DEP	n/a	n/a	0.50

Di-butylphthalate (DBP)

14. The EFSA Panel concluded that effects on reproduction and development were the most sensitive end-points on which to base its risk assessment for DBP, noting that previous reviews had identified as pivotal several rat reproduction studies conducted in the last decade, which gave NOAELs or LOAELs in the region of 50 mg/kg bw/day. The critical effect in these studies was male reproductive development. Among the studies on reproduction and developmental toxicity considered by the Panel, a study by Lee *et al*., 2004[7] showed effects at the lowest

exposure levels and was considered the most appropriate basis on which to establish a TDI[1].

15. In the study by Lee *et al*.[7] maternal rats were given DBP at dietary concentrations of 0, 20, 200, 2000 and 10000 mg/kg during the period from late gestation (gestational day (GD) 15) to the end of lactation on postnatal day (PND) 21. At PND 21, a reduction in spermatocyte development was observed in males, with a decreased number of spermatocytes at dietary concentrations of 20 mg/kg and higher, and increased incidence and/or severity at the higher doses. At postnatal week (PNW) 11, loss of germ cell development was significant at 2000 mg/kg and above in males. This effect differed markedly in severity between animals. Significant increases in vacuolar degeneration in the mammary glands of males were present at dietary concentrations of 20 mg/kg and higher, but with a similar incidence and degree of change across the dose groups. In this study, effects were noted at the lowest dietary concentration - 20mg/kg in the maternal diet equivalent to 1.5-3.0 mg/kg bw/day with default assumptions regarding consumption of feed.

16. Thus, a TDI for DBP of 0.01 mg/kg bw was established by EFSA (2005)[1] based upon a LOAEL of 2 mg/kg bw/day and an uncertainty factor of 200 (twice the normal default factor of 100 because the TDI was derived from a LOAEL).

17. The LOAEL of 2 mg/kg bw/day in the study by Lee *et al.* (2004) was much lower than the NOAELs observed in other studies, which were in the region of 50 mg/kg bw/day. The Committee noted that the study measured a lot of endpoints, not all of which were considered to be relevant, in rather small groups of animals. The effects on testicular spermatocyte development were reversible with continued dosing and lacked clear dose-dependence. The reported mammary gland effects did not accord with other findings since they would be expected to result from an androgenic activity, whereas DBP was anti-androgenic. However some of the reported effects were plausible. After detailed discussion, it was agreed that the findings of the Lee *et al* (2004) study could not be dismissed.

18. The Committee considered relevant studies[8,9,10] reported since the 2005 review by EFSA and concluded that they did not indicate a need to modify the TDI.

Di(2-ethylhexyl)phthalate (DEHP)

19. The EFSA Panel concluded that effects on reproduction and development were the most sensitive end-points on which to base its risk assessment, noting that the available data demonstrated that exposure to DEHP affects both fertility and reproduction in rodents of both sexes, and also produces developmental effects in offspring. In males, DEHP induces severe testicular effects, including testicular

atrophy. Developing male rats have been found to be more sensitive to DEHP-induced testicular toxicity than sexually mature animals[11,12]. The onset of the lesion in young animals is also more rapid. Irreversible effects can occur in rats exposed prenatally and during suckling[13].

20. The EFSA Panel considered a study by Wolfe and Layton (2003)[14] to be more robust than those underpinning the TDI set by the SCF, based on reproductive toxicity, and noted that the methodology used in this study largely complied with Organisation for Economic Co-operation and Development (OECD) Guideline 416. A NOAEL of 5 mg/kg bw/day for testicular toxicity and developmental toxicity was identified from the Wolfe and Layton (2003) study[14], from which the Panel established a TDI of 0.05 mg/kg bw/day, using an uncertainty factor of 100.

21. The Committee considered relevant studies[15,16,17,18] reported since the 2005 review by EFSA and concluded that they did not indicate a need to modify this TDI.

Butylbenzylphthalate (BBP)

22. The EFSA Panel concluded that effects on reproduction and development were the most sensitive end-points on which to base its risk assessment for BBP. They noted that previous reviews had identified as pivotal several rat reproduction studies conducted in the last decade, which gave NOAELs or LOAELs in the region of 20-100 mg/kg bw/day, the critical effect being on male reproductive development. From the literature assessed by the Panel, a study by Tyl *et al.* (2001, 2004)[19,20] was identified as the most appropriate basis for establishing a TDI. This found testicular toxicity and the presence of reduced ano-genital distance (AGD) in F1 and F2 males at birth at a dose of 250 mg/kg bw/day, (NOAEL 50 mg/kg bw/day).

23. Based upon this NOAEL the EFSA Panel established a TDI for BBP of 0.5 mg/kg bw, applying an uncertainty factor of 100.

24. The Committee found one relevant study[21] that had been reported since the 2005 review by EFSA, but concluded that it did not indicate a need to modify the TDI.

Di-isononylphthalate (DiNP)

25. The EFSA Panel concluded that effects on liver, reproduction and development were the endpoints upon which to base its risk assessment for DiNP, noting that earlier reviews of phthalates had identified as pivotal several rat reproduction studies conducted in the previous decade, which gave NOAELs or

LOAELs in the region of 15-150 mg/kg bw/day. The pivotal toxicological effect for risk assessment for DiNP in humans was considered to be hepatic changes, unrelated to peroxisome proliferation, which had been seen in several studies (peroxisome proliferation is rodent specific and therefore not considered relevant for human risk assessment).

26. In a two-year chronic toxicity study in Fischer 344 rats at dietary concentrations of up to 6000 mg/kg, relative testis weights were statistically significantly increased at high doses, with or without concomitant increases in absolute testis weights and decreases in body weights [22]. There was a dose-related increase in relative organ weights of liver and kidney in both males and females with clear NOAELs of 15 and 18 mg/kg bw/day for males and females respectively. In addition to the increased liver and kidney weights at the LOAELs of 152 and 184 mg/kg bw/day for females and males, respectively, the males had an increased incidence of spongiosis hepatis and elevated serum levels of alkaline phosphatase and transaminases. This study was determined to be key.

27. The EFSA Panel agreed to use the NOAEL of 15 mg/kg bw/day for chronic hepatic (non-peroxisomal proliferation-related) and renal effects in establishing a TDI. Using this NOAEL and an uncertainty factor of 100, a TDI of 0.15 mg/kg bw was established for DiNP.

28. The Committee did not identify any relevant new literature indicating effects of DiNP at lower doses, and therefore found no basis to revise the EFSA TDI.

Di-isodecylphthalate (DiDP)

29. The EFSA Panel concluded that effects on liver, reproduction and development were the end points upon which to base their risk assessment, noting that preceding reviews of phthalates had identified as pivotal several rat reproduction studies conducted in the previous decade, which gave NOAELs or LOAELs in the region of 15-150 mg/kg bw/day.

30. In a 13-week study in dogs consuming DiDP at dietary concentrations of 500, 3,000 and 10,000 mg/kg, liver changes (swollen and vacuolated hepatocytes and dose-related increases in liver weight) were seen at the two higher dose levels[23]. A NOAEL of 15 mg/kg bw/day was identified by the study authors.

31. Based on the liver effects in dogs (a species considered insensitive to peroxisome proliferators), with a NOAEL of 15 mg/kg bw/day, and on a decrease in F2 offspring survival in rodent studies with a NOAEL of 33 mg/kg bw/day, a lowest overall NOAEL of 15 mg/kg bw/day was identified. An uncertainty factor of 100 was

applied to the lowest NOAEL of 15 mg/kg bw/day and a TDI of 0.15 mg/kg bw was established.

32. The Committee found one relevant study[24] reported since the 2005 review by EFSA, and concluded that it did not indicate a need to modify the TDI set by the EFSA Panel.

Di-ethylphthalate (DEP)

33. In 2003 the WHO CICAD review concluded that developmental effects were the most relevant endpoint upon which to base their risk assessment.

34. In a study in which DEP was administered at 500, 1600 or 5600 mg/kg bw/day by intra-peritoneal (*i.p.*) injection to pregnant ICR mice from days 0 to 17 of gestation[25], a significant reduction in thymus weight and non-significant (7%) reduction in the spleen weight (not considered adverse) was observed in all dose groups of dams relative to controls. Additionally, the weights of the adrenal glands and kidneys of dams were increased in the highest dose group. A dose of 1600 mg/kg bw/day was identified as the NOAEL for effects on both the mother and the offspring. A lower NOAEL of 750 mg/kg bw/day was identified from a study in which DEP was administered by oral gavage[26], but because only a single dose level had been used, the WHO review did not consider the NOAEL to be sufficiently robust.

35. A TDI of 0.5 mg/kg bw/day was proposed from the NOAEL of 1600 mg/kg bw/day[25] for developmental effects, with an uncertainty factor of 300; 3 for incompleteness of the database and another 10 each for intra- and interspecies variation. No comment was made by the authors on the relevance of the *i.p*. route of administration.

36. The Committee considered relevant studies[27,28,29] reported since the 2003 review by WHO and concluded that they did not indicate a need to modify the TDI proposed by WHO. Members set aside reports of hepatocellular changes associated with peroxisome proliferation, which were not considered relevant for risk assessment since humans are relatively non-susceptible to this effect. The study identified as relevant[27], reported reproductive/developmental effects with a NOAEL (1500 mg/kg bw/day) in the same order as that used for the basis of the assessment by WHO CICAD.

The Total Diet study

Analytical methodology and levels in food

37. The TDS is an important part of the UK Government's surveillance programme for chemicals in food and has been carried out regularly since 1966. Results from the TDS are used to estimate dietary exposures of the general UK population to chemicals in food (including both nutrients and contaminants) to identify trends in exposure, and to make assessments of the safety and quality of the food supply.

38. The design of the UK TDS has been described in detail elsewhere[30]. It involves collecting 119 categories of food from retail outlets in each of 24 towns. Food groups from each town are then pooled into 20 groups of similar foods for analysis. The relative proportion of each food category within a group reflects its importance in the average UK household diet and for the 2007 TDS is largely based on an average of three previous years (2003-2005) of consumption data from the Expenditure and Food Survey. Foods are grouped so that commodities known to be susceptible to contamination (e.g. offal, fish) are kept separate, as are foods which are consumed in large quantities (e.g. bread, potatoes, milk) (see footnote to table 2).

39. Samples from the 2007 TDS were analysed by Food and Environment Research Agency (FERA) using gas chromatography-mass spectrometry. FERA had not previously analysed all of the phthalate diesters, nor any of the monoesters of phthalic acid, nor phthalic acid itself, in foods that were analysed in the TDS samples. Accordingly, the existing methodology for the diesters needed to be validated for the additional chemicals, and a method for the monoesters and phthalic acid had to be developed. In addition to analysing the individual phthalates, a separate analysis was carried out for total phthalates. For this purpose, portions of the samples were first treated chemically to convert all phthalate diesters and monoesters (including any present that were not analysed individually) and phthalic acid to dimethyl phthalate, which was then analysed as an index of total phthalates.

40. The phthalate esters that were analysed, and those detected in the samples, are presented in Table 2.

Table 2: Phthalate esters detected in recent FSA survey.

Chemical	Abbrev.	Number of the 20 food groups in which the phthalate was detected
Diesters:		
Dimethyl phthalate	DMP	0
Diethyl phthalate	DEP	2 (1 confirmed*)
Diisopropyl phthalate	DiPP	0
Diallyl phthalate	DiAP	0
Diisobutyl phthalate	DiBP	9 (4 confirmed*)
Di-n-butyl phthalate	DBP	10 (7 confirmed*)
Di-n-pentyl phthalate	DPP	0
Di-n-hexyl phthalate	DHP	0
Benzyl butyl phthalate	BBP	1 (confirmed*)
Dicyclohexyl phthalate	DCHP	2 (neither confirmed*)
Di-(2-ethylhexyl) phthalate	DEHP	11 (all confirmed*)
Diheptyl phthalate	DHpP	0
Dioctyl phthalate	DOP	0
n-Octyl-n-decyl phthalate	ODP	0
Diisononyl phthalate	DINP	0
Diisodecyl phthalate	DIDP	0
Di-n-decyl phthalate	DDP	0
Monoesters:		
Monoisopropyl phthalate	MiPP	0
Monoisobutyl phthalate	MiBP	0
Mono-n-butyl phthalate	MnBP	3 (all confirmed*)
Mono-n-pentyl phthalate	MPP	0
Monocyclohexyl phthalate	MCHP	0
Monobutyl phthalate	MBP	0
Mono-(2-ethylhexyl) phthalate	MEHP	1 (confirmed*)
Mono-n-octyl phthalate	MOP	0
Monoiisononyl phthalate	MiNP	0
Others:		
Phthalic acid	PA	16 (10 confirmed*)
'Total' phthalates	TPh	20 (all confirmed*)

Notes

* The Standard Operating Procedure used gives confirmation criteria (retention times and ion ratios) that must be met for the response to be confirmed as due to that substance. Lack of confirmation may be due to:

- A response being observed in the quantifying ion but not in the second and/or third ion as the response is low and therefore the ion ratios are not met
- The analyte co-eluting with an interference that contributes to one of the ions monitored so that the ion ratios fail. In this situation it is not known how much, if any, of the response is due to the analyte of interest or none.

Where a phthalate was detected but not confirmed it has been considered a detect in order to calculate exposures throughout this paper.

- The limit of detection (LOD) for each phthalate varies between each of the 20 food groups analysed.
- The 20 food groups analysed were: Bread, Miscellaneous Cereals, Carcase Meat, Offal, Meat Products, Poultry, Fish, Oils and Fats, Eggs, Sugar and Preservatives, Green Vegetables, Potatoes, Other Vegetables, Canned Vegetables, Fresh Fruit, Fruit Products, Beverages, Milk, Dairy Products and Nuts.

Dietary exposure methodology

41. In general the FSA adopts a hierarchical or tiered approach to select the most relevant method for exposure assessment. The assessment methodology is consistent with the approach adopted by the European Food Safety Authority[31] and the World Health Organization[32], and used deterministic and distributional methods.

42. The dietary exposure assessments reported for the 2007 TDS were based on combining phthalate concentration data with corresponding consumption data from the National Diet and Nutrition Survey (NDNS). Dietary exposures to phthalate esters from the TDS were estimated for the following categories: toddlers (1.5 - 4.5 years)[33], young people (4 - 18 years)[34], adults (19 - 64 years)[35], elderly (over 65 years, free living and institutional)[36].

43. The exposure assessments were performed using a bespoke FSA in-house software package known as the Intake Programme. Participants in the NDNS keep a diary of their food consumption, from which calculations are made of the total amount of each food group that each individual consumed. With the assumption that each food group contained a phthalate at the concentration at which it was measured in the TDS, an estimate was made of the total daily amount of the phthalate that each participant consumed. From the distribution of estimated exposures across all participants, high-level (97.5th percentile) exposures were then derived, which represent estimated exposures for individuals who are among the highest consumers of the phthalates. Where a phthalate could not be detected in one or more food groups, two alternative calculations were made. In the first estimate, all undetectable concentrations were assumed to be zero (lower bound), and in the second, they were all assumed to be at the limit of detection for the method of assay (upper bound). High-level exposures were then each expressed as a range, with the lower bound derived under the first assumption and the upper bound under the second.

Estimated dietary exposures to phthalates

44. Table 3 provides a summary of the 97.5th percentile dietary exposures estimated for phthalates identified in the 2007 TDS food categories (food groups not measured were not considered individually in the exposure assessments). Tables 4 a, b and c present exposures from the major contributing food groups in which phthalates were detected, as well as total dietary exposures.

Table 3: Estimated high-level dietary exposure (97.5th percentile) to phthalates from the whole diet

Survey population	Estimated 97.5th percentile dietary exposure (µg/kg bodyweight/day)									
	Diesters							Monoesters		
	DEP	DiBP	DBP	BBP	DCHP	DEHP	PA	MnBP	MEHP	TPh[a]
Toddlers:										
Age >1.5-2.5	0.3 - 0.8	1.4 - 2.7	0.4 – 1.0	0.07 - 1.3	0.04 - 0.8	6.9 - 9.9	0.02 - 0.02	0.4 - 2.4	0.19 - 2.9	20.2
Age >2.5-3.5	0.3 - 0.8	1.3 - 2.1	0.4 - 0.8	0.07 - 1.1	0.04 - 0.6	6.3 - 7.9	0.01 - 0.02	0.33 - 2.0	0.2 - 2.3	18.1
Age >3.5-4.5	0.3 - 0.7	1.2 – 2.0	0.4 - 0.8	0.07 – 1.0	0.04 - 0.5	5.7 - 6.8	0.01 - 0.01	0.3 -1.7	0.19 – 1.9	15.8
Young People										
Age - 4-6 years	0.2 - 0.6	1.0 - 1.8	0.4 - 0.7	0.06 - 0.9	0.03 - 0.4	5.5 - 6.7	0.009 - 0.012	0.28 - 1.6	0.21 - 1.7	13.9
Age - 7-10 years	0.2 - 0.5	0.9 - 1.5	0.3 - 0.6	0.05 - 0.7	0.02 - 0.3	4.6 - 5.2	0.007 - 0.009	0.24 - 1.3	0.18 - 1.4	11.5
Age - 11-14 years	0.13 - 0.4	0.7 - 1.1	0.2 - 0.4	0.04 - 0.5	0.02 - 0.2	3.4 - 4	0.005 - 0.007	0.18 - 0.9	0.13 - 1.1	8.4
Age - 15-18 years	0.12 - 0.3	0.6 – 1.0	0.2 - 0.3	0.03 - 0.4	0.01 - 0.2	2.7 - 3.2	0.004 - 0.005	0.14 - 0.8	0.15 - 0.9	6.7
Adults	0.15 - 0.3	0.6 – 0.9	0.2 - 0.3	0.04 - 0.5	0.03 - 0.2	3.4 - 4	0.003 - 0.007	0.15 – 0.8	0.13 – 1.0	6.4
Free living elderly	0.13 - 0.3[b]	0.5 - 0.8	0.2 - 0.3	0.03 - 0.4	0.06 - 0.2	2.4 - 2.9	0.003 - 0.005	0.14 - 0.7	0.08 - 0.8	5.8
Institutional elderly	0.13 - 0.3	0.6 – 1.0	0.2 - 0.3	0.03 - 0.4	0.04 - 0.2	2.6 - 3.1	0.003 - 0.006	0.12 - 0.7	0.04 - 0.9	6.3
TDI	500[c]	-	10[d]	500[d]	-	50[d]	-	-	-	-

Notes

[a]Total phthalates represents all phthalates present in the samples, not only those specifically targeted, and will therefore not equal the sum of the listed phthalate concentrations

[b] Range represents lower bound (undetectable concentrations were assumed to be zero) to upper bound (undetectable concentrations assumed to be at the limit of detection)

[c] WHO 2003

[d] EFSA 2005

Table 4a. Dietary exposures from selected food groups in which DEP, DiBP and DBP were detected

Age Group	Diethyl phthalate (DEP)			Di-iso-butyl phthalate (DiBP)			Di-n-butyl phthalate (DBP)		
	Total exposure (all food groups combined) (µg/kg bw/d) †	Food groups providing highest exposure in which phthalate was detected	Upper bound exposure from contributing food group (µg/kg bw/d)	Total exposure (all food groups combined) (µg/kg bw/d) †	Food groups providing highest exposure in which phthalate was detected	Upper bound exposure from contributing food group (µg/kg bw/d)	Total exposure (all food groups combined) (µg/kg bw/d) †	Food groups providing highest exposure in which phthalate was detected	Upper bound exposure from contributing food group (µg/kg bw/d)
Toddlers (>1.5 - 2.5 years old)	0.3 - 0.8 [a]	Misc. Cereals	0.18	1.4 - 2.7	Misc. Cereals	1.11	0.4 - 1.0	Beverages	0.26
		Green Veg.	0.15		Bread	0.11		Misc. Cereals	0.19
		-	-		Meat Products	0.11		Bread	0.11
Toddlers (>2.5 - 3.5 years old)	0.3 - 0.8	Misc. Cereals	0.17	1.3 - 2.1	Misc. Cereals	1.04	0.4 - 0.8	Beverages	0.20
		Green Veg.	0.16		Bread	0.11		Misc. Cereals	0.18
		-	-		Meat Products	0.11		Bread	0.11
Toddlers (>3.5 - 4.5 years old)	0.3 - 0.7	Misc. Cereals	0.16	1.2 - 2.0	Misc. Cereals	0.96	0.4 - 0.8	Beverages	0.17
		Green Veg.	0.15		Bread	0.11		Misc. Cereals	0.16
		-	-		Meat Products	0.10		Bread	0.10
Young People (4-6 years old)	0.2 - 0.6	Misc. Cereals	0.15	1.0 - 2.0	Misc. Cereals	0.88	0.4 - 0.7	Misc. Cereals	0.15
		Green Veg.	0.12		Bread	0.11		Beverages	0.12
		-	-		Meat Products	0.10		Bread	0.11
Young People (7-10 years old)	0.2 - 0.5	Misc. Cereals	0.14	0.9 - 1.5	Misc. Cereals	0.84	0.3 - 0.6	Misc. Cereals	0.14
		Green Veg.	0.10		Bread	0.09		Beverages	0.09
		-	-		Meat Products	0.07		Bread	0.09
Young People (11-14 years old)	0.13 - 0.4	Misc. Cereals	0.10	0.7 - 1.1	Misc. Cereals	0.61	0.2 - 0.4	Misc. Cereals	0.10
		Green Veg.	0.06		Bread	0.07		Beverages	0.07
		-	-		Meat Products	0.06		Bread	0.07
Young People (15-18 years old)	0.12 - 0.3	Misc. Cereals	0.09	0.6 - 1.0	Misc. Cereals	0.52	0.2 - 0.3	Misc. Cereals	0.09
		Green Veg.	0.07		Bread	0.06		Beverages	0.07
		-	-		Meat Products	0.05		Bread	0.06
Adults	0.15 - 0.3	Green Veg.	0.09	0.6 - 1.0	Misc. Cereals	0.40	0.2 - 0.3	Beverages	0.09
		Misc. Cereals	0.07		Bread	0.05		Misc. Cereals	0.07
		-	-		Meat Products	0.04		Bread	0.05

Notes

† Range represents lower bound (undetectable concentrations were assumed to be zero) to upper bound (undetectable concentrations assumed to be at the limit of detection).

- Indicates the lack of further major contributing food groups or food groups in which phthalates were detected

Due to the methodology employed in the calculation of chronic exposure assessments, a sum of exposures caused by each major contributing food group will not equal the total exposure to a particular phthalate, nor will any percentages based on these calculations.

Table 4b Dietary exposures from selected food groups in which BBP, DCHP and DEHP were detected

Age Group	Benzyl-butyl phthalate (BBP)			Dicyclohexyl phthalate (DCHP)			Di-(2-ethylhexyl) phthalate (DEHP)		
	Total exposure (all food groups combined) (µg/kg bw/d)†	Food groups providing highest exposure in which phthalate was detected	Exposure from contributing food group (µg/kg bw/d)	Total exposure (all food groups combined) (µg/kg bw/d)†	Food groups providing highest exposure in which phthalate was detected	Exposure from contributing food group (µg/kg bw/d)	Total exposure (all food groups combined) (µg/kg bw/d)†	Food groups providing highest exposure in which phthalate was detected	Exposure from contributing food group (µg/kg bw/d)
Toddlers (>1.5 - 2.5 years old)	0.1 - 1.3	Bread	0.05	0.0 - 0.8	Offal	0.44	6.9 - 9.9	Dairy	5.5
		-	-		Fish	0.03		Fish	3.86
		-	-		-	-		Meat Products	1.96
		-	-		-	-		Misc. Cereals	1.62
Toddlers (>2.5 - 3.5 years old)	0.1 - 1.1	Bread	0.05	0.0 - 0.6	Offal	0.32	6.3 - 7.9	Fish	2.87
		-	-		Fish	0.02		Dairy	2.68
		-	-		-	-		Meat Products	1.99
		-	-		-	-		Poultry	1.48
Toddlers (>3.5 - 4.5 years old)	0.1 - 1.0	Bread	0.05	0.0 - 0.5	Offal	*	5.7 - 6.8	Fish	2.36
		-	-		Fish	0.02		Meat Products	1.90
		-	-		-	-		Dairy	1.82
		-	-		-	-		Misc. Cereals	1.33
Young People (4-6 years old)	0.1 - 0.9	Bread	0.06	0.0 - 0.4	Offal	*	5.5 - 6.7	Fish	2.21
		-	-		Fish	0.02		Meat Products	1.73
								Dairy	1.50
		-	-		-	-		Poultry	1.38
Young People (7-10 years old)	0.1 - 0.7	Bread	0.04	0.0 - 0.3	Offal	0.10	4.6 - 5.2	Fish	1.90
		-	-		Fish	0.02		Meat Products	1.23
		-	-		-	-		Misc. Cereals	1.09
		-	-		-	-		Poultry	1.07
Young People (11-14 years old)	0.0 - 0.5	Bread	0.03	0.0 - 0.2	Offal	0.09	3.4 - 4.0	Fish	1.45
		-	-		Fish	0.01		Meat Products	1.16
		-	-		-	-		Poultry	0.82
		-	-		-	-		Misc. Cereals	0.78
Young People (15-18 years old)	0.0 - 0.4	Bread	0.03	0.0 - 0.2	Offal	*	2.7 - 3.2	Fish	1.11
		-	-		Fish	0.01		Meat Products	0.89
		-	-		-	-		Poultry	0.89
		-	-		-	-		Misc. Cereals	0.67
Adults	0.0 - 0.5	Bread	0.03	0.0 - 0.2	Offal	0.08	3.4 - 4.0	Fish	1.50
		-	-		Fish	0.01		Meat Products	0.80
		-	-		-	-		Poultry	0.78

Notes

† Range represents lower bound (undetectable concentrations were assumed to be zero) to upper bound (undetectable concentrations assumed to be at the limit of detection).

- Indicates the lack of further major contributing food groups or food groups in which phthalates were detected

* Indicates that although phthalate was detected in offal, there was insufficient consumption to allow calculation of a 97.5th percentile consumption value for this age group. However, were there to be sufficient consumers, exposures would probably be be similar to those of other age groups within the same survey population.

Table 4c: Dietary exposures from selected food groups in which MnBP, MEHP and TPh were detected

Age Group	Mono-n-butyl phthalate (MnBP)			Mono-(2-ethylhexyl) phthalate (MEHP)			Total Phthalates (TPh)‡		
	Total exposure (all food groups combined) (µg/kg bw/d)†	Food groups providing highest exposure in which phthalate was detected	Exposure from contributing food group (µg/kg bw/d)	Total exposure (all food groups combined) (µg/kg bw/d)†	Food groups providing highest exposure in which phthalate was detected	Exposure from contributing food group (µg/kg bw/d)	Total exposure (all food groups combined) (µg/kg bw/d)	Food groups providing highest exposure in which phthalate was detected	Exposure from contributing food group (µg/kg bw/d)
Toddlers (>1.5 - 2.5 years old)	0.4 - 2.4	Carcase Meat	0.23	0.2 - 2.9	Poultry	0.21	19.8	Fruit Products	9.74
		Fish	0.22		-	-		Beverages	5.81
		Meat Products	0.19		-	-		Milk	5.26
Toddlers (>2.5 - 3.5 years old)	0.3 - 2.0	Carcase Meat	0.19	0.2 - 2.3	Poultry	0.22	17.3	Fruit Products	9.17
		Meat Products	0.19		-	-		Beverages	4.48
		Fish	0.18		-	-		Misc Cereals	4.39
Toddlers (>3.5 - 4.5 years old)	0.3 - 1.7	Meat Products	0.18	0.2 - 1.9	Poultry	0.23	14.8	Fruit Products	7.00
		Carcase Meat	0.17		-	-		Misc Cereals	4.04
		Fish	0.16		-	-		Beverages	3.83
Young People (4-6 years old)	0.3 - 1.6	Meat Products	0.17	0.2 - 1.7	Poultry	0.23	13.9	Fruit Products	6.37
		Fish	0.15		-	-		Misc Cereals	3.69
		Carcase Meat	0.12		-	-		Beverages	2.62
Young People (7-10 years old)	0.2 - 1.3	Fish	0.13	0.2 -1.4	Poultry	0.18	11.5	Fruit Products	4.68
		Meat Products	0.12		-	-		Misc Cereals	3.55
		Carcase Meat	0.11		-	-		Beverages	2.08
Young People (11-14 years old)	0.2 - 0.9	Meat Products	0.11	0.1 - 1.1	Poultry	0.14	8.4	Fruit Products	3.27
		Fish	0.10		-	-		Misc Cereals	2.54
		Carcase Meat	0.09		-	-		Beverages	1.64
Young People (15-18 years old)	0.1 - 0.8	Meat Products	0.09	0.2 - 0.9	Poultry	0.15	6.7	Fruit Products	2.40
		Carcase Meat	0.08		-	-		Misc Cereals	2.18
		Fish	0.07		-	-		Beverages	1.62
Adults	0.2 - 0.8	Fish	0.10	0.1 - 1.0	Poultry	0.13	6.4	Beverages	1.97
		Meat Products	0.08		-	-		Fruit Products	1.83
		Carcase Meat	0.07		-	-		Misc Cereals	1.69

Notes

† Range represents lower bound (undetectable concentrations were assumed to be zero) to upper bound (undetectable concentrations assumed to be at the limit of detection).

‡ Total phthalates represents all phthalates present in the samples, not only those specifically targeted, and will therefore not equal the sum of the listed phthalate exposures. Range of exposures is not displayed for total phthalates as a detect was confirmed in all 20 food groups.

- Indicates the lack of further major contributing food groups or food groups in which phthalates were detected

Due to the methodology employed in the calculation of chronic exposure assessments, a sum of exposures caused by each major contributing food group will not equal the total exposure to a particular phthalate, nor will any percentages based on these calculations.

45. Of the phthalate esters detected, DEHP was associated with the highest dietary exposures. For DEHP, dairy products, fish, meat products and miscellaneous cereals were the major contributors to dietary exposure for the youngest and oldest toddler age groups, whilst fish, dairy products, meat products and poultry were major contributors to the middle age group. For young people, fish, meat products and poultry provided major contributions in all age groups, with the addition of dairy products in the youngest group and miscellaneous cereals in the older two. For adults, fish, meat products and poultry were identified as providing major contributions to DEHP dietary exposure.

46. The study also investigated the total amount of phthalates (TPh) present in the TDS samples. For TPh, fruit products, beverages and miscellaneous cereals were the major contributors to dietary exposure for toddlers in the two oldest age categories, whilst fruit products, beverages and milk were the major contributors in the youngest class of toddlers. For adults and all age groups of young people, fruit products, miscellaneous cereals and beverages were identified as the major contributors.

Assessment of dietary exposure to phthalates

47. For each of the phthalates detected, calculated upper bound dietary exposure relative to bodyweight was the highest for toddlers in the >1.5 to 2.5 year old age group. The upper bound total dietary DEHP exposure for this age group of toddlers was 9.9 µg/kg bw/day compared to the EFSA TDI of 50 µg/kg bw/day. For BBP, upper bound total dietary exposure for this age group was calculated as 1.3 µg/kg bw/day compared with the EFSA TDI of 500 µg/kg bw/day. For DBP, total dietary exposure for toddlers in the >1.5 to 2.5 age group was 1 µg/kg bw/day compared to the EFSA TDI of 10 µg/kg bw/day. Beverages, miscellaneous cereals and bread were highlighted as the major contributors to dietary exposure for all age groups. For DEP the upper bound total dietary exposure of toddlers aged >1.5 to 2.5 years was 0.8 µg/kg bw/day compared with the WHO TDI of 500 µg/kg bw/day.

48. Diesters of phthalates are hydrolysed to toxicologically active monoesters in the gastrointestinal tract (for example, DEHP is hydrolysed to mono-(2-ethylhexyl) phthalate (MEHP)). The Committee noted that monoester exposure measured in the TDS could be compared to the relevant TDI for each diester by converting the measured levels of monoesters to their diester equivalents using the appropriate molecular ratios. Estimates of high level dietary exposure to combinations of phthalate diesters and their corresponding monoesters converted to diester equivalents are shown in Table 5 for those phthalates for which measurements were available.

Table 5. Dietary exposures to selected phthalate diesters and their corresponding monoester converted to diester equivalents

	Estimated high level (97.5th percentile) dietary exposure (µg/kg bodyweight/day) to selected phthalate combinations		
	DEHP + MEHP converted to DEHP equivalents†	**DBP + MnBP converted to DBP equivalents†**	**DCHP + MCHP converted to DCHP equivalents†**
Toddlers:			
Age >1.5-2.5	7.2 - 13.8	0.9 - 4.0	0.04 - 2.5
Age >2.5-3.5	6.6 - 11.4	0.8 - 3.5	0.04 - 2.1
Age >3.5-4.5	6.0 - 9.6	0.8 - 3.1	0.04 - 1.7
Young People			
Age - 4-6 years	5.8 - 9.1	0.8 - 2.7	0.03 - 1.4
Age - 7-10 years	4.9 - 7.2	0.6 - 2.2	0.02 - 1.1
Age - 11-14 years	3.6 - 5.5	0.4 - 1.5	0.02 - 0.8
Age - 15-18 years	2.9 - 4.5	0.4 - 1.3	0.01 - 0.7
Adults	3.6 - 5.4	0.4 - 1.7	0.03 - 0.7
Free living elderly	2.5 - 4.0	0.4 - 1.2	0.06 - 0.7
Institutional elderly	2.7 - 4.4	0.4 - 1.2	0.04 - 0.7
	TDI for the relevant diester		
	50	10	n/a

$$\text{Total exposure} = (\text{exposure to monoester} \times \left(\frac{\text{molar mass of diester}}{\text{molar mass of monoester}}\right)) + \text{exposure to diester}$$

Notes

† Range represents lower bound (undetectable concentrations were assumed to be zero) to upper bound (undetectable concentrations assumed to be at the limit of detection).

49. The estimated dietary exposures to individual phthalates (alone or in combination with the appropriate monoester) were below the TDI for the relevant diester.

50. In addition, the Committee considered information on combined effects of phthalate esters,[37,38,39,40] and agreed that, in view of their similar structure and toxicological effects (the Committee noted that reproductive effects were seen with most, if not all, of the phthalates for which information was available), as a first tier approach, a cumulative risk assessment was appropriate, based on an assumption of dose-additivity. Due to the lack of established TDIs and limited toxicological information for many of the phthalates a hazard index or relative potency factor approach was not possible.

51. If total exposure is calculated using the estimate for total phthalate in table 3) the highest dietary exposure, for 'toddlers aged >1.5-2.5 years', is approximately double the lowest TDI i.e. that for DBP.

52. Recognising that the TDI for DBP is highly conservative, (as it is based upon a LOAEL that is much lower than the NOAELs and LOAELs identified from other rat reproduction studies), that most of the phthalates are less potent than DBP and that DBP accounts for only approximately 5% of the cumulative exposure, the Committee concluded that the estimated dietary exposures of themselves do not indicate a concern for the health of consumers. However, other sources of exposure would need to be considered in a full assessment of the phthalates.

Conclusions

53. The new data demonstrated the presence of phthalates in a range of food samples.

54. The Committee noted the TDIs set by EFSA and WHO. Members considered that the TDI for DEP established by WHO was not as robust as those established by EFSA for other phthalates, and also that the TDI for DBP was particularly conservative.

55. Evidence was reviewed from the scientific literature that had been published since these TDIs were established. This did not indicate a need to change the TDIs, which the Committee concluded should be used in assessing possible risks from dietary exposure to phthalates.

56. For each of the phthalates detected in the FSA study, calculated dietary exposures (expressed per unit body weight) were highest for toddlers in the >1.5 to 2.5 year old age group. The upper bound estimate of total dietary DEHP exposure of toddlers in this age range was 9.9 µg/kg bw/day, which was lower than the EFSA TDI of 50 µg/kg bw/day. For BBP, the upper bound estimate of total dietary exposure of this age group was 1.32 µg/kg bw/day, which was considerably below the EFSA TDI of 500 µg/kg bw/day. For DBP, the corresponding upper bound estimate of total dietary exposure was 1 µg/kg bw/day, which was lower than the EFSA TDI of 10 µg/kg bw/day. For DEP it was 0.84 µg/kg bw/day, which was considerably below the WHO TDI of 500 µg/kg bw/day. Thus, the estimated dietary exposures to the phthalates individually were not of toxicological concern.

57. Due to the fact that phthalate diesters are hydrolysed to the toxicologically active monoesters in the gastrointestinal tract, the Committee considered it appropriate to sum exposures to corresponding mono and diesters. When this was performed, the combined exposure estimates were also below the TDIs for the relevant individual diesters and were not of toxicological concern.

58. Furthermore, the Committee concluded that as a first tier approach, a cumulative risk assessment for phthalates was appropriate, based on an assumption of dose-additivity.

59. Due to the lack of data for many of the phthalates, a Hazard Index or relative potency factor approach was not possible. If total dietary exposure to all phthalates was estimated the highest level of consumer exposure (in toddlers in age >1.5 to 2.5 years) was approximately double the lowest TDI, i.e. that for DBP. Taking into account that:

- most of the phthalates are less potent than DBP
- the TDI for DBP is likely to be highly conservative
- DBP accounts for only approximately 5% of this cumulative exposure,

the Committee concluded that the estimated dietary exposures do not indicate a concern for health of consumers.

60. Overall the Committee concluded that levels of phthalates that were found in samples from the 2007 TDS do not indicate a risk to human health from dietary exposure alone, either when the compounds are considered individually, or when they are assessed in combination.

61. Other, non-dietary, sources of exposure would need to be considered in a full risk assessment for phthalates.

COT statement 2011/04
May 2011

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Abbreviations

AFC	The European Food Safety Authority Scientific Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food
AGD	Anogenital Distance
BBP	Butylbenzylphthalate
CICAD	Concise International Chemical Assessment Document
COT	Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment
CSL	Central Science Laboratory
DBP	Di-butylphthalate
DCHP	Dicyclohexyl Phthalate
DEP	Di-ethylphthalate
DEHP	Di(2-ethylhexyl)phthalate
DIDP	Di-isodecylphthalate
DINP	Di-isononylphthalate
DPP	Di-n-pentyl phthalate
EFSA	European Food Safety Authority
EPA	Environmental Protection Agency
EU	European Union
FSA	Food Standards Agency
FSIS	Food Safety Information Sheet
GD	Gestational Day
MAFF	Ministry of Agriculture, Fisheries and Food
MEHP	Mono-(2-ethylhexyl) phthalate
NDNS	National Diet and Nutrition Survey
NOAEL	No observed adverse effect level
OECD	Organisation for Economic Co-operation and Development
PND	Postnatal Day
PNW	Postnatal Week
SCF	Scientific Committee for Food
SML	Specific Migration Limits
TDI	Tolerable Daily Intake
t-TDI	Temporary Tolerable Daily Intake
TDS	Total Diet Study
TPh	Total Phthalates
WHO	World Health Organization

Phthalates Literature Search September 2010

Search conducted using – PubMed

Limits imposed on all searches – Only those papers published in or after 2004 i.e. papers not considered by EFSA in their reviews (2005)

DBP SEARCH

Search terms used – (DBP) AND (PHTHALATE) AND (TOXICITY) AND (REPRODUCTION)

Total number of results: 12

Of these, 7 were not ordered for the following reasons:

- A review paper x2
- An *in vitro* study x2
- A study which used an unsuitable species, Xenopus frogs, zebra fish x2
- A multi-component mixtures study administering DBP, 2-3, 7,8 – TCDD, vinclozolin, procymidone and linuron x1

Search terms used – (DBP) AND (PHTHALATE) AND (TOXICITY) AND (DEVELOPMENT)

Total number of results: 32

Of these, 19 were not ordered for the following reasons:

- Paper was identified in the previous search x6
- A study which used an unsuitable species (Zebrafish x3; Xenopus frog x2) x5
- A river ecotox study
- An in vitro study x4
- A statistical study based on medications as a source of exposure to phthalates
- An occupational exposure study which assessed manicurist's exposure to DBP
- A cross-sectional study which assessed exposure of DBP and DEHP in factory workers; exposure via inhalation

Search terms used – (DBP) AND (PHTHALATE) AND (TOXICITY) AND (NEURODEVELOPMENT)

Total number of results: 0

Search terms used – (DBP) AND (PHTHALATE) AND (TOXICITY) AND (REPRODUC*)

Total number of results: 59

Of these, 49 were not ordered for the following reasons:

- Paper was identified in the previous search x 31
- An *in vitro* study x11
- A review paper x3
- A study on hypothyroidism and how it protects against DBP damage
- A study assessing the potential route of exposure of DBP via fingernails
- A study assessing kolaviron and curcumin effects
- A study assessing DBP impact upon growth of a leaf vegetable

BBP SEARCH

Search terms used – (BBP) AND (PHTHALATE) AND (TOXICITY) AND (REPRODUCTION)

Total number of results: 4

Of these, 3 were not ordered for the following reasons:

- Paper was identified in the previous search x3

Search terms used – (BBP) AND (PHTHALATE) AND (TOXICITY) AND (DEVELOPMENT)

Total number of results: 5

Of these, 2 were not ordered for the following reasons:

- An *in vitro* study
- Paper was identified in the previous search

Search terms used – (BBP) AND (PHTHALATE) AND (TOXICITY) AND (NEURODEVELOPMENT)

Total number of results: 0

Search terms used – (BBP) AND (PHTHALATE) AND (TOXICITY) AND (REPRODUC*)

Total number of results: 12

Of these, 11 were not ordered for the following reasons:

- Paper was identified in the previous search x8
- A review paper x1
- Paper reported analysis of phthalates in ham sausages x1
- A multi-component mixtures study which was not specific to BBP

DEHP SEARCH

Search terms used – (DEHP) AND (PHTHALATE) AND (TOXICITY) AND (REPRODUCTION)

Total number of results: 23

Of these, 19 were not ordered for the following reasons:

- Paper was identified in the previous search x8
- An *in vitro* study x2
- A study which used an unsuitable species (Zebrafish, wild boars x 3) x4
- A review paper x3
- A study assessing exposure via inhalation
- A multi-component mixtures study which was not specific to DEHP

Search terms used – (DEHP) AND (PHTHALATE) AND (TOXICITY) AND (DEVELOPMENT)

Total number of results: 27

Of these, 13 were not ordered for the following reasons:

- Paper was identified in the previous search x9
- A review paper x2
- A microbiological study
- An *in vitro* study

Search terms used – (DEHP) AND (PHTHALATE) AND (TOXICITY) AND (NEURODEVELOPMENT)

Total number of results: 2

Of these, 1 was not ordered because of the following reason:

- A study of irrelevant mixtures

Search terms used – (DEHP) AND (PHTHALATE) AND (TOXICITY) AND (REPRODUC*)

Total number of results: 96

Of these, 82 were not ordered for the following reasons:

- Paper was identified in a previous search x36
- A review paper x17
- An *in vitro* study x12
- A study which used an unsuitable species (zebrafish) x3
- A study on effects of warming i.v. bags x2
- A study on exposure of DEHP via bloodbags x2
- A study using bacteria to measure toxicity on phthalate exposure
- A study on the methods used to analyse phthalates
- A study on DEHP and cardiac syncytium
- A study to assess phthalate concentration in soil
- A study on susceptibility to phthalate exposure with allergic conditions
- A study on seven antiandrogens and their productive malformation in rats
- A study measuring DEHT
- A population survey study of exposure to phthalates
- A study on exposure of DEHP to rats with renal dysfunction as a result of intentionally overloading the rats with folic acid
- A study assessing exposure via inhalation

DINP SEARCH

Search terms used – (DINP) AND (TOXICITY)

Total number of results: 14

Of these, 9 were not ordered for the following reasons:

- Paper was identified in a previous search on another phthalate
- A review paper x 2
- An *in vitro* study x3
- A study which used an unsuitable species (Japanese Medeka)
- A genomic microarray analysis study
- A sewage study

DIDP SEARCH

Search terms used – (DIDP) AND (TOXICITY)

Total number of results: 9

Of these, 8 were not ordered for the following reasons:

- Paper was identified in a previous search x 5
- A review paper x2
- A study which used an unsuitable species (Japanese Medeka)

DEP SEARCH

Search terms used – (DEP) AND (PHTHALATE) AND (TOXICITY)

Total number of results: 44

Of these, 39 were not ordered for the following reasons:

- Paper identified in a previous search on another phthalate x3
- A study which used an unsuitable species (Olive flounder paralichthys oliva, Abalone Haliotis diversicolor supertexta, freshwater prawn, giant freshwater prawn, freshwater fish, radish) x10
- A study examining endpoints not considered relevant to reprotoxicology, development, neurodevelopment, i.e. ??? x7
- An *in vitro* study x3
- A study which assessed DEP values in water sources x 3
- A study which assessed DEP values in soil x2
- A study which looked at an alternative phthalate x2
- A biomonitoring study x3
- A review x 3
- A study which investigated amounts of DEP in cosmetic products
- A multi-component mixtures study which was not specific to DEP x 2