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

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

1. At the meeting in November Members considered data from an FSA survey looking at the occurrence of phthalates in the Total Diet Study (TDS). Attached is a draft COT statement describing the study and the Committee's conclusions.

Questions asked of the Committee

2. Members are invited to comment on the draft statement at Annex A.

Secretariat
November 2010

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

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

DRAFT COT STATEMENT ON DIETARY EXPOSURE TO PHTHALATES

This Annex contains a copy of the draft COT statement on Dietary Exposure to Phthalates – Data from the Total Diet Study (TDS)

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

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

Introduction

1. A recent Food Standards Agency (FSA) funded study has looked for the presence of phthalate diesters, a few phthalate monoesters and phthalic acid in Total Diet Study (TDS) samples from 2007. In addition to these, retail samples of a variety of foods (fish, offal, meat, eggs, milk, dairy products, bread, cereals, fruit, vegetables, baby foods and infant formulae) on sale in the UK purchased during 2009-10 were analysed for phthalate diesters only. These 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 advise on whether the levels of phthalates in foods were a health concern.

Phthalate esters

3. Phthalate esters are the dialkyl or alkyl esters of phthalic acid. Phthalates have a variety of industrial uses, such 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, fixatives and personal care products. When incorporated into PVC, phthalates are not covalently bound and are therefore easily released into the environment, consequently resulting in animal and human exposure.

Use of phthalates in food contact materials

4. The food contact materials industry, within Europe, has moved away from use of phthalates in flexible packaging (cling film). Current uses include plastic tubing, and flexible hoses used 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 with fatty food types.

5. The use of certain phthalic acid esters (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. These restrictions have been fully implemented in UK law for the protection of UK consumers.

6. Uses of certain phthalates as plasticisers in gaskets and other plastic applications, the specific migration limits (SMLs) and restrictions vary on their use under different circumstances:

- DBP is permitted as:
  (a) plasticizer in repeated use materials and articles contacting non-fatty foods
  (b) technical support agent in polyolefines in concentrations up to 0,05 % in the final product. SML = 0,3 mg/kg food stimulant

- DEHP is permitted as:
  (a) plasticizer in repeated use materials and articles contacting non-fatty foods
  (b) technical support agent in concentrations up to 0,1 % in the final product. SML = 1,5 mg/kg food simulant.

- BBP is permitted as:
  (a) plasticizer in repeated use materials and articles
  (b) plasticizer in single-use materials and articles contacting non-fatty foods except for infant formulae and follow-on formulae as defined by Directive 91/321/EEC and products according to Directive 96/5/EC
  (c) technical support agent in concentrations up to 0,1 % in the final product. SML = 30 mg/kg food simulant.

- DINP is permitted as:
  (a) plasticizer in repeated use materials and articles

(b) plasticizer in single-use materials and articles contacting non-fatty foods except for infant formulae and follow-on formulae as defined by Directive 91/321/EEC and products according to Directive 96/5/EC
(c) technical support agent in concentrations up to 0,1 % in the final product. SML(T) = 9 mg/kg food simulant.

- DIDP is permitted as:
  (a) plasticizer in repeated use materials and articles
  (b) plasticizer in single-use materials and articles contacting non-fatty foods except for infant formulae and follow-on formulae as defined by Directive 91/321/EEC and products according to Directive 96/5/EC
  (c) technical support agent in concentrations up to 0,1 % in the final product. SML(T) = 9 mg/kg food simulant.

7. DEP and DPP have been removed from the list of positive substances that may be used in manufacturing food contact materials and articles, as industry now use other substance. These esters have previously been in printing inks used on the outside of packaging.

Previous COT evaluations

8. In 1996 based on the results of a Ministry of Agriculture, Fisheries and Food (MAFF) surveillance work on phthalates in food and infant formulae, the COT considered levels of phthalates in infant formulae. The Committee concluded that, on the basis of the evidence available, the total phthalates found in the survey of infant formulae were deemed 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.

9. More recently (May 2010) the Committee considered information from the Danish Environmental Protection Agency's (EPA) report on exposure time trends to phthalates. The Committee focused its discussions on exposure and the endpoints used for each substance's risk assessment.

10. In addition, at the COT meeting in June 2010 data from Scandinavia on phthalate exposure from rubber clogs was presented. The COT's consideration of this topic can be accessed at http://cot.food.gov.uk/pdfs/tox201016.pdf

Previous evaluations by other scientific committees

11. In 1995 the Scientific Committee for Food (SCF, 2005) set temporary Tolerable Daily Intakes (t-TDIs) for DBP and BBP, a Tolerable Daily Intake (TDI) for DEHP, and a group TDI for DINP with DIDP (see Table 1).

12. 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).

13. A TDI for di-ethylphthalate (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[6].

Table 1: Tolerable Daily intake levels for phthalates that were prevalent in FSA-funded survey

Phthalate	Previous TDI (SCF, 1995) mg/kg bw/day	Current TDI, EFSA 2005 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	0.50*

* WHO CICAD, 2003

Di-butylphthalate (DBP)

14. The EFSA Panel concluded that effects on reproduction and development were the most sensitive end-points on which to base the 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, with the critical effect being on male reproductive development. From the studies on reproduction and developmental toxicity considered by the Panel the study by Lee *et al*., 2004[7] showed effects at the lowest exposure levels and was considered the most appropriate basis for establishing a TDI[1].

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

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 (2 times the default factor of 100 due to the fact the TDI is derived from the LOAEL).

17. The Committee reviewed relevant studies[8,9,10] reported since the 2005 review by EFSA and concluded that they did not suggest a need to modify the TDI. Following detailed discussion it was agreed that the Lee *et al* (2004) study could not be dismissed. This study reports a LOAEL of 2 mg/kg bw/day, which is much lower than the NOAELs in the region of 50 mg/kg bw/day reported in other studies. 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, however the biological activity and some endpoints reported were plausible, and as such the results could not be discounted.

Di(2-ethylhexyl)phthalate (DEHP)

18. The EFSA Panel concluded that effects on reproduction and development were the most sensitive end-points on which to base the 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 occur in rats exposed prenatally and during suckling[13].

19. The Panel considered the 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 to a large extent 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.

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

Butylbenzylphthalate (BBP)

21. The EFSA Panel concluded that effects on reproduction and development were the most sensitive end-points on which to base the risk assessment for BBP, 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 20-100 mg/kg bw/day, with the critical effect being male reproductive development. From the literature assessed by the panel the Tyl *et al.* study (2001, 2004)[19,20] which reported testicular toxicity and the presence of reduced AGD in F1 and F2 males at birth at 250 mg/kg bw/day, (NOAEL 50 mg/kg bw/day), was identified as the most appropriate basis for establishing a TDI.

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

23. The Committee reviewed the relevant study[21] reported since the 2005 review by EFSA and concluded that it did not suggest a need to modify the TDI.

Di-isononylphthalate (DiNP)

24. 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. The pivotal toxicological effect for DiNP was considered to be the hepatic changes seen in various studies that were not peroxisome proliferation related effects which are rodent specific and therefore not considered relevant for human risk assessment.

25. In a two-year chronic toxicity study in Fischer 344 rats at dose levels of up to 0.6% in the diet relative testis weights were statistically significantly increased with or without concurrent increase of absolute testis weights and decrease of body weights at high doses[22]. There was a dose-related increase in relative organ weights of liver and kidney in both males and females with a clear NOAEL of 15 and 18 mg/kg bw/day for males and females respectively. In addition to the increased liver and kidney weights at the LOAEL of 152 and 184 mg/kg bw/day for females and males, respectively, the males had increased incidences of spongiosis hepatis and serum levels of alkaline phosphatase and transaminases. This study was determined to be key.

26. The 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 of an uncertainty factor of 100, a TDI of 0.15 mg/kg bw for DiNP was established.

27. No relevant new literature was identified, and therefore there was no basis for reviewing the EFSA TDI.

Di-isodecylphthalate (DiDP)

28. 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.

29. In a 13-week study in dogs consuming dose levels of 0.05, 0.3 and 1% DiDP in the diet, liver changes (swollen and vacuolated hepatocytes and dose-related increases in liver weight increases) were seen at the two higher dose levels[23]. A NOAEL of 15 mg/kg bw/day was identified by the study authors. The fact that dogs are considered to be non-responsive or refractory to peroxisome proliferation could indicate that minor liver damage found in this species occurred by a mechanism other than peroxisome proliferation.

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30. Based on the liver effects in dogs (a species considered as non-sensitive to peroxisome proliferation), with a NOAEL of 15 mg/kg bw/day and on a decrease in F2 offspring survival in rodent studies identifying a NOAEL of 33 mg/kg bw/day, a lowest overall NOAEL of 15 mg/kg bw/day was identified. From this NOAEL and applying an uncertainty factor of 100, a TDI of 0.15 mg/kg bw was established.

31. The Committee reviewed the relevant study[24] reported since the 2005 review by EFSA and concluded that it did not suggest a need to modify the TDI.

Di-ethylphthalate (DEP)

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

33. In a study administering DEP 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 spleen weight of the dams relative to controls were observed in all dose groups. Additionally the weights of the adrenal glands and kidneys of dams were increased in the highest dose group. A dose of 1600 kg body weight per 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 administering DEP by oral gavage[26], but it was not used as the WHO review noted the limitation of the study design to be that only a single dose level had been used.

34. A TDI of 0.5 mg/kg bw/day was proposed from the NOAEL of 1600 mg/kg bw/day[25] for developmental effects applying 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.

35. The Committee reviewed relevant studies[27,28,29] reported since the 2003 review by WHO and concluded that they did not suggest a need to modify the TDI.

The Total Diet study

Analytical methodology and levels in food

36. The TDS is an important part of the UK Government's surveillance programme for chemicals in food and has been carried out on a continuous annual basis since 1966. Results from the TDS are used to estimate dietary exposures of the general UK population to chemicals in food, such as nutrients and contaminants, to identify trends in exposure and make assessments on the safety and quality of the food supply.

37. The design of the UK TDS has been described in detail elsewhere[30] and involves 119 categories of foods combined 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 is largely based on an average of three previous years of consumption data from the National 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).

38. The foods making up the 20 groups of the TDS were obtained from retail outlets in 24 towns throughout the UK. Each food group obtained from each town was analysed for the phthalate monoesters and diesters of interest.

39. Samples were analysed by Food and Environment Research Agency (formerly the Central Science Laboratory (CSL)) using gas chromatography-mass spectrometry. FERA had not previously analysed all of the phthalate diesters nor any of the monoesters or phthalic acid 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 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 to represent total pthalates.

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

Table 2: Phthalate esters detected in recent FSA survey.

Chemical	Abbrev.	Number of times detected in the 20 food groups analysed
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	0
Mono-n-pentyl phthalate	MPP	0
Monocyclohexyl phthalate	MCHP	0
Monobutyl phthalate	MBP	3 (all confirmed*)
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*)

* Note: 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; therefore not confirmed 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 and as such the ion ratios will fail. In this way it is not known whether some of the contribution is due to the analyte of interest or none.

Dietary exposure methodology

41. The dietary exposure assessments reported for the 2007 TDS are based on combining phthalate concentration data following analysis of the food groups with corresponding consumption data. Consumption data from the National Diet and Nutrition Survey (NDNS) were used to estimate dietary exposures for individuals in the population who eat significantly more than average amounts (i.e. 97.5$_{th}$ percentile consumers)[31,32,33,34,].Dietary exposures to phthalate esters from the TDS were estimated for average and high level consumers under the following categories: adults (18 - 64 years), toddlers (1.5 - 4.5years), young people (4 - 18 years), elderly (over 65 years, free living and institutional) using consumption data from the relevant NDNS .

42. In general the FSA adopts a hierarchical or tiered approach to select the most relevant method to carry out exposure assessment. The assessment methodology is consistent with the approach adopted by the European Food Safety Authority[35] and the World Health Organization[36]. Current policy on exposure assessment of chemicals has been to use deterministic and distributional methods.

43. The vast majority of FSA exposure assessments are carried out using in-house software known as Intake2. The Intake2 programme is a bespoke statistical software package which allows the estimation of dietary exposure to food chemicals. The software estimates exposure values by using the levels of chemicals measured in food and combines this information with the amount of that food which is consumed. The food consumption diaries from the NDNS are uploaded onto the Intake2 programme using recipe information and the data are used to derive lists of foods mirroring the TDS samples. The concentrations of the analyte of study in the TDS are also uploaded onto the Intake2 programme. The full distribution of exposure is then calculated by the software and plotted for deriving summary statistics for high-level (i.e. 97.5th percentile) consumers. Exposure values are estimated from a range (lower - upper bound) of mean concentrations; that is, where individual sample analyses were less than the limit of detection, the concentration is expressed as zero (lower bound), or as equal to the limit of detection (upper bound) and the exposure calculated based on the body weights of the individuals in the survey..

Estimated dietary exposures to phthalates

44. The upper and lower bound dietary exposures of selected phthalate combinations are presented in Table 3.

Table 3: Upper and lower bound dietary exposures for high level consumers for selected phthalate combinations

Survey population	**Estimated high level adult dietary exposure (µg/kg bodyweight/day) to selected phthalate combinations from the whole diet**			
Phthalate combinations:	**DEHP + MEHP**	**MnBP + DBP**	**DCHP + MCHP**	**DiBP + DBP**
Free living elderly	2.5 - 3.7	0.3 - 1	0.1 - 0.5	0.6 - 1.1
Institutional elderly	2.6 - 4	0.3 - 1.1	0.04 - 0.6	0.8 - 1.3
Adults	3.5 - 4.9	0.4 - 1.4	0.03 - 0.6	0.8 - 1.5
Young People				
age - 4-6 years	5.7 - 8.5	0.6 - 2.3	0.03 - 1.2	1.4 - 2.5
age - 7-10 years	4.7 - 6.6	0.5 - 1.8	0.02 - 0.9	1.2 - 2.1
age - 11-14 years	3.5 - 5.1	0.4 - 1.4	0.02 - 0.7	0.9 - 1.6
age - 15-18 years	2.8 - 4.1	0.3 - 1.1	0.01 - 0.6	0.8 - 1.4
Toddlers:				
age 1.5-2.5	7.1 - 12.7	0.8 - 3.4	0.04 - 2	1.8 - 3.6
age 2.5-3.5	6.5 - 10.4	0.7 - 3	0.04 - 1.8	1.7 - 3.2
age 3.5-4.5	5.9 - 8.8	0.7 - 2.5	0.04 - 1.4	1.6 - 2.8
Combined prevalence	12	13	2	19

45. Tables 4 a, b and c present the major contributing food groups to overall chronic dietary exposure for each of the phthalates detected in the study, in addition to total phthalates. The major contributing food groups varied greatly across the detected phthalates but only marginally within age groups, this reflects variations in consumption habits across different age groups.

Table 4a: Food groups contributing the highest proportions to dietary DEP, DiBP and DBP exposure

Age Group	Diethyl phthalate (DEP)			Di-iso-butyl phthalate (DiBP)			Di-n-butyl phthalate (DBP)		
	Exposure (all food groups combined) (µg/kg bw/d)	Major contributing food group	Exposure from contributing food group (µg/kg bw/d)	Exposure (all food groups combined) (µg/kg bw/d)	Major contributing food group	Exposure from contributing food group (µg/kg bw/d)	Exposure (all food groups combined) (µg/kg bw/d)	Major contributing food group	Exposure from contributing food group (µg/kg bw/d)
Toddlers (1.5 - 2.5 years old)	0.84	Milk	0.32	2.65	Beverages	1.36	1.00	Milk	0.33
		Fruit Prducts	0.23		Misc. Cereals	1.11		Fruit products	0.33
		Meat Products	0.23		-	-		Beverages	0.26
Toddlers (2.5 - 3.5 years old)	0.79	Milk	0.25	2.11	Beverages	1.05	0.82	Fruit products	0.31
		Meat Products	0.23		Misc. Cereals	1.04		Milk	0.25
		Fruit Prducts	0.22		-	-		Beverages	0.02
Toddlers (3.5 - 4.5 years old)	0.71	Meat Products	0.23	1.97	Misc. Cereals	0.96	0.75	Fruit products	0.23
		Milk	0.17		Beverages	0.90		Milk	0.17
		Fruit Prducts	0.17		-	-		Beverages	0.17
Young People (4-6 years old)	0.64	Meat Products	0.21	1.79	Misc. Cereals	0.88	0.71	Fruit products	0.21
		Fruit Prducts	0.15		Beverages	0.61		Misc. Cereals	0.15
		Misc. Cereals	0.15		-	-		Fresh fruit	0.14
Young People (7-10 years old)	0.52	Meat Products	0.15	1.50	Misc. Cereals	0.84	0.55	Fruit products	0.16
		Misc. Cereals	0.14		Beverages	0.49		Misc. Cereals	0.14
		Fruit Prducts	0.11		-	-		Beverages	0.09

Age Group	Diethyl phthalate (DEP)			Di-iso-butyl phthalate (DiBP)			Di-n-butyl phthalate (DBP)		
	Exposure (all food groups combined) (µg/kg bw/d)	Major contributing food group	Exposure from contributing food group (µg/kg bw/d)	Exposure (all food groups combined) (µg/kg bw/d)	Major contributing food group	Exposure from contributing food group (µg/kg bw/d)	Exposure (all food groups combined) (µg/kg bw/d)	Major contributing food group	Exposure from contributing food group (µg/kg bw/d)
Young People (11-14 years old)	0.41	Meat Products	0.14	1.13	Misc. Cereals	0.60	0.42	Fruit products	0.11
		Misc. Cereals	0.10		Beverages	0.38		Misc. Cereals	0.10
		Fruit Prducts	0.08		-	-		Beverages	0.07
Young People (15-18 years old)	0.34	Meat Products	0.11	1.01	Misc. Cereals	0.52	0.34	Misc. Cereals	0.09
		Misc. Cereals	0.09		Beverages	0.38		Fruit products	0.08
		Fruit Prducts	0.06		-	-		Beverages	0.07
Adults	0.31	Meat Products	0.10	0.91	Beverages	0.46	0.33	Beverages	0.09
		Green Veg.	0.09		Misc. Cereals	0.40		Fresh fruit	0.08
		Misc. Cereals	0.07		-	-		Misc. Cereals	0.07

Notes

Exposures calculated using an upper bound approach

- Indicates the lack of further major contributing food groups

Please note that 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: Food groups contributing the highest proportions to dietary BBP, DCHP and DEHP exposure

Age Group	Benzyl-butyl phthalate (BBP)			Dicyclohexyl phthalate (DCHP)			Di-(2-ethylhexyl) phthalate (DEHP)		
	Exposure (all food groups combined) (µg/kg bw/d)	Major contributing food group	Exposure from contributing food group (µg/kg bw/d)	Exposure (all food groups combined) (µg/kg bw/d)	Major contributing food group	Exposure from contributing food group (µg/kg bw/d)	Exposure (all food groups combined) (µg/kg bw/d)	Major contributing food group	Exposure from contributing food group (µg/kg bw/d)
Toddlers (1.5 - 2.5 years old)	1.32	Fresh Fruit	0.56	0.76	Offals	0.44	9.90	Dairy Products	5.80
		Fruit Products	0.45		Dairy Products	0.38		Fish	3.90
		Milk	0.44		-	-		Milk	2.10
Toddlers (2.5 - 3.5 years old)	1.09	Fresh Fruit	0.46	0.57	Offals	0.32	7.90	Fish	2.80
		Fruit Products	0.42		Fruit Products	0.24		Dairy Products	2.70
		Milk	0.34		-	-		Milk	1.90
Toddlers (3.5 - 4.5 years old)	1.01	Fresh Fruit	0.43	0.48	Offals	*	6.80	Meat	1.90
		Fruit Products	0.32		Fruit Products	0.18		Dairy products	1.80
		Milk	0.23		Dairy Products	0.12		-	-
Young People (4-6 years old)	0.92	Fresh Fruit	0.38	0.44	Fruit Products	0.16	6.70	Fish	2.20
		Fruit Products	0.29		Dairy Products	0.14		Meat	1.70
		Milk	0.19		Milk	0.09		Poultry	1.40
Young People (7-10 years old)	0.71	Fresh Fruit	0.27	0.34	Fruit Products	0.12	5.20	Fish	1.90
		Fruit Products	0.21		Offals	0.10		Meat	1.20
		Misc. Cereals	0.16		Milk	0.09		Poultry	1.10
Young People (11-14 years old)	0.50	Fresh Fruit	0.17	0.24	Offals	0.09	4.00	Fish	1.40
		Fruit Products	0.15		Fruit Products	0.08		Meat	1.20
		Misc. Cereals	0.12		Dairy Products	0.06		Poultry	0.80

Age Group	Benzyl-butyl phthalate (BBP)			Dicyclohexyl phthalate (DCHP)			Di-(2-ethylhexyl) phthalate (DEHP)		
	Exposure (all food groups combined) (µg/kg bw/d)	Major contributing food group	Exposure from contributing food group (µg/kg bw/d)	Exposure (all food groups combined) (µg/kg bw/d)	Major contributing food group	Exposure from contributing food group (µg/kg bw/d)	Exposure (all food groups combined) (µg/kg bw/d)	Major contributing food group	Exposure from contributing food group (µg/kg bw/d)
Young People (15-18 years old)	0.42	Fresh Fruit	0.19	0.20	Offals	*	3.20	Fish	1.10
		Fruit Products	0.11		Fruit Products	0.06		Meat	0.90
		Misc. Cereals	0.10		Dairy Products	0.04		Poultry	0.90
Adults	0.45	Fresh Fruit	0.22	0.19	Fruit Products	0.05	4.00	Fish	1.50
		Fruit Products	0.08		Dairy Products	0.04		-	-
		-	-		Poultry	0.03		-	-

Notes

Exposures calculated using an upper bound approach

* Offals have been included as a major contributor for two age groups, without the presence of an exposure value. This is due to insufficient consumers of offals to calculate 97.5th percentile (high rate) exposures in those age groups ; however, phthalate levels detected in offals are likely to provide relatively high exposure.

- Indicates the lack of further major contributing food groups

Please note that 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 4c: Food groups contributing the highest proportions to dietary MnBP, MEHP and TPh exposure

Age Group	Mono-n-butyl phthalate (MnBP)			Mono-(2-ethylhexyl) phthalate (MEHP)			Total Phthalates (TPh)†		
	Exposure (all food groups combined) (µg/kg bw/d)	Major contributing food group	Exposure from contributing food group (µg/kg bw/d)	Exposure (all food groups combined) (µg/kg bw/d)	Major contributing food group	Exposure from contributing food group (µg/kg bw/d)	Exposure (all food groups combined) (µg/kg bw/d)	Major contributing food group	Exposure from contributing food group (µg/kg bw/d)
Toddlers (1.5 - 2.5 years old)	2.39	Beverages	0.88	2.90	Beverages	1.64	19.79	Fruit Products	9.74
		Dairy Products	0.80		Milk	1.07		Beverages	5.81
		Fruit Products	0.73		-	-		Milk	5.26
Toddlers (2.5 - 3.5 years old)	1.96	Fruit Products	0.69	2.26	Beverages	1.27	17.28	Fruit Products	9.17
		Beverages	0.68		Milk	0.83		Beverages	4.48
		Milk	0.44		-	-		Misc Cereals	4.39
Toddlers (3.5 - 4.5 years old)	1.68	Beverages	0.58	1.93	Beverages	1.08	14.79	Fruit Products	7.00
		Fruit Products	0.52		Milk	0.57		Misc Cereals	4.04
		Dairy Products	0.31		Fruit Products	0.29		Beverages	3.83
Young People (4-6 years old)	1.62	Fruit Products	0.48	1.74	Beverages	0.74	13.86	Fruit Products	6.37
		Beverages	0.40		Milk	0.45		Misc Cereals	3.69
		Misc. Cereals	0.29		Fruit Products	0.26		Beverages	2.62
Young People (7-10 years old)	1.26	Fruit Products	0.35	1.36	Beverages	0.59	11.48	Fruit Products	4.68
		Beverages	0.31		Milk	0.26		Misc Cereals	3.55
		Misc. Cereals	0.28		Fruit Products	0.19		Beverages	2.08
Young People (11-14 years old)	0.94	Beverages	0.25	1.09	Beverages	0.47	8.37	Fruit Products	3.27
		Fruit Products	0.24		Meat Products	0.18		Misc Cereals	2.54
		Misc. Cereals	0.20		Milk	0.17		Beverages	1.64

Age Group	Mono-n-butyl phthalate (MnBP)			Mono-(2-ethylhexyl) phthalate (MEHP)			Total Phthalates (TPh)†		
	Exposure (all food groups combined) (µg/kg bw/d)	Major contributing food group	Exposure from contributing food group (µg/kg bw/d)	Exposure (all food groups combined) (µg/kg bw/d)	Major contributing food group	Exposure from contributing food group (µg/kg bw/d)	Exposure (all food groups combined) (µg/kg bw/d)	Major contributing food group	Exposure from contributing food group (µg/kg bw/d)
Young People (15-18 years old)	0.77	Beverages	0.24	0.90	Beverages	0.46	6.68	Fruit Products	2.40
		Fruit Products	0.18		Poultry	0.15		Misc Cereals	2.18
		Misc. Cereals	0.17		Meat Products	0.14		Beverages	1.62
Adults	0.79	Beverages	0.30	0.96	Beverages	0.56	6.43	Beverages	1.97
		Fresh Fruit	0.15		Poultry	0.13		Fruit Products	1.83
		-	-		-	-		Misc Cereals	1.69

Notes

Exposures calculated using an upper bound approach

† Total phthalates represents all phthalates detected by the study, not only those specifically targeted and will therefore not equal the sum of the listed phthalate exposures

- Indicates the lack of further major contributing food groups

Please note that 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.

46. Of the phthalate esters detected, DEHP was identified as providing the highest dietary exposures. For DEHP; dairy products, fish and milk were the major contributors to dietary exposure for the youngest toddler age groups, whilst meat and dairy were major contributors to the older toddlers. For young people, in all age groups; fish, meat and poultry were identified as major contributors. For adults only fish was identified as providing a major contribution to DEHP dietary exposure.

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

As with DBP and DEHP, exposure in different age groups to remaining phthalate esters that were detected came from different food types.

Assessment of dietary exposure to phthalates

48. For all the phthalates detected, calculated upper bound dietary exposures were the highest for toddlers in the 1.5 to 2.5 year old age group. Total dietary DEHP exposure for toddlers was 9.9 µg/kg bw/day compared to the EFSA TDI of 50 µg/kg bw/day. For BBP, total dietary exposure for this age group was calculated as 1.32 µg/kg bw/day compared with an 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 an EFSA TDI of 100 µg/kg bw/day. For DEP the total dietary exposure of this age group was 0.84 µg/kg bw/day compared with the WHO TDI of 500 µg/kg bw/day.

49. Of the phthalates detected, which also have established TDIs, only di-n-butyl phthalate (DBP) exposure came close to exceeding its stated TDI, this was only the case for 1.5-2.5 year old toddlers. However for DBP, milk, fruit products and beverages were highlighted as the major contributors to dietary exposure for all toddler age groups. For young people and adults, with the exception of the youngest age group, fruit products, miscellaneous cereals and beverages were the major contributors. For the youngest group of young people; fruit products, miscellaneous cereals and fresh fruit were identified as the major contributors to dietary DBP exposure.

50. The Committee noted that exposures to monoesters should be added to those of the corresponding diester (for example, mono-(2-ethylhexyl) phthalate (MEHP) and DEHP) because the diesters are hydrolysed to the toxicologically active monoesters in the gastrointestinal tract. Upper and lower bound dietary exposures for high level consumers for phthalate combinations which are related metabolically and were detected in the analysis are shown in Table 5.

Table 5: Upper and lower bound dietary exposures for high level consumers for selected phthalate combinations

Survey population	**Estimated high level adult dietary exposure (µg/kg bodyweight/day) to selected phthalate combinations from the whole diet**			
Phthalate combinations:	**DEHP + MEHP**	**MnBP + DBP**	**DCHP + MCHP**	**DiBP + DBP**
Free living elderly	2.5 - 3.7	0.3 - 1	0.1 - 0.5	0.6 - 1.1
Institutional elderly	2.6 - 4	0.3 - 1.1	0.04 - 0.6	0.8 - 1.3
Adults	3.5 - 4.9	0.4 - 1.4	0.03 - 0.6	0.8 - 1.5
Young People				
age - 4-6 years	5.7 - 8.5	0.6 - 2.3	0.03 - 1.2	1.4 - 2.5
age - 7-10 years	4.7 - 6.6	0.5 - 1.8	0.02 - 0.9	1.2 - 2.1
age - 11-14 years	3.5 - 5.1	0.4 - 1.4	0.02 - 0.7	0.9 - 1.6
age - 15-18 years	2.8 - 4.1	0.3 - 1.1	0.01 - 0.6	0.8 - 1.4
Toddlers:				
age 1.5-2.5	7.1 - 12.7	0.8 - 3.4	0.04 - 2	1.8 - 3.6
age 2.5-3.5	6.5 - 10.4	0.7 - 3	0.04 - 1.8	1.7 - 3.2
age 3.5-4.5	5.9 - 8.8	0.7 - 2.5	0.04 - 1.4	1.6 - 2.8
Combined exposure	12	13	2	19

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

52. In addition, the committee considered information on combined effects of phthalate esters[37,38,39,40], and concluded that a cumulative risk assessment should be undertaken based on an assumption of dose-addition, unless there was a good rationale for not including individual phthalates (for example, phthalate esters that have different targets).

53. If total exposure is estimated (i.e. adding up all phthalate exposure) the highest level of consumer exposure is approximately double the lowest TDI i.e. that for DBP.

54. Taking into account that most of the phthalates are less potent, and that the TDI for DBP, based on the Lee study showing effects at doses lower than the NOAELs for similar endpoints in other studies is likely to be highly conservative and that DBP accounts for only approximately 10% of this cumulative exposure, the estimated dietary exposures do not indicate a concern for health of consumers. However other sources of exposure need to be considered in a full assessment of the phthalates.

Conclusions

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

56. The Committee noted the TDIs set by EFSA and WHO. It was considered that the WHO review underpinning the TDI for DEP was not as robust as those performed by EFSA.

57. In addition the evidence from the scientific literature that had been published since these opinions were adopted was reviewed. The literature to date did not indicate a need to change the TDIs, thus the Committee concluded these TDIs could be used in assessing dietary exposure to phthalates.

58. For all the phthalates detected in the FSA study, calculated upper bound dietary exposures were the highest for toddlers in the 1.5 to 2.5 year old age group. Total dietary DEHP exposure for toddlers was 9.9 µg/kg bw/day compared to the EFSA TDI of 50 µg/kg bw/day. For BBP, total dietary exposure for this age group was calculated as 1.32 µg/kg bw/day compared with an 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 an EFSA TDI of 100 µg/kg bw/day. For DEP the total dietary exposure of this age group was 0.84 µg/kg bw/day compared with the WHO TDI of 500 µg/kg bw/day.

59. Due to the fact that phthalate diesters are hydrolysed to the toxicologically active monoesters in the gastrointestinal tract, the Committee considered it appropriate to consider the sum of these exposures.

60. The committee concluded that a cumulative risk assessment for phthalates should be undertaken based on an assumption of dose-addition, unless there was a good rationale for not including individual phthalates (for example, phthalate esters that have different targets).

61. If total dietary exposure is estimated (i.e. adding up all phthalate exposure) the highest level of consumer exposure (in toddlers in age 1.5 to 2.5 years) is approximately double the lowest TDI, i.e. that for DBP.

62. The Committee noted that most of the phthalates are less potent than DBP, and that the TDI for DBP, based on the Lee study showing effects at doses lower than the NOAELs for similar endpoints in other studies is likely to be highly conservative; and that DBP accounts for only approximately 10% of this cumulative exposure, thus the estimated dietary exposures do not indicate a concern for health of consumers.

63. Overall the Committee concluded that either individually, or in combination, the high level dietary exposures to phthalates estimated from this survey do not indicate a risk to human health from this exposure route.

64. Other sources of exposure need to be considered in a full assessment of phthalates.

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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
CSL	Central Science Laboratory
DBP	Di-butylphthalate
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 Organisation