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

Health Assessment of Endocrine Disrupting Chemicals – the Danish EPA report and exposure time trends to phthalates

1. At the February 2010 meeting, Members were presented with a paper summarising a recent report by the Danish Environmental Protection Agency (EPA) titled '*Survey and Health Assessment of the exposure of 2 year-olds to chemical substances in Consumer Products*' (DEPA, 2009). At that meeting, the Committee welcomed the approach of studying total exposures from a range of different scenarios, and asked to see the full report where the calculation of the exposure estimates were described for each compound. Similarly, the Committee wanted to review the endpoints used for each compound as the basis of the derived no effect level (DNEL). It was noted that for some compounds, the total calculated exposures were above the DNEL. However, as assessment factors were used in deriving the DNEL, the Committee considered that the margin between the exposure and the minimum effect level in the critical study was likely to be substantial.

2. The Committee also felt that it would be useful to obtain information on time trends in exposure to a selection of the compounds investigated. Some compounds had been withdrawn from use in certain applications, while the use of others was growing, and depending on their chemical properties, this could reduce or increase concerns about the risks of adverse effects.

3. While the Committee wanted to review the full report, it did not consider that the information presented in the summary and conclusions raised concerns that required urgent investigation. It was agreed at the February meeting that the remit of a COT review would need to be defined and expertise in environmental exposure assessment should be sought for further discussion of the topic.

4. The focus of this paper is to provide the Committee with requested information on the endpoints used for each substance in the report's risk assessment, and information on time trends in exposure to endocrine disrupting chemicals. The full Danish EPA report is attached at Annex A.

Danish EPA report (DEPA, 2009)

5. The report's risk assessments focused on the 2-year old child's total exposure to selected endocrine disrupting compounds in consumer products, foods, indoor air and dust. Because of the report's emphasis on substances with endocrine disrupting effects, the risk assessments were based on No Observed Adverse Effect Levels (NOAELs) and Lowest Observed Adverse Effect Levels (LOAELs) from animal

experiments that have shown endocrine disrupting effects. Thus, the selected NOAELs/LOAELs do not necessarily come from the critical effect (the relevant adverse effect seen at the lowest concentration or dose) of the compounds that would traditionally be used in risk assessments; as the aim of the report was to select NOAELs/LOAELs that are used for endocrine disrupting effects in European Union (EU) risk assessments, European Food Safety Authority (EFSA) opinions, or other official risk assessments. In many cases the NOAELs/LOAELs come from studies where the effects were observed following foetal exposure to the substances – the authors deemed this to be a reasonable (although conservative) approach to the risk assessment for 2-year old children.

6. The report follows the EU REACH (**R**egistration, **E**valuation, and **A**uthorisation and Restriction of **Ch**emicals) Guidance Document for risk assessments, using DNELs which are calculated on the basis of a NOAEL/LOAEL and relevant assessment factors (AF): DNEL = (N)LOAEL/AF (ECHA, 2008). The AFs used depended on which study the NOAEL/LOAEL was based on and are given in table 1.

Table 1: The assessment factors employed in the calculation of a DNEL

Parameters	**Value**	**Employed assessment factor**
Inter-species	Allometric scaling: Correction for differences in the metabolic rate per kg body weight.	4 for rats 7 for mice
Inter-species	Remaining inter-species differences.	2.5
Intra-species	Differences between individuals.	10
Dose response	LOAEL to NOAEL, if LOAEL is employed, this is because a NOAEL has not been determined.	3

DNEL: Derived No Effect Level; NOAEL: No Observed Adverse Effect Level; LOAEL: Lowest Observed Adverse Effect Level

Taken from the Danish EPA report: Survey and Health Assessment of the exposure of 2 year-olds to chemical substances in Consumer Products (DEPA, 2009).

7. Seventeen (17) substances were selected based on their known endocrine disrupting effects in animal studies and anticipated exposure of 2-year old children:

- DEHP (di-ethylhexyl phthalate)
- DINP (di-isononyl phthalate)
- DBP (di-butyl phthalate)
- DIBP (di-isobutyl phthalate)
- BBP (butylbenzyl phthalate)
- Prochloraz
- Tebuconazole
- Linuron
- Vinclozolin
- Procymidone

- PCBs (polychlorinated biphenyls)
- Dioxins
- DDTs/DDDs (dichlorodiphenyl trichlorethane/dichlorodiphenyl dichloroethene)
- Propylparaben
- Butylparaben
- Isobutylparaben
- Bisphenol A

8. Exposure calculations (pages 187-253) were made on the basis of the analyses for products relevant to 2-year olds, analyses of relevant products made in prior surveying projects, as well as estimates of the exposure from cosmetic products, food and the indoor climate.

9. Realistic worst-case exposure scenarios were devised for the consumer products based on the EU REACH Guidance Document as well as the RIVM '*Children's Toys Fact Sheet*' (Bremmer and van Veen, 2002). The scenarios were based on calculations of the use and predictable other uses of the products. The exposure assessments were based on sucking/ingestion of the product, dermal contact and/or inhalation of volatile substances from the product or from chemical substances in the indoor climate. The exposure from the indoor climate was based on data from the scientific literature and for foods, the average consumption of food for a 2-year old was used.

10. According to the REACH Guidance Document, health risks are assessed by calculating the Risk Characterisation Ratio (RCR), which uses the DNEL: RCR = Total exposure/DNEL. If the RCR > 1 (i.e. the exposure is greater than the DNEL) then the report concludes that there is a risk. If the RCR < 1 then the report concludes that the exposure does not pose any risk.

11. Table 2 details the endpoints used for the risk assessment of each compound, with comparison to established health based guidance values, where they are available. For the majority of compounds, (BBP, DEHP, DINP, prochloraz, tebucanazole, linuron, procymidone, DDT, and bisphenol A) the DNEL is higher than the health based guidance value, and in all but one case (procymidone), this is because the critical effect identified for derivation of the health based guidance value did not involve endocrine disruption. For procymidone, the same study was used to derive both the DNEL and health based guidance value, but the Danish report assumed a DNEL based on the draft EFSA ADI which identified a NOAEL. However, EFSA subsequently proposed a revised ADI in an addendum based on additional information that was submitted (EFSA, 2009). The ADI was revised to take account of effects observed at the NOAEL (i.e. EFSA derived an ADI based on a LOAEL). For DBP, the DNEL derived was lower than the health based guidance value; and for DIBP, propyl-, butyl-, and iobutyl-parabens, no health based guidance values were derived for comparison. Table 3 summarises the risk characterisation ratios for each compound.

Table 2: Calculation of the derived no effect level (DNEL) and comparison to established health based guidance values

Compound name	NOAEL/ LOAEL (mg/kg bw/day)	Effect	Reference	Assessment factor	DNEL (mg/kg bw/day)	Health based guidance value (mg/kg bw/day)	Basis of health based guidance value
DIBP	NOAEL: 125	Anti-androgenic: reduced AGD and increased retention of nipples	Saillenfait *et al.*, 2008	100 (4x2.5x10)	1.25	SCF evaluated DIBP in 1999 and placed it in List 6B (substances suspected to have toxic properties (other than carcinogenic)) (SCF, 1999). Toxicological data were needed depending on the migration level and if migration exceeds 0.05 mg/kg, then peroxisome proliferation studies were needed too (SCF, 1999). In 2004, EFSA transferred DIBP from List 6B to List 8 (substances for which no or only scanty and inadequate data were available) (EFSA, 2004a). EFSA concluded that more data on migration and use were needed in order to judge if further toxicity data also needed.	
DBP	LOAEL: 2	Anti-androgenic: effects on gamete development and development of mammary tissue	Lee *et al.*, 2004	300 (4x2.5x10x3)	0.0067	0.1[1]	Oral RfD. Based on a NOAEL of 0.25% of diet (125 mg/kg bw/day) for increased mortality in a rat subchronic-to-chronic oral bioassay, and an uncertainty factor of 1000 (US EPA, 1990a).
BBP	NOAEL: 50	Anti-androgenic: reduced AGD	Tyl *et al.*, 2004	100 (4x2.5x10)	0.5	0.2[1]	Oral RfD. Based on a NOAEL of 2800 ppm in diet (159 mg/kg bw/day) for significantly increased liver-to-body weight and liver-to-brain weight ratios in a 6-month rat study, and an uncertainty factor of 1000 (US EPA, 1993a).
DEHP	NOAEL: 5	Anti-androgenic: effects on gametes and reduced testicular weight	Wolfe *et al.*, 2003	100 (4x2.5x10)	0.05	0.02[1]	Oral RfD. Based on a LOAEL of 0.04% of diet (19 mg/kg bw/day) for increased relative liver weight in a guinea pig subchronic to chronic oral bioassay, and an uncertainty factor of 1000 (US EPA, 1991).
DINP	NOAEL: 276	Anti-androgenic: reduced testicular weight	Aristech Chemical Corporation, 1994	175 (7x2.5x10)	1.6	0.15[1]	TDI. Based on a NOAEL of 15 mg/kg bw/day for non-peroxisomal proliferation-related chronic hepatic and renal effects in a 2-year chronic study in rats, and an uncertainty factor of 100 (EFSA, 2005c).

Table 2 *continued*: Calculation of the derived no effect level (DNEL) and comparison to established health based guidance values

Compound name	NOAEL/ LOAEL (mg/kg bw/day)	Effect	Reference	Assessment factor	DNEL (mg/kg bw/day)	Health based guidance value (mg/kg bw/day)	Basis of health based guidance value
Prochloraz	NOAEL: 50	Anti-androgenic: increased retention of nipples	Christiansen *et al.*, 2009	100 (4x2.5x10)	0.5	0.009	Oral RfD. Based on a NOEL of 30 ppm (0.9 mg/kg bw/day) for increases in serum alkaline phosphatase and liver weights, and liver histopathology in a 2-year dog feeding study, and an uncertainty factor of 100 (US EPA, 1989).
						0.01	ADI. Based on two NOAELs for hepatic effects in 2-year studies - 0.9 mg/kg bw/day (dog) and 1.3 mg/kg bw/day (rat), and an uncertainty factor of 100. This ADI was set in 1983 and re-confirmed in 2001 (WHO, 1983 and 2001a).
Tebuconazole	LOAEL: 50	Anti-androgenic: increased retention of nipples	Taxvig *et al.*, 2007	300 (4x2.5x10x3)	0.17	0.03	ADI. Based on a NOAEL of 3 mg/kg bw/day for hypertrophy in zona fasciculate cells of the adrenals in two 1-year dog studies, and an uncertainty factor of 100 (EFSA, 2008a). EFSA noted that the basis of this ADI was supported by a LOAEL of 10 mg/kg bw/day for mouse developmental toxicity.
Linuron	NOAEL: 25	Anti-androgenic: increased retention of nipples	McIntyre *et al.*, 2000	100 (4x2.5x10)	0.25	0.002	Oral RfD. Based on a LEL of 25 ppm diet (0.625 mg/kg bw/day) for abnormal blood pigmentation in a 2-year dog feeding study, and an uncertainty factor of 300 (US EPA, 1990b).
						0.003	ADI. In 2002 an ADI was derived by the European Commission under Directive 91/414/EEC. This ADI was based on results from a 2-year rat study and an uncertainty factor of 500. The background to the derivation of this ADI was not published but reference is made to it by EC (2002).

Table 2 *continued*: Calculation of the derived no effect level (DNEL) and comparison to established health based guidance values

Compound name	NOAEL/ LOAEL (mg/kg bw/day)	Effect	Reference	Assessment factor	DNEL (mg/kg bw/day)	Health based guidance value (mg/kg bw/day)	Basis of health based guidance value
Vinclozolin	LOAEL: 5	Anti-androgenic: increased retention of nipples	Hass *et al.*, 2007	300 (4x2.5x10x3)	0.0167	0.025	Oral RfD. Based on a NOEL of 100 ppm (2.5 mg/kg bw/day) for organ weight changes in a 6-month feeding dog study, and an uncertainty factor of 100 (US EPA, 1992).
						0.005	ADI. In 2006 an ADI was derived by the European Commission under Directive 91/414/EEC. This ADI was based on results from a 2-year rat study and an uncertainty factor of 250. The background to the derivation of this ADI was not published but reference is made to it by EFSA (2008b).
Procymidone	NOAEL: 2.5	Anti-androgenic: decreased AGD, hypospadias, effects on testes	EFSA, 2009	100 (4x2.5x10)	0.025	0.0028	ADI. EFSA set an ADI based on a LOAEL of 50 ppm (2.5 mg/kg bw/day) for increased testes weight, and decreased weight of the prostate, epididymis and seminal vesicles, in a rat multi-generation study. A safety factor of 900 (3 for extrapolating from a LOAEL to a NOAEL, 3 for interspecies variability, 10 for intraspecies variability, and 10 for the severity of the effects) was applied to derive the ADI (EFSA, 2009).

Table 2 *continued*: Calculation of the derived no effect level (DNEL) and comparison to established health based guidance values

Compound name	NOAEL/ LOAEL (mg/kg bw/day)	Effect	Reference	Assessment factor	DNEL (mg/kg bw/day)	Health based guidance value (mg/kg bw/day)	Basis of health based guidance value
Dioxins and dioxin-like PCBs					TDI of 2 pg/kg bw/day[2]	14 pg/kg bw/week	Group TWI for all 2,3,7,8-substituted PCDDs and PCDFs and the dioxin-like PCBs (SCF, 2000 and 2001). In 2000 the SCF derived a temporary TWI of 7 WHO-TEQ/kg bw using a cluster of sensitive LOAELs from monkey and rat studies for neurobehavioural changes, endometriosis, accelerated eye opening, decreased sperm count, and immune suppression. In 2001 the SCF updated its assessment in light of new scientific information on dioxins. The SCF based its updated assessment on the rodent studies. One NOAEL and three LOAELs for the most sensitive effect (developmental effects in rat male offspring) were associated with estimated human daily intakes of either 10 (NOAEL) or 20-50 pg 2,3,7,8-TCDD/kg bw (LOAELs). The SCF recognised that the Wistar rat might be the most sensitive rat strain and therefore applied an uncertainty factor of 9.6 to the estimated human daily intake of 20 pg/kg bw. The SCF concluded that the TDI for 2,3,7,8-TCDD was therefore 2 pg/kg bw/day; and recognising that compounds like 2,3,7,8-TCDD have very long half-lives in the human body, the SCF considered it appropriated to express the TDI on a weekly basis. Therefore, the SCF established a TWI of 14 pg 2,3,7,8-TCDD/kg bw, and extended this TWI to include all 2,3,7,8-substituted PCDDs and PCDFs, and the dioxin-like PCBs, expressed as WHO TEQ (SCF, 2001).
						70 pg/kg bw/month	PTMI for all 2,3,7,8-substituted PCDDs, PCDFs and coplanar compounds (WHO, 2001b).

							The JECFA used a number of rat studies in which the lowest NOELs and LOELs were identified for the most sensitive adverse effects of TCDD (developmental). The two studies with the lowest LOEL (25 ng/kg bw) and NOEL (13 ng/kg bw) were used, and maternal body burdens for effects on male offspring were calculated using both the linear and power model. Estimated human monthly intakes were calculated and an uncertainty factor of either 3.2 (NOEL) or 9.6 (LOEL) was applied, resulting in a range of PTMIs, derived from the two studies, of 40-100 pg/kg bw/month. The Committee chose the midpoint of this range, 70 pg/kg bw/month, as the PMTI. The Committee concluded that this PMTI should be applied to intake of PCDDs, PCDFs and coplanar PCBs expressed as TEFs (WHO, 2001b).
						2 pg TEQ/kg bw/day	TDI for dioxins and dioxin-like PCBs (COT, 2001). The COT agreed that there was sufficient information to assume a threshold existed for the effects of dioxins. The COT considered that the most sensitive and consistent effect was on the developing reproductive system of the male offspring, particularly changes in sperm production and quality. Chemical-specific adjustment factors were applied to the lowest dose level at which effects were observed in the developing male foetus (bolus dose of 25 ng/kg bw before mating and weekly maintenance doses of 5 ng/kg bw). This subcutaneous dosage regime was converted into a steady-state maternal body burden (33 ng/kg bw), and this in turn was subsequently converted into an equivalent human body burden of 3.4 ng/kg bw using an uncertainty factor of 9.6 (3 x 3.2). Estimation of the daily intake that would result in this body burden took into account the bioavailability and the half-life of TCDD.

Table 2 *continued*: Calculation of the derived no effect level (DNEL) and comparison to established health based guidance values

Compound name	NOAEL/ LOAEL (mg/kg bw/day)	Effect	Reference	Assessment factor	DNEL (mg/kg bw/day)	Health based guidance value (mg/kg bw/day)	Basis of health based guidance value
Non-dioxin like PCBs	No assessment available for antiandrogenic effects. Re-assessment of the toxicology of non-dioxin like PCBs with regard to antiandrogenic effects or oestrogenic effects was deemed to lie outside the remit of the project.					In 2005 EFSA carried out a risk assessment on non dioxin-like PCBs in food. In conclusion, no health based guidance value for humans could be established for non dioxin-like PCBs because simultaneous exposure to non dioxin-like PCBs and dioxin-like compounds hampers the interpretation of the results of the toxicological and epidemiological studies, and the database on effects of individual non dioxin-like PCB congeners is limited (EFSA, 2005d).	
DDT	LOAEL: 10 (DDE)	Antiandrogenic: increased retention of nipples	You *et al.*, 1998	300 (4x2.5x10x3)	0.03	0.0005	Oral RfD. Based on a NOEL of 1 ppm diet (0.05 mg/kg bw/day) for liver lesions in a 27-week rat feeding study, and an uncertainty factor of 100 (US EPA, 1996).
Propylparaben	LOAEL: 10	Oestrogenic: decreased daily semen production	Oishi, 2002	300 (4x2.5x10x3)	0.03	In 2004, EFSA reviewed the safety of paraben usage in foods. The Panel established a **group ADI of 0-10 mg/kg bw/day for the sum of methyl and ethyl p-hydroxybenzoic acid esters and their sodium salts.** The Panel considered that propylparaben should not be included in this group ADI because propylparaben, contrary to methyl- and ethyl-paraben, has effects on sex hormones and the male reproductive organs in juvenile rats. The Panel was unable to recommend an ADI for propylparaben because of the lack of a clear NOAEL (EFSA, 2004b). In 2005, the Scientific Committee on Consumer Products (SCCP) of the EC concluded that there was **insufficient information to derive a safe maximal level of usage for propyl-, butyl-, and isobutyl-paraben** and requested further information on these substances, especially related to effects on the male reproductive system (EC, 2005). The SCCP reviewed parabens again in 2006 and their conclusions remain unchanged (EC, 2006).	
Butylparaben	LOAEL: 10	Oestrogenic: effects on sperm quality and production, decreased serum testosterone	Oishi, 2001	300 (4x2.5x10x3)	0.03		
Isobutyl paraben	LOAEL: 72	Oestrogenic: increased uterus weight	Darbre *et al.*, 2002	525 (7x2.5x10x3)	0.14		

Table 2 *continued*: Calculation of the derived no effect level (DNEL) and comparison to established health based guidance values

Substance name	NOAEL/ LOAEL (mg/kg bw/day)	Effect	Reference	Assessment factor	DNEL (mg/kg bw/day)	Health based guidance value (mg/kg bw/day)	Basis of health based guidance value
Bisphenol A	NOAEL: 50	Antiandrogenic: increased duration of pregnancy and incidence of undescended testes, abnormal epididymal cell growth, delayed puberty	Tyl *et al.*, 2008	175 (7x2.5x10)	0.29	0.05	Oral RfD. Based on a LOAEL of 1000 ppm diet (50 mg/kg bw/day) for reduced mean body weight in a rat chronic oral bioassay, and an uncertainty factor of 1000 (US EPA, 1993b).
						0.05	TDI. Based on two NOAELs of 5 mg/kg bw/day and an uncertainty factor of 100. One TDI was based on adult systemic toxicity in a three-generation reproductive study in rats and the other was based on liver effects in a two-generation reproductive study in mice (EFSA, 2006). This TDI was confirmed in 2008 (EFSA, 2008c).

Table Notes:

DIBP: di-isobutyl phthalate; DBP: di-butyl phthalate; BBP: butylbenzyl phthalate; DEHP: di-ethylhexyl phthalate; DINP: di-isononyl phthalate; PCBs: polychlorinated biphenyls

NOAEL: no observed adverse effect level; NOEL: no observed effect level; LOAEL: lowest observed adverse effect level; LOEL: lowest observed effect level; LEL: lowest effect level; DNEL: derived no effect level; AGD: anogenital distance; DDT:dichlorodiphenyltrichloroethane ; DDE: dichlorodiphenyldichloroethylene

ADI: acceptable daily intake; TDI: tolerable daily intake; RfD: reference dose; TWI: tolerable weekly intake; PTMI: provisional tolerable monthly intake; SCF: Scientific Committee for Food; JECFA: Joint FAO/WHO Expert Committee on Food Additives

PCDDs: polychlorinated dibenzo-p-dioxins; PCDFs: polychlorinated dibenzofurans; 2,3,7,8-TCDD: 2,3,7,8-tetrachlorodibenzo-p-dioxin; WHO-TEQ: World Health Organization toxic equivalent; TEF: toxic equivalent factor

[1]In 2005 EFSA concluded that a group TDI could not be set for BBP, DBP, DEHP, DINP and di-isodecylphthalate due to action on different target organs and differences in individual modes of action (EFSA, 2005b).

[2]Equivalent tolerable daily intake (TDI) of 2 pg.kg bw/day for 2,3,7,8-tetrachlordibenzo-p-dioxin (TCDD). The Scientific Committee on Food established a group tolerable weekly intake of 14 pg/kg bw for all 2,3,7,8-substituted PCDDs and PCDFs and the dioxin-like PCBs (SCF, 2000 and 2001). The WHO/FAO Joint Expert Committee on Food Additives established a provisional monthly intake for PCDDs, PCDFs and coplanar compounds of 70 pg/kg bw (WHO, 2001b). The COT recommended a TDI of 2 pg TEQ/kg bw/day for dioxins and dioxin-like PCBs (COT, 2001).

Table 3: Risk characterisation ratios (RCR) for summer and winter scenarios

Substance name	DNEL (mg/kg bw/day)	Health based guidance value (mg/kg bw/day)	Summer scenario with rubber clogs (i.e. max. values)[1,2]		Summer scenario without rubber clogs and no phthalate contribution from toys (i.e. min. value)[1,2]		Winter scenario with no phthalate contribution from toys (i.e. min. value)[3]	
			RCR (50%)[4]	RCR (95% & max)[5]	RCR (50%)[4]	RCR (50%)[4]	RCR (95% and max)[5]	RCR (50%)[4]
DIBP	1.25	None established	0.04	0.04	0	0	0	0.01
DBP	0.0067	0.1	12.67	14.87	1.32	3.62	1.41	3.90
BBP	0.5	0.2	0.01	0.04	0.01	0.04	0.01	0.05
DEHP	0.05	0.02	0.4	1.51	0.39	1.51	0.46	1.98
DINP	1.6	0.15	0.01	0.02	0.01	0.02	0.01	0.02
Prochloraz	0.5	0.009 / 0.01	0	0	0	0	0	0
Tebuconazole	0.17	0.03	0	0	0	0	0	0
Linuron	0.25	0.002 / 0.003	0	0	0	0	0	0
Vinclozolin	0.0167	0.005 / 0.025	0	0	0	0	0	0
Procymidone	0.025	0.0028	0	0	0	0	0	0
Dioxins and dioxin-like PCBs	TDI of 2 pg/kg bw/day[6]	TDI of 2 pg/kg bw/day[6]	2	4	2	4	2	4
Non-dioxin like PCBs	No DNEL derived as no assessment available for antiandrogenic effects.	None established						
DDT	0.03	0.0005	0	0	0	0	0	0
Propylparaben	0.03	None established	3	3	3.03	3.03	0.83	0.83
Butylparaben	0.03	None established	0.71	0.71	0.71	0.71	0.21	0.21
Isobutyl paraben[7]	0.14	None established						
Bisphenol A	0.29	0.05	0	0.02	0	0.02	0	0.02

Table Notes:

Indicates exceedance of the health based guidance value.

DIBP: di-isobutyl phthalate; DBP: di-butyl phthalate; BBP: butylbenzyl phthalate; DEHP: di-ethylhexyl phthalate; DINP: di-isononyl phthalate; PCBs: polychlorinated biphenyls
DNEL: derived no effect level; RCR: risk characterisation ratio

[1]Summer scenario. The following factors were included in the summer scenario: contact with sunscreens and rubber clogs, dermal contact with toys for 9 hours, and ingestion of 50 mg dust. Elements that are common to both the summer and winter are included in both scenarios, e.g. ingestion of foods and contact with objects other than toys (moisturising cream, bath articles, textiles).

[2]Summer scenario without rubber shoes and no phthalate contribution from toys. The content of phthalates in the examined rubber clogs was shown to exceed the permitted values; hence a column has been inserted that does not include the contribution from these clogs. The difference between including the contribution from toys for the phthalate with the maximum contribution and for all the other phthalates, in the calculations of the RCR is minimal.

[3]Winter scenario. The following factors were included in the winter scenario: dermal contact with toys for 6 hours, contact with jackets/mittens for 3 hours, and ingestion of 100 mg dust. Elements that are common to both the summer and winter are included in both scenarios, e.g. ingestion of foods and contact with objects other than toys (moisturising cream, bath articles, textiles). The difference between including the contribution from toys for the phthalate with the maximum contribution and for all the other phthalates, in the calculations of the RCR is minimal.

[4]This is an expression of a total of the remaining scenarios that form a counterpart to the calculated maximum RCR. This has been calculated to show the range between the maximum/95th percentile values and the alternative values.

[5]The maximum RCR value is calculated in such a way that the maximum values are summated. 95th percentile values have been used in the cases where maximum values for the substance were not available. 95th percentiles have also been used for the indoor climate, since there can be extreme differences in the maximum value and the 95th percentile.

[6]Equivalent tolerable daily intake (TDI) of 2 pg.kg bw/day for 2,3,7,8-tetrachlordibenzo-p-dioxin (TCDD). The Scientific Committee on Food established a group tolerable weekly intake of 14 pg/kg bw for all 2,3,7,8-substituted PCDDs and PCDFs and the dioxin-like PCBs (SCF, 2000 and 2001). The WHO/FAO Joint Expert Committee on Food Additives established a provisional monthly intake for PCDDs, PCDFs and coplanar compounds of 70 pg/kg bw (WHO, 2001b). The COT recommended a TDI of 2 pg TEQ/kg bw/day for dioxins and dioxin-like PCBs (COT, 2001).

[7]The RCR value for isobutylparaben was not calculated. This was primarily because the focus was on propyl and butylparaben, not only because they are the two most potent parabens (lowest DNEL value), but also because iosbutylparaben was identified in 1 of 60 sunscreens and creams surveyed in the project.

Di-butyl phthalate

12. To illustrate how the exposure via inhalation, dermal contact and oral contact was assessed in the Danish report, the calculations for di-butyl phthalate are described.

13. The Danish report considered the exposures estimated by Muller *et al.* (2003) and Wormuth *et al.* (2006). Muller *et al.* (2003) estimated a total internal exposure of approximately 400 µg/kg bw/day for 1-6 year olds. Practically all of this exposure is oral, as only approximately 0.4 µg/kg bw/day can be attributed to inhalation, however, it is not known how much of the oral exposure is attributed to foods. Wormuth *et al.* (2006) estimated an internal exposure of approximately 0.4-40 µg/kg bw/day, with a median of approximately 4 µg/kg bw/day, for 1-3 year olds. Approximately 55% of this exposure is attributable to foods, approximately 10% from the ingestion of dust, approximately 2% from textiles and approximately 33% from the inhalation of air. The exposure from foods can therefore be estimated to be a median of 2.2 µg.kg bw/day and a maximum of 22 µg/kg bw/day. It was noted that the data basis for the assessment of the exposure from foods in the Wormuth *et al.* (2006) review was very limited. The Danish report noted that the large difference between the two exposure estimates could be caused by two factors:

- The Wormuth estimate is internal, meaning that only the absorbed amounts are considered.
- The Muller estimate is based on the maximal estimated exposure through the environment.

14. In accordance with the EU Risk Assessment Report for di-butyl phthalate (European Chemicals Bureau, 2004), the following absorptions were applied in the Danish report:

- Dermal: 10%
- Oral: 100%
- Inhalation: 100%

Exposure to di-butyl phthalate from foods

15. As well as the exposure estimates of Muller *et al.* (2003) and Wormuth *et al.* (2006), the Danish report considered the European Food Safety Authority opinion on the use of di-butyl phthalate in food contact materials (EFSA, 2005a). EFSA (2005a) referred to a dietary estimate based on measurements of Danish meals, in which the average and high exposures for adults were calculated to be 4.1 and 10.2 µg/kg bw/day, respectively. According to the Nordic nutrient recommendations, 2 year olds have an energy need per body weight of approximately double that of adults (NNA, 2004). Therefore, the Danish meal exposure estimates of 4.1 and 10.2 µg/kg bw/day for adults correspond to 8.2 and 20.4 µg/kg bw/day, respectively for 2 year olds.

16. Based on the principal of choosing realistic worst case results for the calculations, the Danish report identified an average exposure of 8.2 µg/kg bw/day di-butyl phthalate from foods from the Danish meal survey and, as the maximum exposure from foods, 22 µg/kg bw/day from Wormuth *et al.* (2006).

Exposure to di-butyl phthalate from consumer products

17. Di-butyl phthalate has been found in a number of consumer products in both earlier surveys and in the Danish project, however, migration of di-butyl phthalate from products has only been measured in rare cases. The concentrations measured were generally between 1.8 mg/kg (foam plastic sword) and 780 mg/kg (foam plastic floor jigsaw), with one product containing 3500 mg/kg (scented eraser).

>*toys*

18. No migration was measured on any of the products and therefore no calculations of exposure were performed.

>*erasers*

19. No migration was measured from erasers and therefore no calculations of exposure were performed.

>*baby changing mats/cushions*

20. A migration analysis had been conducted on baby changing mats/cushions but only data concerning di-isononyl phthalate were reported and, so it was assumed that there was no migration of di-butyl phthalate.

>*clothes*

21. No migration was measured from the print on clothes in any of the surveys and therefore no calculations of exposure were performed.

>*jacket zipper strap*

22. In the Danish report, a migration analysis was performed on a zipper strap from a jacket. A migration of 0.51 mg/kg was measured over a period of 3 hours. The calculations assumed that the strap weighed 5g, that approximately half of the strap was sucked, that it was sucked for 3 hours per day, and a 15kg body weight. **The estimated daily ingestion of di-butyl phthalate from a jacket zipper strap was calculated to be 0.084 µg/kg bw/day**.

>*rubber clogs*

23. In the Danish report, migration analyses were performed on rubber clogs. A migration of 249 mg/kg was measured over a period of 6 hours. The calculations assumed that a pair of rubber clogs weighed 69g, that contact occurred with 20-40% of the clog and that as a worst case scenario, no socks were worn with the clogs, and that, rubber clogs were worn for 4-10 hours a day. **The estimated daily ingestion of di-butyl phthalate from rubber clogs was calculated to range from 15.07 to 75.355 µg/kg bw/day, depending on the various exposure scenarios.**

Exposure to di-butyl phthalate from the indoor climate

24. Indoor climate exposure calculations comprise two components: exposure via indoor dust and exposure via the indoor air.

25. For exposure to di-butyl phthalate present in dust, the calculations assumed an oral ingestion of 50 or 100mg dust, a 2-year old body weight of 15.2 kg, and 100% ingestion. The 95th and 50th percentile concentrations of di-butyl phthalate in Swedish household dust were 568 and 150 µg/g, respectively. Thus, estimated daily

ingestion of di-butyl phthalate was calculated to be 1.9 and 3.7 µg/kg bw/day (at the 95th percentile measured value) and 0.49 and 0.99 µg/kg bw/day (at the 50th percentile measured value), for 50mg and 100mg of household dust ingestion, respectively.

26. For exposure to di-butyl phthalate present in the indoor air, the calculations assumed that 2-3 year old children inhale 7m^3 air per day, spend 19 hours inside per day and, that the respirable fraction for di-butyl phthalate is 1 (100%). The 95th and 50th percentile concentrations of di-butyl phthalate in Swedish indoor air were 1.04 and 0.48 µg/m^3, respectively. Thus, estimated daily exposure to di-butyl phthalate was calculated to be 0.38 µg/kg bw/day (at the 95th percentile measured value) and 0.18 µg/kg bw/day (at the 50th percentile measured value).

27. It is evident that the contribution from deposited indoor dust constitutes the largest part of the daily indoor exposure.

28. The total contribution from the indoor climate is the sum of the contribution from the dust and from the air - this is given in table 4 below for both the 95th and 50th percentile concentrations.

Table 4: Daily exposure to di-butyl phthalate through the indoor climate (dust and air) based on 95th and 50th percentile concentrations

	Daily exposure at 50 mg of dust (µg/kg bw/day)	Daily exposure at 100 mg of dust (µg/kg bw/day)
Based on the 50th percentile concentration[1]	0.67	1.17
Based on the 95th percentile concentration[2]	2.28	4.08

[1] 50th percentile concentrations were 150 µg/g for household dust and 0.48 µg/m^3 for indoor air.
[2] 95th percentile concentrations were 568 µg/g for household dust and 1.04 µg/m^3 for indoor air.

Combined exposure to di-butyl phthalate

29. The various contributions to the exposure to di-butyl phthalate can be summed to obtain a combined result for exposure to di-butyl phthalate. Table 5 summarises the various contributions to di-butyl phthalate exposure.

Table 5: Combined exposure to di-butyl phthalate

Source	**Daily exposure to di-butyl phthalate (µg/kg bw/day)**	
	Summer scenario	**Winter scenario**
Foods combined 50th percentile	8.2	8.2
Foods combined maximum[1]	22	22
Indoor climate combined 50th percentile	0.67	1.17
Indoor climate combined 95th percentile	2.28	4.08
Jacket zipper strap		0.08
Rubber clogs low exposure (contact with 20% for 4 hours per day)	15.07	
Rubber clogs high exposure (contact with 40% for 10 hours per day)	75.36	
Total (50th percentile, low exposure)	**23.94**	**9.45**
Total (95th percentile, high exposure)[2]	**99.64**	**26.16**

[1]Only maximum concentration was available.
[2]A maximum contribution from food was used in the estimated total exposure and not a 95th percentile concentration.

30. The calculated exposure to di-butyl phthalate is highly conservative because the calculations use maximum or 95th percentile concentrations, and the total calculated exposure assumes that each 2-year old is exposed to high concentrations through each exposure route (foods, toys, clothes etc).

Time trends in exposure to phthalates

31. In order to obtain information on time trends in exposure to the compounds investigated in the Danish EPA report, a literature search was conducted in PubMed, the full details of which are attached at Annex B. To provide a preliminary indication of the type of data available, focus was placed on phthalates.

32. A number of useful studies were identified that provided information on phthalate exposure through various routes, e.g. food, dust, indoor air, toys, consumer products, and medical devices/medications. These studies do not identify the pattern of phthalate exposure over time. Witttassek *et al.* (2007) conducted a retrospective biomonitoring study to estimate phthalate exposure over 20 years which gives some indication of exposure over time.

33. The primary route of exposure to phthalates is from ingestion of foods, especially fatty foods such as milk, butter, and meats, but low-molecular weight phthalates (diethyl phthalate, di-butyl phthalate, butylbenzyl phthalate) are dermally absorbed through the use of consumer products (Heudorf *et al.*, 2007).

Exposure to phthalates from foods

34. Through a mail survey of the adult Swiss-German population, Dickson-Spillmann *et al*. (2009) modelled consumer's exposure to phthalates through food. Using a food frequency questionnaire covering 29 food items and phthalate concentrations reported from food surveys, exposures to four phthalates (di-ethyhexyl phthalate, di-butyl phthalate, butylbenzyl phthalate, and diethyl phthalate) were estimated in 1,186 participants during January to March 2008. Modelled median daily intakes of the four phthalates were: 1.9 µg/kg bw/day (di-ethyhexyl phthalate), 0.39 µg/kg bw/day (di-butyl phthalate), 0.14 µg/kg bw/day (butylbenzyl phthalate), and 0.02 µg/kg bw/day (diethyl phthalate). Maximum intake levels were 8.21, 7.48, 0.63, and 0.07 µg/kg bw/day, respectively.

35. Much earlier data from the mid-1990s, reported by Schettler (2006) indicate that phthalate levels in food are widely variable. Estimated dietary intakes include: di-butyl phthalate maximum daily intake 0.48 µg/kg bw/day; di-ethylhexyl phthalate 4.9-18 µg/kg bw/day; and butylbenzyl phthalate 0.11-0.29 µg/kg bw/day. Schettler (2006) noted that as these dietary intakes were old, they may not reflect current exposures.

Exposure to phthalates from consumer products

>*toys*

36. In a review of phthalate exposure, Heudorf *et al.* (2007) reports estimated mean exposures in 2002 via mouthing in infants and toddlers of 5-44 µg/kg bw/day (di-isononyl phthalate) and up to 85 µg/kg bw/day (di-ethylhexyl phthalate).

37. Chou and Wright (2006) report similar mean intake levels of di-isononyl phthalate for infants and toddlers (12-23 months): 0.04-21.4 µg/kg bw/day and up to 94.3 µg/kg bw/day. Schettler (2006) report a higher maximum concentration – up to 173 µg/kg bw/day di-isononyl phthalate resulting from children's mouthing activities. Dates of data collection not specified.

>*clothes*

38. No information was located in the scientific literature.

>*personal care products*

39. Sathyanarayana *et al.* (2010) measured 9 phthalate metabolites in 163 infants as part of a multicentre pregnancy cohort study, and investigated the relationship between reported use of dermally applied infant care products. Infants were born between 2000-2005 and the following phthalate metabolites were measured: monobenzyl phthalate, monobutyl phthalate, mono-3-carboxypropyl phthalate, monoisobutyl phthalate, monoethyl phthalate, mono-2-ethylhexyl phthalate, mono-2-ethyl-5-hydroxyhexyl phthalate, mono-2-ethyl-5-oxohexyl phthalate, and monomethyl phthalate. Infants were considered to have been exposed to any baby care products if the mother reported usage on her infant within 24 hours prior to urine collection. Use of baby lotion was found to be associated with increased infant urine concentrations of monoethyl phthalate (mean 178 µg/L, maximum 4481 µg/L) and monomethyl phthalate (mean 4.4 µg/L, maximum 228.3 µg/L). Use of baby shampoo

was associated with an increased infant urine concentration of monomethyl phthalate; and use of baby powder was associated with an increased infant urine concentration of monoisobutyl phthalate (mean 7.8 µg/L, maximum 195 µg/L). Although this study did not estimate the internal exposure to phthalates it does highlight that baby care products can be a source of high exposure to some phthalates.

>*medical devices/medications*

40. Heudorf *et al.* (2007), Chou and Wright (2006), and Schettler (2006) all report internal exposures to di-ethylhexyl phthalate of 0.005-8.5 mg/kg bw/day (adults) and 0.03-22.6 mg/kg bw/day (neonates) from the use of a range of medical devices. Dates of data collection not specified.

41. Using National Health and Nutrition Examination Survey data, Hernandez-Diaz *et al.* (2009) evaluated whether users of phthalate-containing medications had higher urinary concentrations of phthalate metabolites than non-users. During the survey years 1999-2004, four phthalate-containing medications were identified (mesalamine which contains di-butyl phthalate, and didanosine, omeprazole and theophylline which all contain diethyl phthalate). The mean urinary concentration of monobutyl phthalate, the main di-butyl phthalate metabolite, among mesalamine users was approximately 50 times higher than the mean for non-users (2257 µg/L vs. 46 µg/L). Similarly, the mean urinary concentrations of monoethyl phthalate, the main diethyl phthalate metabolite, in users of didanosine, omeprazole, and theophylline were significantly higher than the mean for non-users (1210-4660 µg/L vs.653 µg/L). Although this study did not estimate the internal exposure to phthalates it does highlight that medications can be a source of high exposure to some phthalates.

42. Schettler (2006) report that enteral formulas stored in polyvinyl chloride bags softened with di-ethyhexyl phthalate, result in a daily exposure to di-ethylhexyl phthalate of about 9.5 mg/day (0.14 mg/kg bw/day in adults and 2.5 mg/kg bw/day in infants). Dates of data collection not specified.

Exposure to phthalates from the indoor climate

>*household dust*

43. In a review of phthalate exposure, Heudorf *et al.* (2007) report median levels of: diethyl phthalate <10 µg/g dust, di-butyl phthalate 40-50 µg/g dust, and di-ethylhexyl phthalate 400-700 µg/g dust.

44. Schettler (2006) report total phthalate dust concentrations in offices and homes of 0.3-524 µg/g dust. Di-ethyhexyl phthalate specifically was measured in 38 homes with ingestion of dust estimated to be 64 µg/day in adults.

>*indoor air*

45. In contrast to household dust, Heudorf *et al.* (2007) report median concentrations in indoor air of: diethyl phthalate >350-650 ng/m^3, di-butyl phthalate 600-1200 ng/m^3, and di-ethylhexyl phthalate 150-450 ng/m^3. Dates of data collection not specified.

46. Schettler (2006) report total phthalate air concentrations of 0.005-28 µg/m^3. In 27 houses, inhalation of diethyl phthalate, di-butyl phthalate, butylbenzyl phthalate, di-cyclohexyl phthalate, and di-ethylhexyl phthalate, were estimated to be 2, 78, 0.2, 1.4, and 22 µg/day in adults, respectively.

>*baking modelling clay*

47. Schettler (2006) report air concentrations of phthalates after baking of modelling clay: butylbenzyl phthalate (32-2667 µg/m^3); di-octyl phthalate (not detected – 6670 µg/m^3); and di-ethyhexyl phthalate (6.05-4993 µg/m^3).

48. The dates of data collection for all the indoor climate assessments described above were not specified.

49. Although the information described above on phthalate exposure through different routes is useful, it provides no indication on how phthalate exposure may change over time. Furthermore, the information described has been reported from differing countries and for a range of subgroups of the population. Data gaps over time make it difficult to identify with certainty the various exposure sources to phthalates and their contributions to measured phthalate levels in the general population. Dietary phthalate data are generally considered to be outdated and the presence of phthalates in consumer products may not be apparent (Schettler, 2006).

50. Wittassek *et al.* (2007) conducted a retrospective biomonitoring study in 634 volunteers, predominantly students (age range 20-29 years, 326 females, 308 males), in Germany. Metabolites of di-butyl phthalate, di-isobutyl phthalate, butylbenzyl phthalate, di-ethylhexyl phthalate, and di-isononyl phthalate were determined in 24-hour urine samples that had been collected during the last 20 years. The purpose of the study was to determine internal exposure to phthalates during the last 20 years, and so daily intakes were estimated from the urinary concentrations.

51. The full results are presented in table 6 below. Statistical analyses revealed a significant ($p<0.001$) downtrend in exposure to di-butyl phthalate over the years. In contrast, daily intake of di-isobutyl phthalate increased slightly ($p=0.001$) over the years. There was a weak negative trend ($p=0.002$) in daily intake of butylbenzyl phthalate and from 1998, the median intakes levelled off. A significant ($p<0.001$) downtrend in di-ethylhexyl phthalate exposure was observed; and furthermore, each median before 1996 was significantly higher than each median after 1996 (each $p<0.008$). Continuously increasing intakes for di-isononyl phthalate were observed over the years ($p<0.001$).

52. A limitation of this time trend is that it is not known what exposures (and what proportions) contributed to the overall individual phthalate intake.

53. <u>Questions on which the views of the Committee are sought</u>

i) Do the Committee have any further comments on the Danish EPA study?

ii) Do the Committee wish to specifically discuss and comment on time trends in exposure to phthalates as presented?

iii) Would the Committee like to see time trend exposure data on other selected endocrine disrupting chemicals?

Table 6: Daily intakes of phthalates (µg/kg bw/day) by German students deduced from urinary metabolite levels (taken from Wittassek *et al.* (2007))

Year	*n*	DnBP			DiBP			BBzP			DEHP			DiNP		
		50 P	95 P	Range	50 P	95 P	Range	50 P	95 P	Range	50 P	95 P	Range	50 P	95 P	Range
1988	60	7.0	24.2	0.72-27.8	1.1	3.6	0.27-6.2	0.25	0.77	0.02-6.6	3.9	9.9	0.78-39.8	0.2	1.4	0.04-2.2
1989	60	7.5	21.7	1.5-70.1	1.0	4.2	0.30-12.9	0.30	2.2	0.07-2.8	4.2	10.0	0.84-33.6	0.24	2.2	0.03-12.9
1991	60	6.4	14.3	2.1-28.7	1.2	8.7	0.36-20.2	0.43	1.6	0.11-2.8	4.0	18.8	1.2-23.6	0.22	4.5	0.05-20.2
1993	60	6.6	44.4	1.5-56.3	1.2	2.8	0.39-4.8	0.27	1.9	0.07-2.2	4.2	12.9	1.4-14.1	0.27	1.7	0.04-2.6
1996	145	3.7	15.5	1.1-90.2	1.6	8.4	0.45-29.0	0.29	5.5	0.04-27.3	3.7	13.4	0.76-30.4	0.33	1.6	0.02-3.4
1998	68	3.1	11.9	0.22-20.3	1.4	5.8	0.10-12.2	0.22	1.4	0.01-4.0	3.1	8.1	0.19-10.9	0.30	7.8	0.06-11.7
1999	60	2.8	16.2	0.83-32.8	1.5	4.4	0.41-15.1	0.21	3.7	0.03-10.9	2.7	9.6	1.0-13.9	0.32	1.9	0.05-3.1
2001	60	2.5	19.4	0.81-116	1.6	4.6	0.29-12.6	0.22	0.75	0.02-0.99	3.1	7.4	1.1-20.1	0.34	2.3	0.10-4.4
2003	59	1.9	5.3	0.49-71.8	1.4	3.9	0.46-5.2	0.22	0.91	0.05-1.74	2.4	5.7	0.82-7.1	0.40	1.5	0.12-3.2
Total	632	4.1	19.1	0.22-116	1.4	5.7	0.10-29.0	0.26	1.6	0.01-27.3	3.5	10.1	0.19-39.8	0.29	1.7	0.03-20.2

DnBP: dibutyl phthalate; DiBP: diisobutyl phthalate; BBzP: butylbenzyl phthalate; DEHP: diethylhexyl phthalate; DiNP: diisononyl phthalate
n: number of individuals; P: percentile

References

Aristech Chemical Corporation (1994). 2-Year dietary oral toxicity study in rats with diisononyl phthalate. TSCA 8(e) Submission 8EHQ-0794-13083. CAS number 68515-48-0. Dated July 13, 1994.

Bremmer HJ and van Veen MP (2002). Children's Toys Fact Sheet. To asses the risks for the consumer. RIVM report 612810012/2002, Bilthoven. National Institute of Public Health and the Environment.

Chou K and Wright RO (2006). Phthalates in food and medical devices. *Journal of Medical Toxicology*, **2(3),** 126-135.

Christiansen S, Scholze M, Dalgaard M, Vinggaard AM, Axelstad M, Kortenkamp A and Hass U (2009). Synergistic disruption of external male sex organ development by a mixture of four antiandrogens. *Environmental Health Perspectives*, **117**(12), 1839-1846.

COT (2001). Committees on Toxicity, Mutagenicity, Carcinogenicity of Chemicals in Food, Consumer Products and the Environment. Statement on the tolerable daily intake for dioxins and dioxin-like polychlorinated biphenyls. COT statement 2001/07. Available at:
http://cot.food.gov.uk/cotstatements/cotstatementsyrs/cotstatements2001/dioxinsstate

Darbre PD, Byford JR, Shaw LE, Horton RA, Pope GS and Sauer MJ (2002). Oestrogenic activity of isobutylparaben in vitro and in vivo. *J. Appl. Toxicol.*, **22**(4), 219-226.

DEPA (2009). Danish Environmental Protection Agency. Survey and Health Assessment of the exposure of 2 year-olds to chemical substances in Consumer Products. Survey of chemical Substances in Consumer Products, No. 102. Danish Ministry of the Environment. Available at: http://www2.mst.dk/udgiv/publications/2009/978-87-92548-81-8/pdf/978-87-92548-82-5.pdf

Dickson-Spillmann M, Siegrist M, Keller C and Wormuth M (2009). Phthalate exposure through food and consumers' risk perception of chemicals in food. *Risk Analysis*, **29** (8), 1170-1181.

EC (2002). European Commission Health & Consumer Protection Directorate-General. Review report for the active substance linuron. Finalised in the Standing Committee on the Food Chain and Animal Health at its meeting on 3 December 2002 in view of the inclusion of linuron in Annex I of Directive 91/414/EEC. 7595/VI/97-final, 2 December 2002. Available at:
http://ec.europa.eu/food/plant/protection/evaluation/existactive/list1-30_en.pdf

EC (2005). European Commission Health & Consumer Protection Directorate-General. Scientific Committee on Consumer Products (SCCP) Extended Opinion on

the Safety Evaluation of Parabens. Adopted by the SCCP on 28 January 2005, SCCP/0873/05. Available at: http://ec.europa.eu/health/ph_risk/committees/04_sccp/docs/sccp_o_019.pdf

EC (2006). European Commission Health & Consumer Protection Directorate-General. Scientific Committee on Consumer Products (SCCP) Opinion on Parabens. COLIPA No P82. Adopted by the SCCP during the 9th plenary meeting of 10 October 2006. SCCP/1017/06. Available at: http://ec.europa.eu/health/ph_risk/committees/04_sccp/docs/sccp_o_074.pdf

ECHA (2008). European Chemicals Agency. Guidance on Information Requirements and Chemical Safety Assessment. Available at: http://guidance.echa.europa.eu/docs/guidance_document/information_requirements_en.htm

EFSA (2004a). European Food Safety Authority. Statement of the Scientific Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food (AFC Panel) on the re-classification of some phthalates for consistency with the new SCF guidelines for food contact materials. Expressed on 26 May 2004. Available at: http://www.efsa.europa.eu/en/scdocs/doc/1062.pdf

EFSA (2004b). European Food Safety Authority. Opinion of the Scientific Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food on a Request from the Commission related to para hydroxybenzoates (E 214-219). Question number EFSA-Q-2004-063. Adopted on 13 July 2004. *The EFSA Journal*, **83**, 1-26. Available at: http://www.efsa.europa.eu/en/scdocs/scdoc/83.htm

EFSA (2005a). European Food Safety Authority. Opinion of the Scientific Panel on Food Additives, Flavourings, Processing Aids and Material in Contact with Food (AFC) on a request from the Commission related to Di-Butylphthalate (DBP) for use in food contact materials. Question No EFSA-Q-2003-192, Adopted on 23 June 2005 by written procedure. *The European Food Safety Authority Journal*, **242**, 1-17.

EFSA (2005b). European Food Safety Authority. Statement of the Scientific Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food on a request from the Commission on the possibility of allocating a group-TDI for butylbenzyl phthalate (BBP), di-butylphthalate (DBP), bis(2-ethylexhyl) phthalate (DEHP), di-isononylphthalate (DINP) and di-isodecylphthalate (DIDP). Minutes' statement expressed on 28 June 2005 at its 12th Plenary meeting, corresponding to the item 10 of the agenda. Available at: http://www.efsa.europa.eu/en/home/doc/phthalategroup_minutes_statement.pdf

EFSA (2005c). European Food Safety Authority. Opinion of the Scientific Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food (AFC) on a request from the Commission related to Di-isononylphthalate (DINP) for use in food contact materials. Question Number EFSA-Q-2003-194, adopted on 30 July 2005. *The EFSA Journal*, **244**, 1-18. Available at: http://www.efsa.europa.eu/EFSA/Scientific_Opinion/afc_op_ej244_dinp_en2.pdf?ssbinary=true

EFSA (2005d). European Food Safety Authority. Opinion of the Scientific Panel on Contaminants in the Food Chain on a request from the Commission related to the presence of non dioxin-like polychlorinated biphenyls (PCBs) in feed and food. *The EFSA Journal*, **284**, 1-137. Available at: http://www.efsa.europa.eu/en/scdocs/doc/284.pdf

EFSA (2006). European Food Safety Authority. Opinion of the Scientific Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food on a request from the Commission related to 2,2-BIS(4-HYDROXYPHENYL)PROPANE (Bisphenol A). Question number EFSA-Q-2005-100. Adopted on 29 November 2006. *The EFSA Journal*, **428**, 1-75. Available at: http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1178620772817.htm

EFSA (2008a). European Food Safety Authority. Conclusion on pesticide peer review. Conclusion regarding the peer review of the pesticide risk assessment of the active substance tebuconazole. Issued on 25 September 2008. *EFSA Scientific Report*,**176**, 1-109. Available at: http://www.efsa.europa.eu/en/scdocs/doc/176r.pdf

EFSA (2008b). European Food Safety Authority. Reasoned opinion of EFSA prepared by PRAPeR on MRLs of concern for the active substance vinclozolin. *EFSA Scientific Report*, **166**, 1-36. Available at: http://www.efsa.europa.eu/en/scdocs/doc/166r.pdf

EFSA (2008c). European Food Safety Authority. EFSA updates advice on bisphenol. Available at: http://www.efsa.europa.eu/en/press/news/cef080723.htm

EFSA (2009). European Food Safety Authority. Reasoned Opinion of EFSA prepared by the Pesticides Unit on MRLs of concern for the active substance procymidone (revised risk assessment). *EFSA Scientific Report*, **227**, 1-26. Available at: http://www.efsa.europa.eu/en/scdocs/doc/227r.pdf

European Chemicals Bureau (2004). European Union Risk Assessment Report. Dibutyl phthalate (with addendum). Volume 29, 1st priority list. Available at: http://ecb.jrc.ec.europa.eu/DOCUMENTS/Existing-Chemicals/RISK_ASSESSMENT/REPORT/dibutylphthalatereport003.pdf

Hass U, Scholze M, Christiansen S, Salgaard M, dalgaard M, Vinggaard AM, Axelstad M, Metzdorff SB and Kortenkamp A (2007). Combined exposure to anti-androgens exacerbates disruption of sexual differentiation in the rat. *Environ. Health Pespect.*, **115**(Suppl 1), 122-128.

Hernandez-Diaz S, Mitchell AA, Kelley KE, Calafat AM and Hauser R (2009). Medications as a potential source of exposure to phthalates in the US population. *Environmental Health Perspectives*, **117**(2), 185-189.

Heudorf U, Mersch-Sundermann V and Angerer J (2007). Phthalates: toxicology and exposure. *Int. J. Hyg. Environ. Health*, **210**, 623-634

Lee KY, Shibutani M, Takagi H, Kato N, Takigami S, Uneyama C and Hirose M (2004). Diverse developmental toxicity of di-n-butyl phthalate in both sexes of rat offspring after maternal exposure during the period from late gestation through lactation. *Toxicology*, **203**(1-3), 221-238.

McIntyre BS, Barlow NJ, Wallace DG, Maness SC, Gaido KW and Foster Pm (2000). Effects of in utero exposure to linuron on androgen-dependent reproductive development in the male Crl:CD(SD)BR rat. *Toxicol. Appl. Pharmacol.*, **167**(2), 87-99.

Muller AK, Nielsen E, Ladefoged O (2003). Human exposure to selected phthalates in Denmark. 1st edition, 2003.

NNA (2004). Nordic Nutrition Recommendations 2004, 4th edition. Nord 2004:13. Nordic Council of Ministers, Copenhagen.

Oishi S (2001). Effects of butylparaben on the male reproductive system in rats. *Toxicol. Ind. Health*, **17**, 31-39.

Oishi S (2002). Effects of propyl paraben on the male reproductive system. *Food Chem. Toxicol.*, **40**(12), 1807-1813.

Saillenfait AM, Sabate JP and Gallissot F (2008). Diisobutyl phthalate impairs the androgen-dependent reproductive development of the rat. *Reprod. Toxicol.*, **26**(2), 107-115.

Sathyanarayana S, Karr CJ, Lozano P, Brown E, Calafat AM, Liu F and Swan SH (2010). Baby care products: possible sources of infant phthalate exposure. *Paediatrics*, **121**(2), e260-e268.

SCF (1999). Reports of the Scientific Committee for Food (42nd Series). Compilation of the evaluations of the Scientific Committee for Food on certain monomers and additives used in the manufacture of plastics materials intended to come into contact with foodstuffs until 21 March 1997. European Commission Directorate-General Consumer Policy and Consumer Health Protection, 1999). Available at: http://ec.europa.eu/food/fs/sc/scf/reports/scf_reports_42.pdf

SCF (2000). Scientific Committee on Food. Opinion of the SCF on the Risk Assessment of Dioxins and Dioxin-like PCBs in Food. Adopted on 22 November 2000. European Commission, SCF/CS/CNTM/DIOXIN/8 Final. Available at: http://ec.europa.eu/food/fs/sc/scf/out78_en.pdf

SCF (2001). Scientific Committee on Food. Opinion of the SCF on the Risk Assessment of Dioxins and Dioxin-like PCBs in Food. Update based on new scientific information available since the adoption of the SCF opinion of 22 November 2000. Adopted on 30 May 2001. European Commission, CS/CNTM/DIOXIN/20 final. Available at: http://ec.europa.eu/food/fs/sc/scf/out90_en.pdf

Schettler T (2006). Human exposure to phthalates via consumer products. *International Journal of Andrology*, b29**, 134-139.**

Taxvig C, Hass U, Axelstad M, Dalgaard M, Boberg J, Andeasen HR and Vinggaard AM (2007). Endocrine-disrupting activities in vivo of the fungicides tebuconazole and epoxiconazole. *Toxicol. Sci.*, **100**(2), 464-473.

Tyl RW, Myers CB, Marr MC, Fail PA, Seely JC, Brine DR, Barter RA and Butala JH (2004). Reproductive toxicity evaluation of dietary butyl benzyl phthalate (BBP) in rats. *Reprod. Tox.*, **18**(2), 241-264.

Tyl RW, Myers CB, Marr MC, Sloan CS, Castillo NP, Veselica MM, Seely JC, Dimond SS, Van Miller JP, Shiotsuka RN, Beyer D, Hentges SG, Maechter JM Jr (2008). Two-generation reproductive toxicity study of dietary bisphenol A in CD-1 (Swiss) mice. *Toxicol. Sci.*, **104**(2), 362-384.

US EPA (1989). US Environmental Protection Agency Integrated Risk Information System: Prochloraz. Available at: http://www.epa.gov/ncea/iris/subst/0378.htm

US EPA (1990a). US Environmental Protection Agency Integrated Risk Information System. Dibutyl phthalate. Available at: http://www.epa.gov/ncea/iris/subst/0038.htm

US EPA (1990b). US Environmental Protection Agency Integrated Risk Information System: Linuron. Available at: http://www.epa.gov/ncea/iris/subst/0170.htm

US EPA (1991). US Environmental Protection Agency Integrated Risk Information System. Di(2-ethylhexyl)phthalate (DEHP). Available at: http://www.epa.gov/ncea/iris/subst/0014.htm

US EPA (1992). US Environmental Protection Agency Integrated Risk Information System: Vinclozolin. Available at: http://www.epa.gov/ncea/iris/subst/0126.htm

US EPA (1993a). US Environmental Protection Agency Integrated Risk Information System. Butyl benzyl phthalate. Available at: http://www.epa.gov/ncea/iris/subst/0293.htm

US EPA (1993b). US Environmental Protection Agency Integrated Risk Information System: Bisphenol A. Available at: http://www.epa.gov/ncea/iris/subst/0356.htm

US EPA (1996). US Environmental Protection Agency Integrated Risk Information System: p,p'-Dichlorodiphenyltrichloroethande (DDT). Available at: http://www.epa.gov/ncea/iris/subst/0147.htm

WHO (1983). Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues. Geneva, 5-14 December 1983. Prochloraz. Available at: http://www.inchem.org/documents/jmpr/jmpmono/v83pr37.htm

WHO (2001a). Pesticide residues in food 2001. Toxicological evaluations: prochloraz. Available at: http://www.inchem.org/documents/jmpr/jmpmono/2001pr11.htm#4.0

WHO (2001b). Safety evaluation of certain food additives and contaminants. Polychlorinated dibenzodioxins, polychlorinated dibenzofurans, and coplanar polychlorinated biphenyls. Prepared by the fifty-seventh meeting of the Joint FAO/WHO Expert Committee on Food Additives. WHO Food Additive Series 48. World Health Organization, Geneva.

Wittassek M, Wiesmuller GA, Koch HM, Eckard R, Dobler L, Muller J, Angerer J and Schluter C (2007). Internal phthalate exposure over the last two decades – a retrospective human biomonitoring study. *Int. J. Hyg. Environ. Health*, **210**, 319-333.

Wolfe NL *et al.* (2003). Multigeneration reproduction toxicity study in rats (unaudited draft): Diethylhexylphthalate: Multigenerational reproductive assessment by continuous breeding when administered to Sprague-Dawley rats in the diet. TherImmune Research Corporation (Gaithersburg, Maryland), TRC Study No 7244-200.

Wormuth M, Scheringer M, Vollenweider M *et al.* (2006). What are the sources of exposure to eight frequently used phthalic acid esters in Europeans? *Risk Anal.*, **26**(3), 803-824.

You L, Casanova M, Archibeque-Engle S, Sar M, Fan LQ and Heck HA (1998). Impaired male sexual development in perinatal Sprague-Dawley and Long-Evans hooded rats exposed in utero and lactationally to p,p'-DDE. *Toxicol. Sci.*, **45**(2), 162-173.

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

Health Assessment of Endocrine Disrupting Chemicals – the Danish EPA report and exposure time trends to phthalates

Danish EPA report: Survey and Health Assessment of the exposure of 2 year-olds to chemical substances in Consumer Products

A copy of the full report is available from
http://www2.mst.dk/udgiv/publications/2009/978-87-92548-81-8/pdf/978-87-92548-82-5.pdf

Secretariat
June 2010

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

Health Assessment of Endocrine Disrupting Chemicals – the Danish EPA report and exposure time trends to phthalates

Timeline search on exposure to chemicals listed in the Danish EPA Survey of Chemical Substances in Consumer Products.

Secretariat
June 2010

Key =

A = Useful Paper

B = Previously Identified Paper

C = Potentially Useful Paper

Exclusion Criteria

- Papers that do not include human exposure data
- Papers providing limited dietary exposure data
- Papers concerned with the effects of exposure
- Papers focussed on data recorded due to the proximity of a significant point source emission
- Papers discussing data modelling methodology or the determination of an analytical methodology

Timeline search on exposure to chemicals listed in the Danish EPA Survey of Chemical Substances in Consumer Products

DEHP SEARCH

Databases interrogated –

- PubMed

Search Terms – (DEHP OR “di-octyl phthalate” OR “di-ethyl-hexyl-phthalate”) AND (“Exposure Assessment” OR “Human exposure” OR “Environmental level*” OR “Time trend” OR “Temporal trend”)

Search Dates (From/To) – Not specified

Number of Abstracts Identified – 55

Papers Identified

13. Environ Int. 2007 Nov;33(8):1012-20. Epub 2007 Jul 3.

A Intake of phthalates and di(2-ethylhexyl)adipate: results of the Integrated Exposure Assessment Survey based on duplicate diet samples and biomonitoring data.

Fromme H, Gruber L, Schlummer M, Wolz G, Böhmer S, Angerer J, Mayer R, Liebl B, Bolte G.

Department of Environmental Health, Bavarian Health and Food Safety Authority, Veterinärstrasse 2, D-85764 Oberschleissheim, Germany.
hermann.fromme@lgl.bayern.de

Phthalates are ubiquitous environmental chemicals with potential detrimental health effects. The purpose of our study was to quantify dietary intake of phthalates and of DEHA (Di-ethylhexyl adipate) using duplicate diet samples and to compare these data with the calculated data based on urinary levels of primary and secondary phthalate metabolites. 27 female and 23 male healthy subjects aged 14-60 years collected daily duplicate diet samples over 7 consecutive days.

Overall, 11 phthalates were measured in the duplicates by GC/MS and LC/MS methods. Urinary levels of primary and secondary phthalate metabolites are also available. The median (95th percentile) daily intake via food was 2.4 (4.0) microg/kg b.w. (Di-2-ethylhexyl phthalate, DEHP), 0.3 (1.4) microg/kg b.w. (Di-n-butyl phthalate, DnBP), 0.6 (2.1) microg/kg b.w. (Di-isobutyl phthalate, DiBP) and 0.7 (2.2) microg/kg b.w. for DEHA. MEPH (Mono-2-ethylhexyl phthalate) was detectable only in minor concentrations in the samples, thus conversion of DEHP to MEHP and dietary intake of MEHP were negligible. When comparing back-calculated intake data of the DEHP metabolites with dietary DEHP intake from the day before significant correlations were observed for most of the metabolites. No correlation was found for DnBP and only a weak but significant correlation for DiBP. The median and 95th percentile daily dietary intake of all target analytes did not exceed the recommended tolerable daily intake. Our data indicated that food was the predominant intake source of DEHP, whilst other sources considerably contributed to the daily intake of DnBP and DiBP in an adult population.

PMID: 17610953 [PubMed - indexed for MEDLINE]

15. Int J Hyg Environ Health. 2007 May;210(3-4):345-9. Epub 2007 Feb 23.

A Integrated Exposure Assessment Survey (INES) exposure to persistent and bioaccumulative chemicals in Bavaria, Germany.

Fromme H, Albrecht M, Angerer J, Drexler H, Gruber L, Schlummer M, Parlar H, Körner W, Wanner A, Heitmann D, Roscher E, Bolte G.

Department of Environmental Health, Bavarian Health and Food Safety Authority, Veterinaerstrasse 2, 85764 Oberschleissheim, Germany.
hermann.fromme@lgl.bayern.de

The Integrated Exposure Assessment Survey (INES) was started in the year 2005. Altogether 50 healthy adults living in Bavaria, Germany, were included into the study. Monitoring was conducted in accordance with relevant routes of human exposure (inhalation, ingestion) and integrated different pathways (indoor air, food, house dust). This approach consisted of a combination of external measurements of contaminants with the determination of these substances or their metabolites in body fluids. The target substances were phthalates, perfluorinated compounds (PFC), polychlorinated biphenyls (PCBs), polychlorinated dibenzo-p-dioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs), and polybrominated diphenylethers (PBDEs). This paper gives a brief description of the objectives and the concept of INES as well as methods of sampling and analyses of target compounds. Some preliminary results of biomonitoring data for PFC and phthalates as well as of the dietary intake of DEHP will be discussed.

PMID: 17321208 [PubMed - indexed for MEDLINE]

26. Int J Hyg Environ Health. 2005;208(4):237-45.

A Evaluation of the effect of governmental control of human exposure to two phthalates in Japan using a urinary biomarker approach.

Itoh H, Yoshida K, Masunaga S.

Graduate School of Environment and Information Sciences, Yokohama National University, Japan.
itoh-hiroaki@umin.ac.jp

In Japan, the use of certain phthalates has been regulated. We analyzed the effectiveness of these measures using an analytical biomarker approach. We measured two phthalate metabolites, mono-n-butyl phthalate (MBP) and mono-2-ethylhexyl phthalate (MEHP) in urine samples from 36 participants using enzymatic deconjugation, offline solid phase extraction, and HPLC-ESI-MS/MS. From the levels measured and individual values of creatinine excretion rate the daily intake was determined and compared to each corresponding tolerable daily intake (TDI). The levels of urinary MBP and MEHP were < 1.8-280 and 0.76-25 microg/l, respectively. The ranges of the estimated daily intake of di-n-butyl phthalate (DBP) and di-2-ethylhexyl phthalate (DEHP) from 35 adult urine samples were 0.22-4.5 and 0.37-7.3 microg/kg/ day, respectively. These values were lower than the corresponding TDIs. After comparing these values to previous exposure assessment data on DEHP in Japan, it could be seen that the DEHP intake dropped over the period from 1998 to 2001. Children were not covered in the present study, so the results may only be applicable to adults, not to the Japanese population at large. Even so, the small number of people in one specific geographic area cannot be considered representative of the adult Japanese population. In addition to MEHP, the

secondary metabolites of DEHP, which are more suitable biomarkers should be measured in the future.

PMID: 16078637 [PubMed - indexed for MEDLINE]

38. Environ Health Perspect. 2004 Mar;112(3):327-30.

A Mono(2-ethyl-5-hydroxyhexyl) phthalate and mono-(2-ethyl-5-oxohexyl) phthalate as biomarkers for human exposure assessment to di-(2-ethylhexyl) phthalate.

Kato K, Silva MJ, Reidy JA, Hurtz D 3rd, Malek NA, Needham LL, Nakazawa H, Barr DB, Calafat AM.

Division of Laboratory Sciences, National Center for Environmental Health,
Centers for Disease Control and Prevention, 4770 Buford Highway NE, Atlanta, GA 30341, USA.

Exposure to di-(2-ethylhexyl) phthalate (DEHP) is prevalent based on the measurement of its hydrolytic metabolite mono-(2-ethylhexyl) phthalate (MEHP) in the urine of 78% of the general U.S. population studied in the 1999-2000 National Health and Nutrition Examination Survey (NHANES). However, despite the high level of production and use of DEHP, the urinary MEHP levels in the NHANES samples were lower than the monoester metabolites of phthalates less commonly used than DEHP, suggesting metabolic differences between phthalates. We measured MEHP and two oxidative DEHP metabolites, mono-(2-ethyl-5-oxohexyl) phthalate (MEOHP) and mono (2-ethyl-5-hydroxyhexyl) phthalate (MEHHP) to verify whether these other metabolites account for a greater proportion of DEHP metabolic products in 127 paired human urine and serum samples. We found that the urinary levels of MEHHP and MEOHP were 10-fold higher than levels of MEHP; concentrations of urinary MEOHP and MEHHP were strongly correlated (r = 0.928). We also found that the serum levels of MEOHP and MEHHP were comparatively lower than those in urine. Furthermore, the glucuronide-bound conjugates of the oxidative metabolites were the predominant form in both urine and serum. MEOHP and MEHHP cannot be formed by serum enzymes from the hydrolysis of any contamination from DEHP potentially introduced during blood collection and storage. Therefore, concentrations of MEHHP and MEOHP in serum may be a more selective measure of DEHP exposure than is MEHP. However, additional data on the absorption, distribution, metabolism, and elimination of these oxidative metabolites are needed to completely understand the extent of DEHP exposure from the serum concentrations of oxidative DEHP metabolites.

PMCID: PMC1241862
PMID: 14998748 [PubMed - indexed for MEDLINE]

DINP SEARCH

Databases interrogated –

- PubMed

Search Terms – (DINP OR “di-iso-nonyl-phthalate”) AND (“Exposure Assessment” OR “Human exposure” OR “Environmental level*” OR “Time trend” OR “Temporal trend”)

Search Dates (From/To) – Not specified

Number of Abstracts Identified – 10

Papers Identified

9. NTP CERHR MON. 2003 Mar;(2):i-III90.

A NTP-CERHR Monograph on the Potential Human Reproductive and Developmental Effects of Di-isononyl Phthalate (DINP).

National Toxicology Program.

The National Toxicology Program (NTP) Center for the Evaluation of Risks to Human Reproduction (CERHR) conducted an evaluation of the potential for di-isononyl phthalate (DINP) to cause adverse effects on reproduction and development in humans. DINP is one of 7 phthalate chemicals evaluated by the NTP CERHR Phthalates Expert Panel. These phthalates were selected for evaluation because of high production volume, extent of human exposures, use in children's products, and/or published evidence of reproductive or developmental toxicity. DINP is a mixture of branched, C-9 phthalate isomers used to add flexibility to a wide variety of plastic products such as toys, garden hoses, flooring tiles, tarps, and pool liners. The results of this evaluation on DINP are published in a NTP-CERHR monograph which includes: 1) the NTP Brief, 2) the Expert Panel Report on the Reproductive and Developmental Toxicity of Di-isononyl Phthalate, and 3) public comments received on the Expert Panel Report. As stated in the NTP Brief, the NTP reached the following conclusions regarding the possible effects of exposure to DINP on human development and reproduction. First, although DINP could possibly affect human development if exposures are sufficiently high, there is minimal concern for DINP causing adverse effects to human reproduction or fetal development. There is no direct evidence that exposure of people to DINP adversely affects reproduction or development, but studies show that oral exposure of pregnant rats to high doses (500 and 1000 mg/kg bodyweight/day) of DINP can adversely affect fetal development. Effects on pup growth were noted in a 2-generation reproductive toxicity study in rats at doses of 143-285 mg/kg body weight/day. Human exposure information for DINP was not available but it was assumed that the general US population would be exposed to 3-30 mug/kg body weight/day, based upon the range of estimated exposures for DEHP, a more widely used phthalate. Second, based on estimates of exposure of children to DINP from mouthing toys and other objects, the NTP has minimal concern for developmental effects in children. After the expert panel meeting, a US Consumer Products Safety Commission panel estimated that the majority of children exposed to DINP had a "minimum to non-existent risk of injury" from mouthing toys. Children's exposure was estimated at 70-280 mug/kg body weight/day, a level 1000-fold lower than exposures resulting in developmental effects in rats. NTP-CERHR monographs are transmitted to federal and state agencies, interested parties, and the public and are available electronically in PDF format on the CERHR web site

(http://cerhr.niehs.nih.gov) and in printed text or CD-ROM from the CERHR (National Institute of Environmental Health Sciences, P.O. Box 12233, MD EC-32, Research Triangle Park, NC; fax: 919-316-4511).

PMID: 15995726 [PubMed - in process]

DBP SEARCH

Databases interrogated –

- PubMed

Search Terms – (DBP OR “di-butyl-phthalate” OR “di-n-butyl phthalate”) AND (“Exposure Assessment” OR “Human exposure” OR “Environmental level*” OR “Time trend” OR “Temporal trend”)

Search Dates (From/To) – Not specified

Number of Abstracts Identified – 41

Papers Identified

17. Environ Int. 2007 Nov;33(8):1012-20. Epub 2007 Jul 3.

B Intake of phthalates and di(2-ethylhexyl)adipate: results of the Integrated Exposure Assessment Survey based on duplicate diet samples and biomonitoring data.

(See Above)

23. Int J Hyg Environ Health. 2005;208(4):237-45.

B Evaluation of the effect of governmental control of human exposure to two phthalates in Japan using a urinary biomarker approach.

(See Above)

DIBP SEARCH

Databases interrogated –

- PubMed

Search Terms – (DIBP OR “di-iso butyl-phthalate”) AND (“Exposure Assessment” OR “Human exposure” OR “Environmental level*” OR “Time trend” OR “Temporal trend”)

Search Dates (From/To) – Not specified

Number of Abstracts Identified – 2

Papers Identified

2. Environ Int. 2007 Nov;33(8):1012-20. Epub 2007 Jul 3.

B Intake of phthalates and di(2-ethylhexyl)adipate: results of the Integrated Exposure Assessment Survey based on duplicate diet samples and biomonitoring data.

(See Above)

BBP SEARCH

Databases interrogated –

- PubMed

Search Terms – (BBP OR “butyl-benzyl-phthalate”) AND (“Exposure Assessment” OR “Human exposure” OR “Environmental level*” OR “Time trend” OR “Temporal trend”)

Search Dates (From/To) – Not specified

Number of Abstracts Identified – 6

Papers Identified

NONE

PROCHLORAZ SEARCH

Databases interrogated –

- PubMed

Search Terms – Prochloraz AND (“Exposure Assessment” OR “Human exposure” OR “Environmental level*” OR “Time trend” OR “Temporal trend”)

Search Dates (From/To) – Not specified

Number of Abstracts Identified – 2

Papers Identified

NONE

TEBUCONAZOLE SEARCH

Databases interrogated –

- PubMed

Search Terms – Tebuconazole AND (“Exposure Assessment” OR “Human exposure” OR “Environmental level*” OR “Time trend” OR “Temporal trend”)

Search Dates (From/To) – Not specified

Number of Abstracts Identified – 1

Papers Identified

NONE

LINURON SEARCH

Databases interrogated –

- PubMed

Search Terms – (Linuron OR “3-(3,4-dichlorophenyl)-1-methoxy-1-methylurea “) AND (“Exposure Assessment” OR “Human exposure” OR “Environmental level*” OR “Time trend” OR “Temporal trend”)

Search Dates (From/To) – Not specified

Number of Abstracts Identified – 6

Papers Identified

NONE

VINCLOZOLIN SEARCH

Databases interrogated –

- PubMed

Search Terms – (Vinclozolin OR "(*RS*)-3-(3,5-dichlorophenyl)-5-methyl-5-vinyl-1,3-oxazolidine-2,4-dione") AND ("Exposure Assessment" OR "Human exposure" OR "Environmental level*" OR "Time trend" OR "Temporal trend")

Search Dates (From/To) – Not specified

Number of Abstracts Identified – 6

Papers Identified

NONE

PROCYMIDONE SEARCH

Databases interrogated –

- PubMed

Search Terms – (Procymidone OR "*N*-(3,5-dichlorophenyl)-1,2-dimethylcyclopropane-1,2-dicarboximide") AND ("Exposure Assessment" OR "Human exposure" OR "Environmental level*" OR "Time trend" OR "Temporal trend")

Search Dates (From/To) – Not specified

Number of Abstracts Identified – 2

Papers Identified

NONE

PCB's SEARCH

Databases interrogated –

- PubMed

Search Terms – (PCB* OR "poly-chlorinated-biphenyl*" OR "Polychlorinated biphenyl*") AND ("Exposure Assessment" OR "Human exposure" OR "Environmental level*" OR "Time trend" OR "Temporal trend")

Search Dates (From/To) – Not specified

Limits – Human and English

Number of Abstracts Identified – 201

Papers Identified

19. Chemosphere. 2008 Oct;73(6):907-14. Epub 2008 Aug 20.

A Fourth WHO-coordinated survey of human milk for persistent organic pollutants (POPs): Belgian results.

Colles A, Koppen G, Hanot V, Nelen V, Dewolf MC, Noël E, Malisch R, Kotz A, Kypke K, Biot P, Vinkx C, Schoeters G.

Flemish Institute for Technological Research (VITO), Department Environmental Toxicology, Boeretang 200, BE-2400 Mol, Belgium. Ann.colles@vito.be

Persistent organic pollutants (POPs) are chemicals that accumulate in the food chain and are toxic to humans and wildlife. The fourth World Health Organization (WHO) survey on POP levels in human milk (2006-2009) aims to provide baseline and trend information on human exposure to POPs. So far Belgium participated in all three previous rounds (1988, 1992, 2001). Whereas the first three rounds focused on determination of dioxins and PCBs in pooled (mixed) samples, the fourth survey comprised the analyses of individual milk samples for nine "basic POPs" (chlorinated pesticides and indicator PCBs) and of pooled milk samples for "basic POPs", "advanced POPs" (dioxins and dioxin-like PCBs) and "optional POPs" (polybrominated diphenylethers [PBDEs], polybrominated dioxins and dibenzofurans [PBrDD/F], mixed halogenated dioxins and dibenzofurans [PXDD/F] and hexabromocyclododecane [HBCD]). For the Belgian participation human milk samples were collected during the summer of 2006 from 197 women between 18 and 30 years old distributed over all Belgian provinces. The individual samples were analyzed in a Belgian Laboratory for "basic" POPs. A pooled sample was made from 178 individual samples and analyzed by the WHO Reference Laboratory for the "basic, advanced and optional" POPs. The results indicate that most organochlorinated pesticides banned 25-30 years ago were below or around detection limits in Belgian human milk samples although DDE was still found at low levels in all samples. Over the last five years the levels of marker PCBs and PCDD/Fs in Belgian human milk decreased, respectively, by 58% and 39%. For some of the other emerging or older compounds recent international data are needed to allow comparison. This shows the importance of international studies as run by WHO.

PMID: 18718632 [PubMed - indexed for MEDLINE]

21. Curr Drug Saf. 2007 May;2(2):163-72.

C A review of environmental exposure to persistent organochlorine residuals during the last fifty years.

Lucena RA, Allam MF, Jiménez SS, Villarejo ML.

Department of Preventive Medicine and Public Health, Faculty of Medicine,
University of Cordoba, Public Health Research Group, Spain.

Environmental exposure to persistent toxic organochlorines (Pesticides and
Polychlorinated biphenyls) is ever changing over time and space, as a result of their agricultural and industrial use and the control measures being adopted.

Scientific investigations have revealed the great toxicity of these compounds and their severe impact on human health so that it is quite important to evaluate the risk of human exposure to these toxic compounds by means of a biomarker, such as human milk. The determination of persistent organochlorine compounds in human milk permits the monitoring (time-place) of these toxicants in the human body after its environmental exposure. For this reason, we have reviewed different papers published over the past 50 years in different countries and continents to find out the dynamics of exposure to persistent organochlorine residuals. Scientific progress in analytical methods and toxicological mechanisms, which are changing due to the discovery of certain compounds together with the use and introduction of derived products and the establishment of sanitary measures, has caused a succession of publications on pesticides and PCBs in human milk. These have reflected exposure to these compounds, their great persistence, and the correlation of the levels detected with diverse epidemiological factors (age, profession, number of children, number of them breast fed, residence in rural or urban areas, etc.) with the aim of establishing their association and the effectiveness of protection measures. Our review found that the greatest number of publications on this topic were from European countries, but the trend in these determinations was seen to be similar on the other continents (America, Asia and Africa) with a clear reduction in the levels of organochlorine residuals (Pesticides and PCBs) in human milk. These levels served as biomarkers (time-place) suggesting that the control and prohibition of their use would minimize their impact on public health.

PMID: 18690963 [PubMed - indexed for MEDLINE]

25. Regul Toxicol Pharmacol. 2008 Aug;51(3):278-87. Epub 2008 Apr 24.

C Dietary exposure to dioxins and dioxin-like PCBs in The Netherlands anno 2004.

De Mul A, Bakker MI, Zeilmaker MJ, Traag WA, Leeuwen SP, Hoogenboom RL, Boon PE, Klaveren JD.

RIKILT-Institute of Food Safety, Wageningen University and Research Centre, P.O. Box 230, Bornsesteeg 45, AE Wageningen, The Netherlands.

In this study, representative occurrence data for PCDD/Fs and dioxin-like PCBs in food were obtained and used to estimate dietary exposure of the Dutch population.

Food composite samples were analyzed as well as single fish and vegetables samples. Total dioxin concentrations in animal products ranged from 0.05 pg TEQ/g product in poultry to 2.5 pg TEQ/g product (using TEF(2006)) in fish (shrimp), with 0.12pg TEQ/g product being the lowest concentrations measured in fish (tuna). In vegetable products, concentrations ranged from 0.00002 pg TEQ/g product (white kale) to 0.19 pg TEQ/g (oils and fats). A long-term dietary exposure distribution was calculated using Monte Carlo Risk Assessment software.

The lower bound median exposure of the Dutch population to PCDD/Fs and dioxin-like PCBs was estimated at 0.8 pg WHO-TEQ/kgbw/d, half of which were dioxin-like PCBs. Dairy was the main source (38%) due to its high consumption. Time-trend analysis shows that the exposure to dioxins has further decreased by 35% over the past five years. This is due to lower levels of dioxin-like compounds in most of the foods, mainly influenced by lower levels in meat and milk. The use of the

new TEFs gives an exposure reduction of 10% with respect to TEF(1998). Still, 4% of the Dutch population exceeds the exposure limit of 14 pg/kgbw/week as set by the EU.

PMID: 18554765 [PubMed - indexed for MEDLINE]

28. Chemosphere. 2008 Aug;73(1 Suppl):S220-7. Epub 2008 May 6.

A Persistent environmental contaminants in human milk: concentrations and time trends in Italy.

Abballe A, Ballard TJ, Dellatte E, di Domenico A, Ferri F, Fulgenzi AR, Grisanti G, Iacovella N, Ingelido AM, Malisch R, Miniero R, Porpora MG, Risica S, Ziemacki G, De Felip E.

Italian National Institute for Health, I-00161 Rome, Italy.

Comment in:
Chemosphere. 2008 Oct;73(6):1016-7.

Breast milk monitoring studies of persistent and toxic environmental contaminants are of primary importance for carrying out an adequate risk assessment at the actual levels of human exposure and represent a major source of information on infant perinatal exposure. Milk specimens from mothers of the general population of the Venice and Rome areas were collected over the 1998-2001 period, pooled, and analyzed for selected persistent organic pollutants such as polychlorodibenzodioxins (PCDDs), polychlorodibenzofurans (PCDFs), polychlorobiphenyls (PCBs), organochlorinated pesticides (p,p'-DDE, p,p'-DDT, hexachlorobenzene), and polybromodiphenyl ethers (PBDEs), and the heavy metals Cd, Co, Cu, Hg, Mn, Pb, Sn, and Zn. The goal was to verify whether mother milk from the Venice area, whose lagoon is partly under direct industrial impact, had a contaminant load greater than that from the Rome area, primarily urban. For mothers from the Venice area, the correlation between fish and fishery product consumption and contaminant concentrations in milk was also explored, with however inconclusive results. The concentrations of PCDDs, PCDFs, dioxin-like PCBs, and organochlorinated pesticides determined in this study were compared with those available from a previous analytical work carried out on 1987 human milk pools of domestic origin: the declining trend of the aforesaid contaminants in milk is confirmed to be in agreement with what was observed in other European countries. The breast milk content of (137)Cs and (40)K radionuclides was also determined and compared with data obtained in other research programmes carried out in Italy: the health risk for breastfed infants was deemed to be not significant.

PMID: 18462773 [PubMed - indexed for MEDLINE]

41. Int J Hyg Environ Health. 2007 May;210(3-4):345-9. Epub 2007 Feb 23.

B Integrated Exposure Assessment Survey (INES) exposure to persistent and bioaccumulative chemicals in Bavaria, Germany.

(See Above)

48. Chemosphere. 2007 Apr;67(9):S65-70. Epub 2007 Jan 9.

C A total diet study to estimate PCDD/Fs and dioxin-like PCBs intake from food in Taiwan.

Hsu MS, Hsu KY, Wang SM, Chou U, Chen SY, Huang NC, Liao CY, Yu TP, Ling YC.

Department of Chemistry, National Tsing Hua University, Hsinchu 30013, Taiwan.

Concentrations of 17 dibenzo-p-dioxins/dibenzofurans (PCDD/Fs) and 12 dioxin-like polychlorinated biphenyls (dl-PCBs) were measured in total diet study samples of 14 food groups of animal origin from 11 locations in Taiwan, collected in 2003.
Pork meat possessed the lowest background concentration level of 0.058 pg WHO-TEQ(PCDD/Fs+dl-PCBs)/g fresh weight. The dl-PCBs contribution were 31%, 59%, 36%, 46%, and 13% for meat and meat products, muscle meat of fish, milk and dairy products, fat and oil, and egg, respectively. The estimated monthly intake (EMI) was 44.7 and 39.5 pg WHO-TEQ(PCDD/Fs+dl-PCBs)/kg b.w./month for a male and female adult weighing 64.8 kg and 56.3 kg, respectively. Muscle meat of fish contributes 46% to the mean EMI. Factors affecting the EMI, in order of increasing importance are analytical method uncertainty, sample compositional difference, and food consumption data. In addition to the continuous efforts to identify and reduce the source of PCDD/Fs and dl-PCBs releases into the environment and the food-chain, the practice of a healthy dietary habit, i.e., eating foods of lower TEQ levels, was suggested to effectively reduce human exposure to PCDD/Fs and dl-PCBs.

PMID: 17215025 [PubMed - indexed for MEDLINE]

49. Chemosphere. 2007 Apr;67(9):S295-300. Epub 2007 Jan 17.

C Concentrations of polychlorinated biphenyls (PCBs) and polybrominated diphenyl ethers (PBDEs) in milk of women from Catalonia, Spain.

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In this study, the concentrations of polychlorinated biphenyls (PCBs) and polybrominated diphenyl ethers (PBDEs) in milk from women living in the vicinity of a new hazardous waste incinerator (HWI) in Catalonia, Spain, were determined.

The study was performed after 4 years of regular operations in the facility and the present PCB levels were compared with baseline concentrations obtained in a pre-operational program. PCBs and PBDEs levels were determined by HRGC/HRMS in 15 samples. In the present study planar PCBs ranged from 1.3 to 6.3 pg WHO-TEQ/g fat with a mean value of 3.8 pg WHO-TEQ/g fat. After adding dioxin-like mono-ortho-PCBs the total PCB-TEQ concentrations ranged from 3.8 to 13.3 pg WHO-TEQ/g fat (mean value: 8.7 pg WHO-TEQ/g fat). A comparison of the current data with those obtained in the baseline study showed significant decreases for both planar and total WHO-TEQ of

PCBs: 47.9% and 44.6%, respectively. PCB concentrations in milk of women living in urban zones were higher than those living near industrial areas (10.1 and 7.4 pg WHO-TEQ/g fat, respectively). Mean PBDE concentrations were 2.2 and 2.5 ng/g fat for women living in urban and industrial zones, respectively. Dietary intake of PCBs and PBDEs for a standard adult woman samples were 898 and 843 ng/day for PCBs, and 72 and 63 ng/day for PBDEs, for residents in urban and industrials areas, respectively. This study suggests that dietary intake is more relevant for human exposure to PCBs and
PBDEs than living near the HWI.
54. Mol Nutr Food Res. 2006 Oct;50(10):922-33.

A Dioxins, polychlorinated biphenyls and other organohalogen compounds in human milk. Levels, correlations, trends and exposure through breastfeeding.

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Polychlorinated dibenzo-p-dioxins (PCDD) and dibenzofurans (PCDF), together simplified termed "dioxins", polychlorinated biphenyls (PCB), polybrominated diphenylethers (PBDE) and organochlorine pesticides constitute lipophilic, persistent organic pollutants that bioaccumulate in the food chain and consequently can be found in humans at considerable concentrations. During the past 30 years our institute analyzed far more than 2,000 individual human milk samples for organochlorine pesticides and PCB and over 1,000 specimens for PCDD/PCDF. The results of these analyses provide an overview and reliable basis as to contamination of human milk with these compounds, their correlations among each other, the temporal trend of exposure through breastfeeding and the predominant parameters that influence the maternal body burden. It was found that the levels of most persistent organohalogen compounds in human milk decreased significantly over the past three decades and equally did their exposure through breastfeeding. Exceptions are PBDE, which are still extensively used as flame-retardants. PBDE levels in milk samples collected in the early 2,000s are approximately 60% higher compared to specimens sampled 10 years before. Moreover, in contrast to PCB, PBDE show no significant correlation with PCDD/PCDF in human milk, which might be interpreted as an indication for another mode of human exposure.

PMID: 17009213 [PubMed - indexed for MEDLINE]

61. Environ Health Perspect. 2006 Aug;114(8):1179-85.

C Levels and concentration ratios of polychlorinated biphenyls and polybrominated diphenyl ethers in serum and breast milk in Japanese mothers.

Inoue K, Harada K, Takenaka K, Uehara S, Kono M, Shimizu T, Takasuga T,
Senthilkumar K, Yamashita F, Koizumi A.

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Blood and/or breast milk have been used to assess human exposure to various environmental contaminants. Few studies have been available to compare the concentrations in one matrix with

those in another. The goals of this study were to determine the current levels of polybrominated diphenyl ethers (PBDEs) and polychlorinated biphenyls (PCBs) in Japanese women, with analysis of the effects of lifestyle and dietary habits on these levels, and to develop a quantitative structure-activity relationship (QSAR) with which to predict the ratio of serum concentration to breast milk concentration. We measured PBDEs and PCBs in 89 paired samples of serum and breast milk collected in four regions of Japan in 2005. The geometric means of the total concentrations of PBDE (13 congeners) in milk and serum were 1.56 and 2.89 ng/g lipid, respectively, whereas those of total PCBs (15 congeners) were 63.9 and 37.5 ng/g lipid, respectively. The major determinant of total PBDE concentration in serum and milk was the geographic area within Japan, whereas nursing duration was the major determinant of PCB concentration. BDE-209 was the most predominant PBDE congener in serum but not in
milk. The excretion of BDE 209 in milk was lower than that of BDE 47 and BDE 153. QSAR analysis revealed that two parameters, calculated octanol/water partition and number of hydrogen-bond acceptors, were significant descriptors. During the first weeks of lactation, the predicted partitioning of PBDE and PCB congeners from serum to milk agreed with the observed values. However, the prediction became weaker after 10 weeks of nursing.

PMCID: PMC1552037
PMID: 16882522 [PubMed - indexed for MEDLINE]

62. Arch Environ Contam Toxicol. 2006 Aug;51(2):296-313. Epub 2006 May 22.

A Human blood monitoring program in Japan: contamination and bioaccumulation of persistent organochlorines in Japanese residents.

Minh TB, Watanabe M, Kajiwara N, Iwata H, Takahashi S, Subramanian A, Tanabe S, Watanabe S, Yamada T, Hata J.

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Japan.

Concentrations of persistent organochlorines (OCs)-such as polychlorinated
biphenyls (PCBs), 1,1,1-trichloro-2,2-bis(p-chlorophenyl)ethane (DDT) and its
metabolites (DDTs), hexachlorocyclohexane isomers (HCHs), chlordane compounds (CHLs),
hexachlorobenzene, and tris(4-chlorophenyl)methane [TCPMe]-were determined in plasma samples from residents of three sub-metropolitan locations in Japan (Miyako, Saku, and Tottori) for the purpose of studying the geographic variation and specific accumulation of OCs. Residue concentrations of PCBs and DDTs were the highest in samples collected in Saku (400 and 370 ng/g lipid wt, respectively) whereas samples from Miyako contained greater CHL residues (70 ng/g lipid wt) than those from the other two locations. This contamination pattern reflects the historic use of OCs in each area. For the first time, tris (4-chlorophenyl) methane (TCPMe) concentrations were detected in most of the plasma sample analyzed. Concentrations of TCPMe which ranged from <0.1 to 8.1 n/g lipid wt eight, were lower than those previouly reported in other human tissue. Larger geographic differences in OC accumulation were observed for PCBs and CHLs, whereas DDTs and HCHs exhibited little variability. PCB concentrations in samples from Saku residents were higher than those from residents of countries in the circumpolar Arctic region but lower than those reported for some populations in the United States and Western European countries. Interestingly, CHL residue concentrations in human blood from Japan are among the highest values reported for the countries examined, suggesting continued increased exposure to CHLs of the Japanese population. Time-trend

analysis of CHLs in human blood samples from Miyako (Okinawa prefecture) showed that CHL residues have decreased substantially during the last decade, indicating the effect of the official ban of CHLs in 1986 in Japan. Isomer-specific analysis of PCBs revealed lower proportions of higher chlorinated congeners such as hepta- and octachlorobiphenyls in women than in men, suggesting the possibility of preferential elimination of higher chlorinated biphenyls in women. The difference in sex-dependent accumulation of OC compounds in healthy and ill persons was suggested. To our knowledge, this is the first report on the specific accumulation of persistent QCs, including TCPMe, in human blood samples from Japan.

PMID: 16783626 [PubMed - indexed for MEDLINE]

70. Chemosphere. 2006 Aug;64(9):1601-8. Epub 2006 Jan 4.

A Contamination status of persistent organochlorines in human breast milk from Japan: recent levels and temporal trend.

Kunisue T, Muraoka M, Ohtake M, Sudaryanto A, Minh NH, Ueno D, Higaki Y, Ochi M, Tsydenova O, Kamikawa S, Tonegi T, Nakamura Y, Shimomura H, Nagayama J, Tanabe S.

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Contamination levels of persistent organochlorines (OCs) such as polychlorinated dibenzo-p-dioxins (PCDDs), dibenzofurans (PCDFs), biphenyls (PCBs), dichlorodiphenyltrichloroethane and its metabolites (DDTs), hexachlorocyclohexane isomers (HCHs), hexachlorobenzene (HCB), and chlordane compounds (CHLs) was examined in human breast milk collected during 2001-2004 from Fukuoka prefecture in Japan. The concentrations of OCs such as dioxins and related compounds, DDTs, CHLs and HCB in human breast milk from primiparae were comparable to or slightly higher than the data obtained during 1998, indicating that the levels of these contaminants in Japanese human breast milk have not decreased since 1998 and Japanese are continuously exposed to these chemicals, presumably via fish intake.
In addition, OC levels in human breast milk from primiparae were significantly higher than those from multiparae, implying elimination of OCs via lactation.
Furthermore, significant positive correlations were observed between levels of OCs in human breast milk and the age of primiparae. These results indicate that the mothers with higher age may transfer higher amounts of OCs to the first infant than to the infants born afterwards through breast-feeding, and hence the first born children might be at higher risk by OCs.

PMID: 16386779 [PubMed - indexed for MEDLINE]

74. Environ Res. 2005 Sep;99(1):31-9. Epub 2005 Jan 22.

A Assessment of human exposure to polychlorinated biphenyls and polybrominated diphenyl ethers in Japan using archived samples from the early 1980s and mid-1990s.

Koizumi A, Yoshinaga T, Harada K, Inoue K, Morikawa A, Muroi J, Inoue S, Eslami B, Fujii S, Fujimine Y, Hachiya N, Koda S, Kusaka Y, Murata K, Nakatsuka H, Omae K, Saito N, Shimbo S, Takenaka K, Takeshita T, Todoriki H, Wada Y, Watanabe T, Ikeda M.

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Persistent organic pollutants have been linked to various adverse effects on human health. We conducted a retrospective exposure assessment for 11 polychlorinated biphenyl (PCB) congeners and 4 polybrominated diphenyl ether (PBDE) congeners. We analyzed paired samples of blood and food duplicate portions collected in the 1980s (1980 survey, N=40) and the mid-1990s (1995 survey, N=40) from females (five participants from each of eight sites per survey) living throughout Japan, from Hokkaido to Okinawa. The study populations in the 1980 and 1995 surveys were different but had lived in the same community. We measured PCBs and PBDEs in serum and PCBs in diet. Total serum PCBs (ng/g lipid) [geometric mean (geometric standard deviation)] were similar in the 1980 [163.0 (1.7)] and the 1995 [142.6 (2.0)] surveys. In contrast, dietary intake (ng/day) between 1980 and 1995 decreased significantly, from 522.8 (2.5) to 165.9 (3.3), respectively, ($P<0.05$). We classified the participants by birth year-before 1941 (older generation) and equal to or after 1941 (younger generation). Serum PCB levels decreased significantly in the younger generation, from 179.1 (1.8) in the 1980 survey to 115.4 (2.0) in the 1995 survey ($P<0.05$). However, in the older generation, serum levels (ng/g lipid) did not change: 150.4 (1.6) in the 1980 survey and 180 (1.8) in the 1995 survey. Total PBDE serum levels (ng/g lipid) increased significantly during the 15 years, from 0.5 (3.5) to 1.8 (3.7) ($P<0.05$). At the Shimane site, PBDE serum levels (ng/g lipid) increased 20-fold, from 1.3 (4.8) to 26.0 (5.0). The serum levels of PCBs decreased in the younger generation but not in the older, although levels in daily intakes decreased significantly. Exposure levels of PBDEs appear to be increasing in an area-specific manner.

PMID: 16053925 [PubMed - indexed for MEDLINE]

92. Sci Total Environ. 2004 Sep 1;330(1-3):55-70.

C Circumpolar maternal blood contaminant survey, 1994-1997 organochlorine compounds.

Van Oostdam JC, Dewailly E, Gilman A, Hansen JC, Odland JO, Chashchin V, Berner J, Butler-Walker J, Lagerkvist BJ, Olafsdottir K, Soininen L, Bjerregard P, Klopov V, Weber JP.

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During the past 20 years a number of studies have found neurological and immunological effects in the developing fetus and infants exposed to background or only slightly elevated levels of persistent organic pollutants (POPs) such as polychlorinated biphenyls (PCBs). To address concerns arising from possible increased human exposure in the Arctic and possible effects of POPs, all circumpolar countries agreed in 1994 to monitoring of specific human tissues for contaminants in the Arctic under the Arctic Monitoring and Assessment Program (AMAP). Mothers in eight circumpolar countries contributed blood samples that were analysed at a single laboratory for 14 PCB congeners (IUPAC No. 28, 52, 99, 105, 118, 128, 138, 153, 156, 170, 180, 183, 187) and 13 organochlorine pesticides (aldrin, beta-hexachlorocyclohexane (beta-HCH), dichlordiphenyltrichloroethane (p,p'-DDT), diphenyldichloroethylene (p,p'-DDE), dieldrin, heptachlorepoxide, hexachlorobenzene (HCB), mirex, and the chlordane derivatives alpha-chlordane, gamma-chlordane, cis-nonachlor, oxychlordane and trans-nonachlor). Inuit mothers from Greenland and Canada have significantly

higher levels of oxychlordane, transnonachlor and mirex than mothers from Norway, Sweden, Iceland and Russia. Inuit mothers from Greenland also have significantly higher levels of these contaminants than Inuit mothers from Canada and Alaska.

These differences among Inuit groups may represent regional dietary preferences or different contaminant deposition patterns across the Arctic. Levels of PCBs are also elevated among some arctic populations due to their consumption of marine mammals and are in the range where subtle effects on learning and the immune system have been reported. The Russian mothers who consume mainly food imported from southern Russia have elevated levels of DDT, DDE, beta-HCH and a higher proportion of lower chlorinated PCB congeners. This study has allowed an assessment of the variation of contaminants such as PCBs and various organochlorine pesticides (DDT, chlordane, etc.) in human populations around the circumpolar north.

PMID: 15325158 [PubMed - indexed for MEDLINE]

100. Environ Health Perspect. 2004 May;112(6):654-8.

A Retrospective time-trend study of polybrominated diphenyl ether and polybrominated and polychlorinated biphenyl levels in human serum from the United States.

Sjödin A, Jones RS, Focant JF, Lapeza C, Wang RY, McGahee EE 3rd, Zhang Y, Turner WE, Slazyk B, Needham LL, Patterson DG Jr.

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Comment in:
Environ Health Perspect. 2004 Dec;112(17):A978-9; author reply A979.

Six polybrominated diphenyl ethers (PBDEs), one hexabromobiphenyl [polybrominated biphenyl (PBB)], and one hexachlorobiphenyl [polychlorinated biphenyl (PCB)] were measured in 40 human serum pools collected in the southeastern United States during 1985 through 2002 and in Seattle, Washington, for 1999 through 2002. The concentrations of most of the PBDEs, which are commercially used as flame retardants in common household and commercial applications, had significant positive correlations with time of sample collection, showing that the concentrations of these compounds are increasing in serum collected in the United States. In contrast, PCB and PBB levels were negatively correlated with sample collection year, indicating that the levels of these compounds have been decreasing since their phaseout in the 1970s.

PMCID: PMC1241957
PMID: 15121506 [PubMed - indexed for MEDLINE]

118. Arch Environ Contam Toxicol. 2002 Nov;43(4):473-80.

A Organochlorine pesticides and polychlorinated biphenyl residues in foodstuffs and human tissues from china: status of contamination, historical trend, and human dietary exposure.

Nakata H, Kawazoe M, Arizono K, Abe S, Kitano T, Shimada H, Li W, Ding X.

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Concentrations of persistent organochlorine pesticides such as DDTs, hexachlorocyclohexanes (HCHs), chlordane compounds (CHLs), hexachlorobenzene (HCB), and polychlorinated biphenyls (PCBs), were determined in a wide variety of foodstuffs and human tissues collected from Shanghai and its vicinity in China in 2000-2001. Among the organochlorines analyzed, DDT and its metabolites were prominent compounds in most of the foodstuffs. In particular, mussels contained noticeable residues of DDTs (34,000 ng/g lipid weight), which are one to three orders greater than those reported levels in bivalves from other Asian countries.

Concentrations of HCHs, CHLs, HCB, and PCBs in foodstuffs were generally low, suggesting small amounts of inputs into the environment. Temporal trends examined by comparing the results of previous studies of organochlorine levels in Chinese foodstuffs in 1970s and 1992 revealed a greater amounts of declines of DDTs and HCHs residues and the average daily intakes during the past 30 years. In contrast, very high concentrations of DDTs and HCHs were detected in human tissues from Shanghai, with the maximum values as high as 19,000 ng/g lipid weight (mean: 7,600 ng/g) and 17,000 ng/g (mean: 7,400 ng/g), respectively.

Considering that foodstuffs are a main source of human exposure to contaminants, the greater concentrations of DDTs and HCHs in Chinese people might be due to past extensive usage of these compounds as agricultural pesticides. Continuous monitoring and epidemiological studies of organochlorine pesticides in humans are warranted in China. To our knowledge, this is the first report to present the residue levels of persistent organochlorine pesticides and PCBs in human tissues of China.

PMID: 12399919 [PubMed - indexed for MEDLINE]

141. Chemosphere. 2000 May-Jun;40(9-11):1111-23.

A Certain organochlorine and organobromine contaminants in Swedish human milk in perspective of past 20-30 years.

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The investigations of organochlorine compounds in breast milk from women living in the Stockholm region started in 1967. The present study summarises the investigations of polychlorinated biphenyls (PCBs), naphthalenes (PCNs),
dibenzo-p-dioxins (PCDDs), dibenzofurans (PCDFs), polybrominated diphenyl ethers (PBDEs) and pesticides (DDT, DDE, hexachlorobenzene, dieldrin) as well as methylsulfonyl metabolites of PCBs and DDE in human milk sampled during different periods up to 1997. During the course of 20-30 yr the levels of organochlorine compounds in human milk have decreased to various extent. A decrease to the half of the original concentration was attained in the range of 4-17 yr periods. On the contrary to the organochlorine compounds, the concentrations of PBDEs have increased during the period

1972-1997, indicating a doubling of the levels by 5 yr. The levels reflect the environmental contamination and background levels in the population. The accumulation and ongoing increase in the levels of PBDEs calls for immediate measures to stop the environmental pollution and human exposure to PBDEs.

PMID: 10739053 [PubMed - indexed for MEDLINE]

155. Sci Total Environ. 1998 Apr 23;215(1-2):31-9.

A Organochlorine pesticides and polychlorinated biphenyls in human milk of mothers living in northern Germany: current extent of contamination, time trend from 1986 to 1997 and factors that influence the levels of contamination.

Schade G, Heinzow B.

Landesamt für Natur und Umwelt, Flintbek, Germany.

This study reports the concentration levels of PCB, DDT, HCB and beta-HCH in the human milk of women living in northern Germany over a period of 12 years and determines factors that may influence these levels. From 1986 to 1997 more than 3500 milk samples were analyzed for organochlorine compounds. A questionnaire was used to obtain information regarding personal characteristics, life style factors and eating habits. Descriptive statistics of concentration levels were computed to characterize the current extent of contamination. To follow time trends across the years homogeneous subgroups were compared and multiple regression analyses were used to investigate associations between determining factors and specific contaminants. Between summer 1995 and summer 1997 the median PCB concentration level was 0.502 mg/kg, the median DDT level 0.202 mg/kg, the median HCB level 0.065 mg/kg and the median beta-HCH level 0.036 mg/kg, all values expressed on a fat basis. The median concentration levels decreased by 80-90% during the past 12 years and the median PCB levels by 60%. The concentration levels of all substances were positively correlated with maternal age and negatively associated to parity, to the total period of breast-feeding and to a weight increase of mothers before and after delivery. Post-pregnancy BMI was a significant predictor of the likelihood of having higher concentrations for DDT, HCB and beta-HCH and of having lower concentrations for PCB levels. A balanced diet for at least 3 years was related to lower HCB and beta-HCH levels. Women who ate more than 100 g of fish or more than 700 g of meat per week were more likely to have higher PCB and beta-HCH levels or higher HCB levels, respectively. Higher HCB and beta-HCH concentration levels were associated with lower birth weights of female infants.

PMID: 9599454 [PubMed - indexed for MEDLINE]

Databases interrogated –

- PubMed

Search Terms – Dioxin* AND (“Exposure Assessment” OR “Human exposure” OR “Environmental level*” OR “Time trend” OR “Temporal trend”)

Search Dates (From/To) – Not specified

Limits – Human and English

Number of Abstracts Identified – 213

Papers Identified

15. Chemosphere. 2008 Oct;73(6):907-14. Epub 2008 Aug 20.

B Fourth WHO-coordinated survey of human milk for persistent organic pollutants (POPs): Belgian results.

(See Above)

21. Chemosphere. 2008 Aug;73(1 Suppl):S220-7. Epub 2008 May 6.

B Persistent environmental contaminants in human milk: concentrations and time trends in Italy.

(See Above)

47. Int J Hyg Environ Health. 2007 May;210(3-4):345-9. Epub 2007 Feb 23.

B Integrated Exposure Assessment Survey (INES) exposure to persistent and bioaccumulative chemicals in Bavaria, Germany.

(See Above)

60. Mol Nutr Food Res. 2006 Oct;50(10):922-33.

B Dioxins, polychlorinated biphenyls and other organohalogen compounds in human milk. Levels, correlations, trends and exposure through breastfeeding.

(See Above)

71. Chemosphere. 2006 Aug;64(9):1601-8. Epub 2006 Jan 4.

B Contamination status of persistent organochlorines in human breast milk from Japan: recent levels and temporal trend.

(See Above)

85. Food Chem Toxicol. 2005 May;43(5):671-9.

A Human exposure to dioxins from food, 1999-2002.

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In response to aggressive attempts to control dioxin emissions over the last 35 years, human exposures to dioxins from the environment have declined significantly. The primary source of human exposure to dioxins at present is food. The sources of dioxins in food are not well understood and are probably varied. Data on the levels of dioxins measured in various foods for samples collected from 2000 to 2002 have recently been released by the US Food and Drug Administration as part of its Total Diet Study. Data on samples collected in 1999, and released in 2002, are also available. Based on those data and on the US Department of Agriculture's most recent food consumption survey (1994-1996 & 1998 Continuing Survey of Food Intakes by Individuals), estimates of dioxin intake for the total US population and for three age groups of children were obtained.

Results show that the most recent mean dietary exposures for all groups are below 2 pg TEQ/kg BW/day, the tolerable daily intake established for dioxins by the World Health Organization. Between 1999 and 2002 mean dioxin intakes from food appear to have decreased, but when estimates are adjusted based on a standardized limit of detection and evaluating only those {congenerxfood} combinations common to all 4 years, no trend is apparent. When dioxin concentrations below the limit of detection are represented by one-half the limit, approximately 5% of the intake estimates for 2-year-olds and 1% of the intake estimates for 6-year-olds exceed the tolerable daily intake by about 10%, although such upper-percentile estimates should not be equated with excess risk. When non-detectable dioxin values are set to zero (i.e., when only dioxin values actually measured are used), only 1% of intake estimates exceed the tolerable daily intake for

2-year-olds. As expected, about 50% of daily dietary dioxin intake by the total US population is attributable to meat and dairy products, based on the same food group classifications used by the National Academy of Sciences' Committee on the Implications of Dioxin in the Food Supply. This information may be useful for targeting future risk management activities.

PMID: 15778006 [PubMed - indexed for MEDLINE]

136. Chemosphere. 2000 May-Jun;40(9-11):1111-23.

B Certain organochlorine and organobromine contaminants in Swedish human milk in perspective of past 20-30 years.

(See Above)

163. J Toxicol Environ Health. 1995 Oct;46(2):133-48.

A PCDDs, PCDFs, and PCBs in human milk from different parts of Norway and Lithuania.

Becher G, Skaare JU, Polder A, Sletten B, Rossland OJ, Hansen HK, Ptashekas J.

Department of Environmental Medicine, National Institute of Public Health, Oslo, Norway.

Concentrations of 2,3,7,8-substituted polychlorinated dibenzo-p-dioxins (PCDDs) and dibenzofurans (PCDFs) as well as 16 polychlorinated biphenyls (PCBs) have been determined in pooled samples of breast milk from 10-12 mothers living in three different geographical areas in both Norway and Lithuania. The results indicate no apparent dependency of the PCDD/PCDF levels, expressed as toxic equivalents (TEQs), and total PCB levels on the geographical residence of the donors within a country. This confirms the findings from a corresponding Norwegian study in 1985/1986 where individual samples from the same areas were analyzed. Teh total TEQs, including dioxin-like PCBs, ranged from 31 to 42 pg TEQs/g fat in Norway and from 45 to 49 pg TEQs/g fat in Lithuania. The mean concentration of PCDDs/PCDFs in the Norwegian samples (10.4 pg TEQs/g fat) was slightly lower than in the Lithuanian samples (14.8 pg TEQs/g fat). Dioxin-like PCBs were found to contribute two to three times more to the total TEQs than the PCDDs and PCDFs. Major contributors among the dioxin-like PCBs were PCBs 126, 156, 114, 118, and 170. Comparison of the present data with those obtained in the
Norwegian study in 1985/1986 shows that for PCDDs/PCDFs the mean TEQ levels have decreased by about 37% in the 7-yr time span, while the levels of total PCBs, as determined by packed-column gas chromatography, have remained unchanged or only slightly decreased. Future studies are necessary to confirm this potential temporal trend.

PMID: 7563213 [PubMed - indexed for MEDLINE]

172. Environ Health Perspect. 1994 Jan;102 Suppl 1:173-85.

C PCDD and PCDF exposure and levels in humans in Germany.

Beck H, Dross A, Mathar W.

Bundesgesundheitsamt, Berlin, Germany.

For nonoccupationally exposed persons, the daily intake via food consumption has been calculated to be 0.35 pg/kg body weight per day for 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) and 2.3 pg/kg body weight per day for TCDD equivalents (TEqs). As compared to food, other sources and pathways are of minor importance. Food of animal origin contributes most, although human exposure begins with atmospheric emissions depositing these compounds on plant surfaces.

In the meantime, a possible additional body burden from cardboard containers for cow's milk and coffee filters has been practically excluded. Of the 210 existing PCDDs and PCDFs, only 15 2,3,7,8-substituted isomers with a characteristic congener pattern can be found in samples of human origin. In adipose tissue and milk samples, mean levels for 2,3,7,8-TCDD of 7.2 and 3.6 pg/g fat, respectively, and of 56 (range 18-122) and 30 (range 10-72) pg TEqs/g fat, respectively, were determined. Human data revealed a dependency of polychlorinated dibenzo-p-dioxins/polychlorinated dibenzofurans (PCDD/PCDF) levels on age. In human milk, levels became reduced with the number of children born to mothers and duration of breast-feeding period. The average daily intake for a breast-fed child has been calculated to be 17 pg 2,3,7,8-TCDD/kg body weight per day and 142 pg TEqs/kg body weight per day, respectively. Levels in adipose tissue of infants, even if breast fed, were distinctly lower compared to human milk. In human milk, adipose tissue, and whole blood, PCDD/PCDF concentrations have been found to be equal on a fat-weight basis. Liver fat accumulated PCDD/PCDF with an alteration in the congener distribution pattern, whereas brain, even on a fat-weight basis, showed the lowest concentrations. Elevated or even high levels were found in occupationally exposed persons working in special chemical plants or involved in specific processes. There are limited data suggesting slightly elevated PCDD/PCDF levels are due to long-term consumption of a large share of food produced near point sources with a heavy emission or ingestion of soil or dust from such areas.

PMCID: PMC1566882
PMID: 8187706 [PubMed - indexed for MEDLINE]

182. Sci Total Environ. 1991 May 1;104(1-2):97-127.

C Human exposure to dioxin.

Travis CC, Hattemer-Frey HA.

Office of Risk Analysis, Health and Safety Research Division, Oak Ridge National Laboratory, TN 37831-6109.

Because 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) is the most potent chemical carcinogen evaluated by the U.S. Environmental Protection Agency (EPA), many people fear that exposure to even small amounts of TCDD could lead to serious health effects. Ambient measurements confirm that environmental TCDD contamination is widespread. The public is concerned about TCDD exposure from such diverse sources as municipal solid waste incinerators, pulp and paper mills, and contaminated fish and soil. This paper evaluates several critical issues including: (i) the extent of background contamination; (ii) accumulation in the food chain and the potential for human exposure from ingesting contaminated food items; (iii) the magnitude of TCDD emissions into the

U.S. environment, and the relative contribution of various known TCDD sources to the total TCDD load; and (iv) setting environmental standards for TCDD.

PMID: 1871593 [PubMed - indexed for MEDLINE]

DDT's / DDD's SEARCH

Databases interrogated –

- PubMed

Search Terms – (DDT OR DDD OR "dichloro-diphenyl-trichloroethane" OR "dichloro-diphenyl-dichloroethane") AND ("Exposure Assessment" OR "Human exposure" OR "Environmental level*" OR "Time trend" OR "Temporal trend")

Search Dates (From/To) – Not specified

Limits – Human and English

Number of Abstracts Identified – 71

Papers Identified

8. Chemosphere. 2008 Aug;73(1 Suppl):S220-7. Epub 2008 May 6.

B Persistent environmental contaminants in human milk: concentrations and time trends in Italy.

(See Above)

16. Arch Environ Contam Toxicol. 2006 Aug;51(2):296-313. Epub 2006 May 22.

B Human blood monitoring program in Japan: contamination and bioaccumulation of persistent organochlorines in Japanese residents.

(See Above)

22. Sci Total Environ. 2004 Sep 1;330(1-3):55-70.

B Circumpolar maternal blood contaminant survey, 1994-1997 organochlorine compounds.

(See Above)

30. Arch Environ Contam Toxicol. 2002 Nov;43(4):473-80.

B Organochlorine pesticides and polychlorinated biphenyl residues in foodstuffs and human tissues from china: status of contamination, historical trend, and human dietary exposure.

(See Above)

42. Chemosphere. 2000 May-Jun;40(9-11):1111-23.

B Certain organochlorine and organobromine contaminants in Swedish human milk in perspective of past 20-30 years.

(See Above)

46. Sci Total Environ. 1998 Oct 8;221(2-3):201-4.

A Time trend of organochlorine pesticide residues in human adipose tissue in Veracruz, Mexico: 1988-1997 survey.

Waliszewski SM, Aguirre AA, Infanzón RM, Rivera J, Infanzón R.

Instituto de Medicina Firense, Universidad Veracruzana, Boca del Río, Mexico.

The monitoring study of 287 human adipose tissue samples collected from 1988 to 1997 was used to determine the contamination levels of organochlorine pesticides.

The results obtained indicate DDT as dominant. The fluctuation of DDT levels during the study period reveal a descent tendency and are closely related to the pp'-DDE content. The results, classified according to the origin of donors, indicate a higher contamination of the suburban zone. This difference was caused by diminished use of DDT and its substitution by Malathion and pyrethroids.

PMID: 9842747 [PubMed - indexed for MEDLINE]

51. Sci Total Environ. 1998 Apr 23;215(1-2):31-9.

B Organochlorine pesticides and polychlorinated biphenyls in human milk of mothers living in northern Germany: current extent of contamination, time trend from 1986 to 1997 and factors that influence the levels of contamination.

(See Above)

70. Pestic Monit J. 1977 Sep;11(2):61-3.

A Effects of reducing DDT usage on total DDT storage in humans.

Kutz FW, Yobs AR, Strassman SC, Viar JF Jr.

Agricultural uses of the insecticide DDT were cancelled by the U.S. Environmental Protection Agency December 31, 1972. However, the domestic use of DDT had begun to decline before this action. Beginning July 1969, residues of DDT and its metabolites were measured in human adipose tissue collected through an annual national survey. Levels of total DDT equivalent residues in human adipose have decreased slightly, but the frequencies of finding DDT or its metabolites have remained high. The most marked decline in residue concentration has been found in the youngest age group (0-14 years). Approximately 80 percent of the total DDT equivalent found in this survey was DDE. These data show that the reduction of the agricultural uses of DDT has decreased human exposure to and storage of this chemical.

PMID: 600675 [PubMed - indexed for MEDLINE]

PROPYLPARABEN SEARCH

Databases interrogated –

- PubMed

Search Terms – Propylparaben AND (“Exposure Assessment” OR “Human exposure” OR “Environmental level*” OR “Time trend” OR “Temporal trend”)

Search Dates (From/To) – Not specified

Number of Abstracts Identified – 1

Papers Identified

NONE

BUTYLPARABEN SEARCH

Databases interrogated –

- PubMed

Search Terms – Butylparaben AND (“Exposure Assessment” OR “Human exposure” OR “Environmental level*” OR “Time trend” OR “Temporal trend”)

Search Dates (From/To) – Not specified

Number of Abstracts Identified – 1

Papers Identified

NONE

ISOBUTYLPARABEN SEARCH

Databases interrogated –

- PubMed

Search Terms – Isobutylparaben AND (“Exposure Assessment” OR “Human exposure” OR “Environmental level*” OR “Time trend” OR “Temporal trend”)

Search Dates (From/To) – Not specified

Number of Abstracts Identified – 0

Papers Identified

NONE

BISPHENOL A SEARCH

Databases interrogated –

- PubMed

Search Terms – (BPA OR “Bisphenol A”) AND (“Exposure Assessment” OR “Human exposure” OR “Environmental level*” OR “Time trend” OR “Temporal trend”)

Search Dates (From/To) – Not specified

Limits – Human and English

Number of Abstracts Identified – 65

Papers Identified

6. Environ Health Perspect. 2009 May;117(5):784-9. Epub 2009 Jan 28.

C Bisphenol A data in NHANES suggest longer than expected half-life, substantial nonfood exposure, or both.

Stahlhut RW, Welshons WV, Swan SH.

Environmental Health Sciences Center, University of Rochester Medical Center, Rochester, New York 14642, USA. richard_stahlhut@urmc. rochester.edu

Comment in:
Environ Health Perspect. 2009 May;117(5):A210.

BACKGROUND: It is commonly stated in the literature on human exposure to bisphenol A (BPA) that food is the predominant BPA exposure source, and that BPA is rapidly and completely cleared from the body. If this is correct, BPA levels in fasting individuals should decrease with increased fasting time.

OBJECTIVES:
We set out to investigate the relationship between urine BPA concentration and fasting time in a population-based sample. METHODS: We modeled log BPA urine concentration as a function of fasting time, adjusted for urine creatinine and other confounders, in 1,469 adult participants in the 2003-2004 National Health and Nutrition Examination Survey. We estimated the BPA "population-based half-life" (pop(1/2)) for a fasting time of 0-24 hr, < 4.5 hr, 4.5-8.5 hr, and > 8.5 hr.

RESULTS: The overall pop(1/2) for the 0- to 24-hr interval was 43 hr [95% confidence interval (CI), 26-119 hr]. Among those reporting fasting times of
4.5-8.5 hr (n = 441), BPA declined significantly with fasting time, with a pop (1/2) of 4.1 hr (95% CI, 2.6-10.6 hr). However, within the fasting time intervals of 0-4.5 hr (n = 129) and 8.5-24 hr (n = 899), we saw no appreciable decline. Fasting time did not significantly predict highest (> 12 ng/mL) or lowest (below limit of detection) BPA levels.

CONCLUSIONS: Overall, BPA levels did not decline rapidly with fasting time in this sample. This suggests substantial nonfood exposure, accumulation in body tissues such as fat, or both.

Explaining these findings may require experimental pharmacokinetic studies of chronic BPA exposure, further examination of BPA levels and effects in fat, and a search for important nonfood sources.

PMCID: PMC2685842
PMID: 19479022 [PubMed - indexed for MEDLINE]