MAN-MADE CHEMICALS IN HUMAN BLOOD.

LEVELS OF FORTY-SIX CHEMICALS IN

A DUTCH COHORT.

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Abstract

Human beings are continuously exposed to man-made chemicals introduced in the environment. Studies in animals have shown negative health effects of some of these compounds. Limited information is available regarding the levels of these compounds in the human as well as their potential health effects.

The aim of this study is to measure blood levels of 46 man-made chemicals in a random Dutch population. Ninety-one healthy volunteers were included, 48 males and 43 females. The age ranged from 19 till 78 years.

Thirty-six of the 46 chemicals were detected. Some compounds were detected in all individuals, some only in one individual. The brominated flame retardant BDE-153 was detected in 76 samples, with a median of 8.0 pg/g. The newer brominated compounds HBCD and TBBPA were detected in 11 and 32 of the samples. The phthalates, DEHP and DBP were detected in 84 respectively. 68 of the samples, both showed a wide range of levels. The synthetic musk compounds, AHTN and HHCB, were detected in 88 and 91 samples respectively. Remarkably, Musk Ambrette, which has been banned in the European Union since 1995, was still observed in 48 samples. Organotin compounds were hardly detected. Bisphenol-A was above detection limit in 36 of the samples.

We did not observe a correlation between any of the levels and age, sex, occupation and living area. Only BDE-153 showed a higher level in males. Levels of chemicals belonging to the same group were related to each other. Relations between the levels of different groups were found for phthalates and synthetic musk compounds and for phthalates and Bisphenol-A.

We conclude that the Dutch population is exposed to a variety of man-made chemicals. In all blood samples man-made chemicals were detected. A wide range of levels was detected for some compounds. The most likely explanation is differences in exposure, although we were not able to relate these to a single factor. The results of this study also show that the introduction of any new agent almost immediately results in detectable levels in the human, while a reduction in production results in a reduction in levels in human.

Studies are needed regarding the way the human is exposed to these compounds as well as regarding potential negative health effects. Studies on other, older environmental contaminants like dioxins and PCBs have shown negative effects of these pollutants for human health. Special emphasis is needed regarding the effect of exposure to a mixture of compounds. Animal studies usually evaluate the effect of one single agent. Both a reduction in the use of man-made chemicals as well as studies concerning the potential negative effects of these products for human health is very much needed.

Samenvatting.

Mensen zijn continu blootgesteld aan kunstmatig geproduceerde chemische stoffen. Dierstudies tonen aan dat een aantal van deze stoffen negatieve gezondheidseffecten kan hebben. Over de concentraties die aanwezig zijn in de lichamen van mensen en over de mogelijke gezondheidseffecten voor mensen is slechts beperkt informatie beschikbaar.

Doel van deze studie is de concentraties te meten van 46 chemische stoffen in het bloed van een willekeurige groep Nederlanders. In de studie zijn 91 vrijwilligers betrokken, 48 mannen en 43 vrouwen. Hun leeftijd varieerde van 19 tot 78 jaar.

Van de 46 chemische stoffen waren 36 aantoonbaar. Sommige stoffen werden aangetroffen in het bloed van alle individuen, andere slechts in één individu. De broomhoudende vlamvertrager BDE-153 werd aangetroffen in 76 bloedmonsters, met een mediaan van 8,0 pg/g. De nieuwere broomhoudende vlamvertrages HBCD en TBBPA zijn aangetroffen in 11 en 32 monsters. Van de ftalaten werden DEHP en DBP aangetoond in resp. 84 en 68 monsters, waarbij de gehaltes een grote spreiding lieten zien. De synthetische muskverbindingen AHTN en HHCB werden aangetroffen in resp. 88 en 91 bloedmonsters. Musk ambrette, sinds 1995 verboden in de Europese Unie, werd nog steeds aangetroffen in 50% van de monsters. Organotinverbindingen zijn nauwelijks aangetroffen. Bisfenol-A werd aangetoond in 36 monsters.

Correlaties tussen de verschillende gehaltes en leeftijd, sekse, beroep en woongebied zijn niet gevonden. Alleen BDE-153 is bij mannen in een hoger gehalte aangetroffen. Gehaltes van chemische stoffen die tot dezelfde stofgroep behoren zijn aan elkaar gerelateerd. Relaties tussen de gehaltes van verschillende groepen zijn gevonden tussen ftalaten en muskverbindingen en tussen ftalaten en bisfenol-A.

Samenvattend: de Nederlandse bevolking staat bloot aan uiteenlopende chemische stoffen. In alle bloedmonsters zijn meerdere van de onderzochte stoffen aangetroffen. De gehaltes van sommige stoffen liepen sterk uiteen. De meest voor de hand liggende verklaring is dat de blootstellingen sterk verschillen, hoewel we de verschillen niet in verband konden brengen met één factor. Uit deze studie blijkt ook dat zodra een nieuwe stof wordt geïntroduceerd, deze vrijwel onmiddellijk aantoonbaar is in mensen. Omgekeerd resulteert een verminderde productie van een stof in lagere gehaltes in mens.

Onderzoek is nodig naar de wijze waarop mensen aan de onderzochte stoffen zijn blootgesteld en naar potentiële negatieve gezondheidseffecten. Studies naar oudere milieuvervuilende stoffen als dioxinen en PCB's toonden negatieve effecten aan op de gezondheid van mensen. In het bijzonder is aandacht nodig voor het effect van blootstelling aan een combinatie van stoffen. Dierstudies onderzoeken meestal slechts het effect van één stof. Zeer noodzakelijk zijn zowel een reductie in het gebruik van kunstmatig geproduceerde chemicaliën, als en onderzoeken naar de potentiële negatieve effecten van deze producten op de gezondheid van mensen.

Introduction.

There is increasing concern regarding the effects of the presence of man-made chemicals in the environment on human health. A number of these chemicals, especially the lipophyllic compounds, accumulate in animal fat and also in human tissues (1,2). The human is exposed to these chemicals through a variety of ways. The most important route is food, as the chemicals accumulate in the food chain (3). The human is also exposed through the presence of chemicals in dust and air and by direct contact. The latter might for instance be important for chemicals present in cosmetics (4). The working environment can cause unusual high levels of exposure. All these ways of exposure can lead to accumulation of these compounds in human tissues.

A number of the analyzed man-made chemicals show negative health effects in animals (5,6). For example, endocrine disruptive effects have been described, not only in laboratory animals but also in wildlife (7). Less is known regarding the effects of these compounds on human health as only a limited number of studies have been done (8,9,10). The human is exposed to a variable levels and combination of compounds. Studies in animals usually concern single compounds. It is impossible to translate the results of these single compound studies directly to the situation in the human who is exposed to a combination of compounds. The chemicals might act synergistically as well as antagonistically. The objective of the present study is to determine the levels of forty-six man-made chemicals in healthy volunteers in the Netherlands. The groups of chemicals studied are brominated flameretardants, organotin compounds, artificial musk compounds, alkylphenols, bisphenol-A and phthalates. We evaluated whether plasma levels of different compounds are related to each other. We also evaluated the relation with age, sex, living area, occupation and food intake.

Methods.

Healthy volunteers were recruited for this study. The recruitment was done through an advertisement in a nationally broadcasted radio program where the purpose and design of the study was explained. People interested to participate as a volunteer were asked to send an e-mail. Thirteen hundred and one volunteers indicated their interest to participate in the study.

A stratified sample of volunteers was made based on the following criteria. The Netherlands was divided, based on population, into 10 areas. From each area two males and two females born before 1960 were randomly selected as well as two males and two females born after 1960. In addition to these 80 volunteers, eleven randomly selected but well-known individuals from the Netherlands were invited to participate in the study.

After giving informed consent, the participants were visited at their homes. 60 ml blood was taken from each participant via venipuncture and collected in BD-vacutainer tubes. Samples were kept cool (between 2° C and 8° C) until delivered at the laboratory within 24 hrs. Thereafter samples were stored at 4° C until analysis. All participants filled in two questionnaires. One, custom-made questionnaire contained questions regarding the background of the participant, including age, sex, smoking and occupation. The use of cosmetics was also recorded. A second, previously validated questionnaire concerned the dietary habits of the participants (11).

Analyses.

The laboratory of TNO Environment, Energy and Process innovation in Apeldoorn, The Netherlands, performed all laboratory analyses. The list of chemicals that were measured is given in table 1.

Materials and methods.

Before the start of the project, all methods used in this study were validated for the analytes under study. The validation experiments were carried out using fresh calf's blood and spiked with the analytes of interest. The validation study resulted in standard operation procedures that were tested on a limited number of human blood samples and subsequently used in this study.

Sample pre-treatment.

Upon receipt of the whole sample, a sub-sample was collected for the organotin analysis. The remaining part was allowed to clot at room temperature for 20 min and centrifuged at 4000 rpm for 15 min. The serum was transferred into PTFE-capped glass vials and stored at 4°C until further analysis.

Sample analysis. Extraction of serum samples.

All glassware used in the analyses was cleaned, rinsed with deionised water and baked in an oven for 16 hours at 280°C prior to use. All solvents were distilled prior to use to achieve low blank results. The latter was especially important for the determination of the phthalates.

The serum sample was weighed into a clean glass 60 ml vial. Methanol, 0.1 M HCl and a set of internal standards (one or more for each group of chemicals) was added to the sample. The sample was extracted twice with a hexane-diethyl ether mixture and centrifuged to separate the organic phase. The combined extracts were washed with a 1% KCl-solution and dried with anhydrous sodium sulphate. The extract was split into two equal parts, A and B.

Bisphenol-A, tetrabromobisphenol-A, alkylphenols and alkylphenol ethoxylates.

Part A of the extract was concentrated to a small volume without further purification. Methanol was added to the extract and the extract was concentrated further to remove all hexane-diethyl ether residues. The methanol extract was used for the determination of BPA, TBBPA, NP, OP, NPEO and OPEO. The final extracts were analysed with liquid chromatography coupled with mass spectrometry (LC/MS) in the selected ion monitoring mode (SIM).

Brominated flame retardants, phthalates and musk compounds.

Part B of the extract was concentrated to a small volume. The extract was purified using a florisil cleanup procedure and separate fractions were collected containing the component groups. The purified extracts were concentrated to a small volume and an injection standard was added. The final extracts were analysed with gas chromatography coupled with mass spectrometry (GC/MS) in the selected ion monitoring mode (SIM).

Organotin compounds.

The whole blood sample was weighed into a 60 ml vial and internal standards were added. After the addition of a sodium dithiocarbamate solution in ethanol, the sample was sonicated, left overnight, and sonicated once more. The residue was removed and an acetate buffer and a sodium tetra-ethylborate solution in ethanol were added. The mixture was extracted twice with hexane for 30 minutes and purified using a silica clean-up procedure. The purified extract was concentrated and an injection standard was added. The final extracts were analysed with gas chromatography coupled with mass spectrometry (GC/MS) in the selected ion monitoring mode (SIM).

Identification, quantification and expression of results.

The identification of analytes was based on correct retention times and qualifier ion ratios, compared to an external standard. The quantification was based on an external standard analysed together with the

samples. The recovery of the added internal standards was used to determine the performance of the analysis, but not to correct the results of the target compounds.

The results in this report are expressed in pg/g serum (flame retardants) and ng/g serum (other analytes). The study was approved by the Medical-Ethical Committee of the University Hospital Groningen. All participants provided written informed consent.

Statistical analysis.

Median (50th-percentile) and range were determined for all compounds. Other percentiles were calculated to provide additional information about the shape of the distribution. The relation between levels and demographic data was analysed by comparison in pairs. The relation between levels of individual compounds was analysed by regression analysis. All analyses were done with only the levels above detection limit as well as with the non detectables set at 50% of the detection limit. The percentiles are calculated from the results above detection limit.

Results

In total 91 volunteers were included in the study. The personal data of the subjects are given in table 2. According to the study design there were at least 8 participants per area. The age of the participants ranged from 19 to 78 years. There were no significant differences in distributions of sex, age and occupation between the groups in the different areas.

Of the brominated flame retardants, BDE-153 was most abundant present and detectable in 76 of the 91 samples (table 3). BDE-47 was found in 40 of the samples, BDE-28 and BOG-49 in only one sample while BDE-17 and 85 were not above detection limit in any of the samples. Of the other flame retardants identified, BDE-209 (deca-BDE) was found in 11 samples, while HBCD and TBBPA were above detection limits in 11 and 32 samples respectively

Overall, concentrations of brominated compounds varied widely; this however was mainly due to a small number of particularly high levels in the different compounds. For instances, for BDE-153 about 10% of the samples have values of more than three times the median, clearly indicating that they significantly deviate from the other results. The same is true for BDE-47, -99, -100, -154, -183 and TBBPA. The organotin compounds were only detectable in very few samples, while all detectable levels were only just above detection limit (table 4). DBT, MPT, DPT and TPT were not detectable in any of the samples.

Of the artificial musk compounds, the more recently introduced compounds AHTN and HHCB were detectable in 88 and 91 samples respectively of the 91 samples.(Table 5) For AHTN, one sample contained more than 10 ng/g, 7 samples between 1 and 2 ng/g while all others contained less than 1 ng/g. Detected HHCB concentrations ranged from 0.2 to 9.2 with a median concentration of 1.3 ng/g. Four samples contained concentrations of 4.3, 6.7, 8.7 and 9.2 ng/g which is more than 3 times the median HHCB concentration. Surprisingly, of the older, nitromusk compounds, musk ambrette was surprisingly detectable in 48 of the samples. The other musk compounds were detectable only in low levels and in very few samples.

Bisphenol-A was the most frequently detected compound of the phenolic agents, appearing in 36 of the samples at above limits of detection (table 6). If BPA was detected about two third of the concentrations were below 2 ng/g. The other third showed concentrations up to 16 ng/g. For NP, detected in 16 samples, the distribution is more or less comparable to that of BPA.

The phthalates and especially DBP, BzBP and DEHP were detected in a majority of the samples (table 7). DEHP was present in 84 of the 91 samples, showed at a remarkably wide range of levels, from 25 to 5863 ng/g plasma.

For none of the compounds, except for BDE-153, was a difference between the levels in males vs females found. BDE-153 showed a value of 23 ± 6 (mean \pm SE) pg/g in man compared to 10 ± 6 pg/g in woman (p<. 0.011). No consistent difference was observed for any of the different age groups for the level of any of the compounds. The level of none of the compounds was related to the area of residence.

We divided the occupation of the participants in five categories: office workers, education, production labor, medical employees and politicians. Levels of BDE-153 tended to be higher in the production labor group compared to the other groups, though this was not statistically significant (p = 0.08). For the other brominated compounds, no apparent relation to occupation was found, and this was the case also for phenolic agents, musks and phthalates. No analysis was conducted for potential relationships between the occupation and the organotin compounds due to the small number of samples yielding levels above detection limit. Fifty-six of the participants smoked at present, or had been smoking in the past. Smoking did not appear to influence concentrations of any of the analytes quantified in this study. The amount of body fat, expressed as body mass index, was correlated negatively with BDE-209, MA, BPA and DEP, and positively with BDE-47.

Finally we analysed if the levels of the different compounds measured were related to each other. The levels of the brominated compounds BDE-47, -99, -100, -153 and -183 were all related to each other but not to the levels of BDE-209 or to the newer compounds HBCD and TBBPA. The levels of these latter compounds were not related to each other either. Furthermore, the levels of the brominated compounds did not correlate with any of the other chemicals determined.

A strong association was found, however, between the two newer musks, AHTN and HHCB (r = 0.78, p 0.001). Within the phtalates, DEHP showed a significant negative correlation with DBP (r = -0.48, p 0.001) and a positive correlation with BzBP (r = 0.27, p 0.01). The phthalate DBP showed a significant correlation with the musk compounds AHTN and HHCB, while DEHP was negatively correlated with AHTN and positively with bisphenol-A.

In a multi-regression analysis where we included age, sex, occupation and living area, no statistical significant effect of a combination of these factors on levels of chemicals in blood was found. When the analyses were repeated with the non-detectable levels set at 50% of the detection limit, no differences in results were found.

Discussion.

To our knowledge, this is the first study to measure in total 46 man-made chemicals in healthy volunteers in The Netherlands. The results obtained give an indication of the blood levels of environmental contaminants in our country. Ten of the 46 chemicals were not detected in any of the samples. The other 36 were present at rather variable levels. We did not observe a relation between age, sex, area of residence or occupation with any of the levels except for BDE-153 which was apparently dependent on sex and occupation.

Our data indicate that, although levels do vary between individuals, there is a widespread presence of chemical contaminants in blood serum in the population. The sources of exposure of the different groups of compounds seem to be different as correlations between levels were mainly found within groups of chemicals. Since levels for most compounds show a clear variation, it is reasonable to assume that the exposure between individuals varies. A range in plasma levels of 100 to 1000 fold is hard to explain from genetically-determined differences in metabolism. Possibly due to the number of participants included in the study we were not able to establish areas of high contamination causing high levels in a number of individuals.

In this study it was decided to analyse 46 man-made chemicals belonging to six different chemical

groups. This approach was chosen to obtain information about a wide range of pollutants and about possible relations between levels within the same individual. Animal studies usually evaluate the effect of one single agent. There is increasing evidence that the human is exposed to a variety of chemicals which either might augment or oppose the effects seen when encountered singly. This might especially be true regarding endocrine disrupting effects. A downside of this approach was the limited number of participants that could be included in the study due to financial constraints. The number at the same time is in our opinion sufficient to provide an impression of the levels in the Netherlands.

For the study volunteers were recruited via a call on the Dutch radio. A selection was made from the respondents based on area of living, age and gender. We can not exclude some bias in the participants who either might have been concerned about pollution in general or have concerns due to their specific living conditions. As we made a random selection of only seven percent of all volunteers we believe the risk of bias is small. As the participants were informed already at the recruitment that they would not be informed about their own levels, we expected not to include participants who only were interested in their own level of pollution.

In this study we did not observe any relation between levels and demographic data. Age, living area, sex and smoking, at present or in the past, were not related to levels of the different chemicals. Occupation only was found to be related to BDE-153. The amount of body fat showed a negative correlation with a number of compounds. At the same time, a rather wide range of levels was detected for some compounds. The most likely explanation is differences in exposure, although we were not able to relate these to a single factor. Special studies are needed to pinpoint sources of contamination. Given the range in levels, it is unlikely that the variation in levels is only due to differences in metabolism and excretion. The levels of brominated flame retardants found in this study are comparable to results of other studies in Western Europe but significantly lower compared to levels reported from the USA (12,13). The use of some of these chemicals is considerably higher in the USA due in part to the specifics of regulations on fire prevention.

The most commonly detected congener in this study is BDE-153, though in the vast majority of volunteers levels were not above 10 pg/gram serum. One individual, a process operator, showed a value of 206 pg/gram with high levels also for BDE-28, -47, -99, -100, -159, -183 and -209. We did not detect the source of contamination in this individual. BDE 209, found in 11 of the individuals, showed one high value of 1944 pg/gram. However, none of the other congeners were observed in this individual and no explanation for this single value was found. HBCD and TBBPA, two flame retardants which are increasingly widely used, were found in 11 and 32 of the 91 samples. The correlation between BDE-47, -99, -100, -153 and -183 is to be expected since these compounds commercially are available as mixtures (penta- and octa-). BDE- 209, HBCD and TBBPA on the other hand, are commercially available as more or less pure compounds

The organotin compounds were hardly detectable is this population. The low levels might be due to the restricted use of these chemicals in our country and a limited fish consumption. Musk is originally a sexual scent signal. Nowadays many different artificial musk compounds are used in perfumes, detergents, soap, body lotions and deodorizers. The older (nitromusk) compounds MK and MX, as well as MM and MT were found in only very few samples. This is in accordance with a study of Kafferlein et al (14,15) who showed declining levels after reducing the use of these chemicals. Remarkably, MA, also an older musk, was still observed in over 50% of the samples. Whether this is due to continued use or a higher persistence needs further study. The two most abundant musk compounds were AHTN and HHCB. Looking at the high correlation between levels of these, it is most likely that these compounds are commonly used together. It is unknown however if the combined exposure cause more or less health effect in the human. We are not aware of any study regarding the

potential health effects of these chemicals on the human. A study in fish showed that AHTN and HHCB exert anti-estrogenic effects on the human estrogen receptor alpha and beta (16).

A number of studies in animals have shown that some phthalates are able to suppress the androgen synthesis during development thereby inducing testicular dysgenesis together cryptorchidism and hypospadia (17,18). An equivalent in the human is the so-called testicular dysgenesis syndrome, what is related to a reduced fertility in the human (19). It is unknown, however, if the present level of exposure and thereby levels in the human are able to impact on the human male reproductive health. One study in prepubertal females in Puerto Rico showed a relation between levels of phthalates, especially DEHP and premature breast development (20). The levels of DEHP observed in that study were comparable to levels found in our study.

The highest level of DEHP found in this study, 5863 ng/gram plasma was in a man who used to work in a factory making paint. His level therefore can very well be explained by occupational exposure. However, almost equal levels were observed in humans where no clear explanation was found. In view of the potential severe negative effects of phthalates as seen in animals and the levels observed in this study, more studies are needed regarding the potential health effects of these compounds in man.

Conclusion.

In summary, we observed detectable levels of a number of man-made chemicals in human plasma. The results also indicates that the introduction of any new agent results in detectable or higher levels in the human, while a reduction of the use of such compounds results in a reduction in levels in human. Absorption of these products by the human is an unintended side effect of these compounds. Studies regarding the potential effect of these compounds on human health are very scarce. Studies on other, older environmental contaminants like dioxins and PCBs have shown negative effects of these pollutants for human health (1,2,6,8,9,10). Both a reduction in the use of man-made chemicals as well as studies concerning the potential negative effects of these products for human health is very much needed.

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Table 1. Compounds analysica and acted on min	Table 1.	Compounds	analysed	and de	etection	limi
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Compound	Abbreviation	Method detection limit
Brominated flame retardants:		
2,2',4-tribromo diphenylether	BDE 17	1 pg/g serum
2,4,4'-tribromo diphenylether	BDE 28	1 pg/g serum
2,2',4, 4- tetrabromo diphenylether	BDE 47	2 pg/g serum
2,2',4,5'- tetrabromo diphenylether	BDE 49	1 pg/g serum
2,2',3,4,4'-pentabromo diphenylether	BDE 85	3 pg/g serum
2,2',4,4',5- pentabromo diphenylether	BDE 99	3 pg/g serum
2,2',4,4',6- pentabromo diphenylether	BDE 100	2 pg/g serum
2,2',4,4',5,5'-hexabromo diphenylether	BDE 153	1 pg/g serum
2,2',4,4',5,6'- hexabromo diphenylether	BDE 154	1 pg/g serum
2,2',3,4,4',5',6-heptabromo diphenylether	BDE 183	2 pg/g serum
decabromo diphenylether	BDE 209	150 pg/g serum
hexabromo cyclododecane	HBCD	80 pg/g serum
tetrabromodisphenol-A	TBBPA	50 pg/g serum
Phthalates:		
dimethyl phthalate	DMP	1 ng/g serum
diethyl phthalate	DEP	2 ng/g serum
d-iso-butyl phthalate	DIBP	2 ng/g serum
di-n-butyl phthalate	DBP	2 ng/g serum
butylbenzyl phthalate	BBP	1 ng/g serum
dicyclohexyl phthalate	DCHP	1 ng/g serum
di-(2-ethylhexyl)phthalate	DEHP	10 ng/g serum
di-n-octyl phthalate	DOP	1 ng/g serum
di-iso-nonyl phthalate	DINP	10 ng/g serum
di-iso-decyl phthalate	DIDP	10 ng/g serum
Musk compounds:		
celestolide	ADBI	0.05 ng/g serum
tonalide	AHTN	0.1 ng/g serum
traseolide	ATTI	0.05 ng/g serum
cashmeron	DPMI	0.05 ng/g serum
galaxolide	ННСВ	0.1 ng/g serum
musk ambrette	MA	0.1 ng/g serum
musk ketone	MK	0.05 ng/g serum
musk moskene	MM	0.05 ng/g serum
musk tibetene	MT	0.05 ng/g serum
musk xylene	MX	0.05 ng/g serum
Organotin compounds:		
monobutyltin	MBT	0,1 ng/g blood
dibutyltin	DBT	0,1 ng/g blood
tributyltin	TBT	0,1 ng/g blood
monoctyltin	MOT	0,1 ng/g blood
dioctyltin	DOT	0,1 ng/g blood
monophenyltin	MPT	0,2 ng/g blood
diphenyltin	DPT	0,2 ng/g blood
triphenyltin	TPT	0,4 ng/g blood
Phenols and phenol ethoxylates:		
bisphenol-A	BPA	0,5 ng/g serum
nonylphenol	NP	0,5 ng/g serum
octylphenol	OP	0,5 ng/g serum
nonylphenol ethoxylates	NPEO	2,5 ng/g serum
octylphenol ethoxylates	OPEO	2,5 ng/g serum

Table 2. Characteristics of participants.Male n=48Female n=43Total

Age in groups			
18-29	8	9	17
30-39	11	6	17
40-49	14	11	25
50-59	9	13	22
60-69	3	2	5
70-79	2	2	4
Unknown	1		1

Area			
Westland	7	5	12
Centre of The	5	4	9
Netherlands			
Friesland	4	4	8
Groningen	4	4	8
Overijssel	4	4	8
Gelderland east	5	4	9
Limburg	4	4	8
Middle Brabant	4	4	8
South-west Brabant	4	4	8
North-Holland	7	6	13

Profession groups			
Office	10	14	24
Education	9	7	16
Production	16	8	24
Medical	5	8	13
Politics	3	2	5
Other	5	4	9

Parameter	BDE-17	BDE-28	BDE-47	BDE-49	BDE-85
	Pg/g serum	pg/g serum	pg/g serum	Pg/g serum	pg/g serum
method detection limit	<1	<1	<2	<1	<3
(MDL)					
minimum		2.0	2.3	3.0	
maximum		2.0	226	3.0	
median		2.0	5.0	3.0	
25th percentile			3.0		
75th percentile			9.0		
number of samples above MDL	0	1	40	1	0
Parameter	BDE-99	BDE-100	BDE-153	BDE-154	BDE-183
	pg/g serum	pg/g	pg/g	pg/g serum	pg/g serum
		serum	serum		
method detection limit (MDL)	<3	<2	<1	<1	<2
minimum	3.6	2.4	1.9	1.2	2.2
maximum	401	132	253	46	308
median	6.3	5.8	8.0	3.1	5.6
25th percentile	5.2	3.2	5.8	1.9	2.7
75th percentile	7.8	11.1	11	7.2	23
number of samples above	23	21	76	19	10
MDL					
Parameter	BDE-209	HBCD	TBBPA		
	pg/g serum	pg/g	pg/g		
		serum	serum		
method detection limit (MDL)	<150	<80	<50		
minimum	151	96	56		
maximum	1944	356	787		
median	307	197	128		
25th percentile	187	135	80		
75th percentile	383	250	235		
number of samples above	11	11	32		
MDL					

Table 3. Level of brominated flame retardants (n= 91)

Parameter	MBT ng/g blood	DBT ng/g blood	TBT ng/g blood	MOT ng/g blood	DOT ng/g blood
method detection limit (MDL)	<0.1	<0.1	<0.1	<0.1	<0.1
minimum	0.1		0.1	0.1	0.2
maximum	0.1		0.1	0.5	2.4
median	0.1		0.1	0.1	0.7
25th percentile				0.1	0.4
75th percentile				0.2	1.6
number of samples above	3	0	3	12	13
MDL					

Table 4 . Level of organotin compounds (n=91)

Parameter	MPT	DPT	ТРТ
	ng/g blood	ng/g blood	ng/g
			blood
method detection limit	< 0.2	< 0.2	<0.4
(MDL)			
minimum			
maximum			
median			
25th percentile			
75th percentile			
number of samples above	0	0	0
MDL			

Parameter	ADBI ng/g serum	AHTN ng/g serum	ATTI ng/g serum	DPMI ng/g serum	HHCB ng/g serum
method detection limit	< 0.05	<0.1	< 0.05	< 0.05	<0.1
minimum	0.05	0.1	0.29	8.0	0.2
maximum	0.05	11	0.67	8.0	9.2
median	0.05	0.44	0.32	8.0	1.3
25th percentile		0.22			0.83
75th percentile		0.72			2.0
number of samples above MDL	1	88	4	1	91

Table 5. Level of the musk compounds (n=91)

Parameter	MA ng/g serum	MK ng/g serum	MM ng/g serum	MT ng/g serum	MX ng/g serum
method detection limit (MDL)	<0.1	< 0.05	< 0.05	<0.05	<0.05
minimum	0.10	0.06	0.15	0.14	0.10
maximum	4.0	1.47	0.15	0.20	0.27
median	0.40	0.17	0.15	0.17	0.13
25th percentile	0.21				
75th percentile	0.81				
number of samples above MDL	48	9	1	3	6

Parameter	BPA ng/g serum	OP ng/g serum	NP ng/g serum	OPEO ng/g serum	NPEO ng/g serum
method detection limit (MDL)	<0.5	<0.5	<0.5	<2.5	<2.5
minimum	0.57	2.0	0.58		
maximum	16	2.3	16		
median	1.4	2.2	1.4		
25th percentile	0.80		0.93		
75th percentile	2.7		3.0		
number of samples above MDL	36	2	16	0	0

Table 6. Biphenol-A, alkylphenols and ethoxylates (n=91)

Parameter	DMP ng/g serum	DEP ng/g serum	DIBP ng/g serum	DBP ng/g serum	BzBP ng/g serum
method detection limit (MDL)	<1	<2	<2	<2	<1
minimum	1.0	2.2	3.2	2.6	1.1
maximum	10	14	93	136	305
median	1.9	6.4	54	12	1.7
25th percentile	1.4	2.8	10	6.1	1.3
75th percentile	3.3	9.6	66	31	2.2
number of samples above	26	21	18	68	35
MDL					

Table 7. Levels of Phthalates (n=91) 1

Parameter	DCHP ng/g serum	DEHP ng/g serum	DOP ng/g serium	DINP ng/g serum	DIDP ng/g serum
		beruin	Serum		
method detection limit	<1	<25	<1	<10	<10
minimum	1.0	28	2		
maximum	4	5863	17		
median	1.5	209	9		
25th percentile		65			
75th percentile		572			
number of samples above	4	84	2	0	0
MDL					