RIVM report 310305002/2003

Exposure assessment of Dutch nursing infants to brominated flame retardants via breast milk

R. de Winter-Sorkina[1], M.I. Bakker[1],
R.A. Baumann[2], R. Hoogerbrugge[2],
M.J. Zeilmaker[1]

[1]Centre for Substances and Integrated Risk Assessment
[2] Laboratory for Analytical Chemistry

coworker:
W.C. Hijman

This investigation has been performed by order and for the account of Inspectorate for Health Protection and Veterinary Public Health, within the framework of project 310305, Dioxins in Food.

RIVM, Postbus 1, 3720 BA Bilthoven, telefoon: 030 - 274 91 11, fax: 030 - 274 29 71

Abstract

As part of a national survey on the occurrence of persistent organic contaminants in breast milk, a group of brominated flame retardants (polybrominated diphenyl ethers or PBDEs) was measured in breast milk which had been collected in 1998 from Dutch primiparous women on day 6 to 10 after labour. Together with data on milk intake, body weight and the duration of breast feeding these data were taken as a starting point for the calculation of the exposure to PBDEs via breast milk. The cumulative exposure was calculated for 10 PBDE congeners and for breast feeding periods of 8 days and 1, 2, 3, 4, 5, 6, 7.5 and 9 months. The mean, standard deviation, minimum, maximum, 5^{th} and 95^{th} percentile of these exposure doses were calculated. The mean cumulative exposure of the sum of the PBDEs was 2.9 µg/kg bw (95^{th} percentile 6.6 µg/kg bw) for a breast feeding period of 6 months and 3.8 µg/kg bw (95^{th} percentile 8.6 µg/kg bw) for a period of 9 months. BDE #47 contributed about 35 % to the total intake, while BDEs #153, #99, #183 en #100 contribute ~10-25 % each. It appears that at 6 months the daily exposure of nursing infants to PBDEs via breast milk is about 6 times higher than the exposure of adults via food (the latter was calculated in an earlier study). In addition to the exposure to PBDEs, nursing infants are also expected to be exposed to the brominated flame retardant hexabromocyclododecane (HBCD). Consequently, measurements of HBCD in breast milk, followed by a risk assessment for nursing infants, is recommended.

Contents

Samenvatting

De blootstelling van Nederlandse zuigelingen aan polybroomhoudende bifenylethers (PBDEs) via moedermelk is berekend. Dit is gedaan met behulp van gemeten concentraties PBDEs in moedermelk die in 1998 bij Nederlandse vrouwen verzameld is en met gegevens over de melkinname van zuigelingen, hun lichaamsgewicht en de duur van de borstvoedingsperiode. Hierbij werd een probabilistische benadering toegepast. Dat wil zeggen dat de distributie van de inname werd bepaald rekening houdend met de variabiliteit van de PBDE concentratie in moedermelk, de variabiliteit van de melkinname en die van het lichaamsgewicht van de zuigeling. De cumulatieve blootstelling (gemiddelde, standaard afwijking, minimum, maximum, 5 en 95 percentiel waarden) werd berekend voor 10 PBDEs en voor borstvoedingsperioden variërend van 8 dagen tot 1-9 maanden.
De gemiddelde cumulatieve blootstelling van de som van de PBDEs (#17, #28, #47, #66, #85, #99, #100, #153, #154 en #183) bedroeg 2,9 µg/kg lg (95^{e} percentiel: 6,6 µg/kg lg) voor een borstvoedingsperiode van 6 maanden en 3,8 µg/kg lg (95^{e} percentiel 8,6 µg/kg lg) voor een periode van 9 maanden. De grootste bijdrage aan de blootstelling werd geleverd door BDE #47 (~35 %). Ook de BDEs #153, #99, #183 en #100 leverden grote bijdragen (elk congeneer ~10-25 %, samen ~55 %). De procentuele bijdragen van #17, #28, #66, #85 en # 154 waren slechts gering.
Een eerdere studie naar de blootstelling van volwassenen aan gebromeerde vlamvertragers via de voeding heeft laten zien dat naast blootstelling aan PBDEs (3,2-3,5 ng/kg lg/dag voor de som van PBDEs), ook blootstelling aan hexabroomcyclododecaan (HBCD, 2,9 ng/kg lg/dag) optreedt. Gegeven deze inname en de chemische eigenschappen van HBCD mag verwacht worden dat HBCD in Nederlandse moedermelk aanwezig is. Hierdoor zal, naast blootstelling aan PBDEs, ook blootstelling van zuigelingen aan HBCD optreden. Het verdient daarom aanbeveling om de analytisch-chemische methoden voor broomhoudende vlamvertragers in moedermelk uit te breiden met een HBCD-bepaling. De gebromeerde vlamvertrager tetrabroombisphenol-A bevindt zich ook in voeding, maar zal naar verwachting niet accumuleren in de mens.
Tenslotte moet worden opgemerkt dat de geschatte blootstelling van zuigelingen aan PBDEs uit moedermelk hoger is dan die van Nederlandse volwassenen uit voeding. Voor de in Nederland aanbevolen borstvoedingsperiode van 6 maanden is de gemiddelde dagelijkse blootstelling van zuigelingen aan de som van PBDEs ongeveer 6 keer hoger dan de geschatte blootstelling van volwassenen aan deze verbindingen via voedsel.

Summary

The exposure of nursing children via breast milk to a group of brominated flame retardants (polybrominated diphenyl ethers or PBDEs) was calculated with concentrations in breast milk which had been collected in 1998 and with data on milk intake, body weight and the duration of breast feeding. A probabilistic approach was followed i.e., the distribution of the intake rate was determined, taking into account the variability of the PBDE concentration in breast milk, the variability of the milk intake rate and that of the nursing infant's body weight. The cumulative exposure was calculated for 10 PBDE congeners and for breast feeding periods of 8 days and 1, 2, 3, 4, 5, 6, 7.5 and 9 months. The mean, standard deviation, minimum, maximum, 5th and 95th percentile of these exposure doses were calculated.
The mean cumulative exposure to the sum of PBDEs is 2.9 μg/kg bw (95th percentile: 6.6 μg/kg bw) for 6 months of breast feeding and 3.8 μg/kg bw (95th percentile 8.6 μg/kg bw) for a period of 9 months of breast feeding. The highest contribution to the total intake via breast milk is given by BDE #47 (~35 %), while BDEs #99, # 100, #153 and #183 and #100 was ~10-25 % each. The BDEs #17, #28, #66, #85 and #154 only had small contributions to the total exposure.
The exposure assessment of adults to brominated flame retardants (BFRs) via food showed that adult exposure is not restricted to PBDEs (intake: 3.5 ng/kg bw/day for the sum of PBDEs) but also comprises hexabromocyclododecane (HBCD, intake: 2.9 ng/kg bw/day). Given this intake and the intrinsic chemical properties of HBCD it is expected that HBCD will be present in Dutch breast milk in quantities high enough to contribute significantly to the exposure of nursing infants to BFRs via breast milk The flame retardant tetrabromobisphenol-A (TBBP-A) is also present in food, but is not expected to accumulate in humans. In order to improve the exposure assessment of nursing infants to brominated flame retardanats the development of analytic chemical methods to quantify HBCD in breast milk is therefore recommended.
The exposure of nursing infants to these compounds via breast milk appeared to be higher than the exposure of adults via food. For example, taking the recommended breast feeding period in The Netherlands as a reference, i.e. 6 months, the mean daily exposure of nursing infants to the sum of PBDEs is about 6 times higher than the exposure of adults via food.

1. Introduction

Brominated flame retardants (BFRs) are widely used in electronic household equipment (e.g. personal computers and television sets), plastics, textile and polyurethane foam in furniture and cars for safety reasons (Boon et al., 2002).
The annual world production of flame retardants is roughly 600,000 tons, of which about 150,000 are brominated compounds. Of the brominated products, about one-third contain tetrabromobisphenol-A (TBBP-A) and derivatives, another third contain various bromines, including polybrominated biphenyls (PBBs) and hexabromo-cyclododecane (HBCD) and the last third contain PBDEs.
The waste from the products mentioned above is either incinerated or deposited in landfills. Potential routes of discharging of BFRs into the environment is through incineration, sewage, leaching from landfills and through volatilisation from electrical components during their lifetime. (Darnerud et al., 2001 and references therein)
BFRs are persistent, bioaccumulative and toxic substances. PBDEs for example act on the thyroid gland and can cause immunotoxicity. The environmental fate of BFRs is similar to the fate of other persistent organic pollutants, such as PCBs and dioxins. The presence of BFRs in the environment has been shown in air, sewage sludge, sediments, fish, birds and mammals, including human breast milk and adipose tissue (De Wit, 2002, Boon et al., 2002).
While a steady decline of the amount of pesticides, dioxins, furans and PCBs in breast milk is found by Dutch monitoring campaigns in the 1988-1998 period (Zeilmaker et al., 2002), the levels of PBDEs in Swedish breast milk have increased exponentially from 1972 to 1997, with concentrations doubling every 5 years (Noren et al., 1998). Hereafter, the levels of PBDEs tend to decrease (Darnerud et al., 2002).
As mentioned, BFRs are excreted in breast milk. Consequently, ingestion of contaminated breast milk forms an important route of exposure for nursing children. However, up to now quantitative information is not available on such exposure. Regarding the situation in the Netherlands this report fills this deficiency by assessing the intake of 10 PBDEs by Dutch nursing infants via breast milk. In short, the concentration of PBDEs was measured in breast milk which was collected in 1998 from 108 Dutch primigravidae. As the exposure of nursing children is not only determined by the PBDE concentration of breast milk but also by the amount of milk ingested, the duration of the breast feeding period and the child’s body weight the exposure was assessed by combining the measured PBDE concentrations with data on milk intake, nursing infant body weight and breast feeding period, resulting in the cumulative intake per kg body weight. In the determination of the exposure of a nursing infant a probabilistic approach was followed i.e., the intake rate was quantified as a variable entity being determined by the inter-individual variability of the PBDE concentration in breast milk, the milk intake rate and the nursing infant’s body weight.

2. Model structure and model parameterisation

2.1 Model description.

The methodology of the assessment is based on Hoover (1999). The cumulative exposure of Dutch nursing infants to brominated flame retardants (PBDEs) via breast milk is expressed as:

$$\textit{Cumulative exposure}\ \text{(ng/kg body weight)} = \int_0^T \frac{C_m(t) \times I_m(t)}{W(t)} dt \qquad (1)$$

$$C_m(t) = C_f(t) \times F(t) \qquad (2)$$

Where T is breast feeding period duration in days, C_m is the concentration of the contaminant in breast milk ng/g milk, C_f is the concentration of the contaminant in breast milk fat in ng/g fat, F is the fat content in breast milk in g fat/g milk, I_m is the intake of breast milk in g milk per day, W is the nursing infant body weight (bw) in kg and t is time (in this particular case time is equivalent to the age of the nursing child). The concentration of the contaminant in breast milk C_m, the intake of breast milk I_m and the nursing infant body weight W are characterised as specific probability distribution functions. The latter two parameters vary with the age of a nursing infant (see below).
Available information on PCBs, dioxins and furans in breast milk suggest a depuration, i.e. a time-related decline of the concentration as the breast feeding period increases (LaKind et al., 2001). However, currently data on the depuration of PBDEs in breast milk are not available. For this reason the concentration of PBDEs in breast milk was assumed constant during the breast feeding period ($C_m(t) = C_m$).
Probability distributions were determined for 10 PBDE congeners from 25000 random trials by Latin Hypercube sampling following equation (1). With Latin Hypercube, the samples more accurately reflect the distribution of values in the input probability distribution than with the Monte Carlo method. Calculations are performed with @Risk (version 4.0.5, Palisade Corporation) for MS Excel.

2.2 Probability density functions

2.2.1 Concentration of PBDEs in breast milk

The concentrations of polybrominated diphenyl ethers (PBDEs) measured in breast milk samples were taken from Baumann et al. (2002, see Table 1). These 103 breast milk samples were obtained from Dutch primiparous women 6 to 10 days after labour in 1998 and analysed on 11 different PBDE congeners. The BDE #138 congener was not found in any of the breast milk samples in concentrations exceeding its limit of detection. Therefore exposure calculations were not carried out for this congener. In calculating the exposure, the concentrations of congeners lying below the level of detection were assumed to have a value of half the value of the detection limit.

Table 1. Summary of polybrominated diphenyl ethers (PBDEs) congener concentrations measured in 103 Dutch breast milk samples in 1998.

	n >LOD[1]	**Minimum ng/g fat**	**Maximum ng/g fat**	**Median ng/g fat**	**Mean, ng/g fat**	**sd[2] ng/g fat**	**rel. sd[3] (%)**
BDE #17	10	<0.03	0.13	<0.03			
BDE #28	108	0.05	0.43	0.11	0.13	0.07	0.50
BDE #47	108	0.45	6.50	1.23	1.56	1.09	0.70
BDE #66	36	<0.06	0.32	<0.06			
BDE #85	13	<0.08	0.17	<0.08			
BDE #99	108	0.17	2.70	0.40	0.53	0.40	0.76
BDE #100	108	0.09	1.72	0.31	0.37	0.25	0.67
BDE #138	0	<0.1	0.00	<0.1			
BDE #153	108	0.33	3.88	0.91	1.02	0.52	0.51
BDE #154	51	<0.08	0.26	<0.08			
BDE #183	105	<0.09	1.90	0.42	0.45	0.28	0.61

[1] n >LOD: number of samples exceeding the limit of detection.
[2] sd: standard deviation
[3] rel. sd: relative standard deviation

The concentrations of PBDE congeners are expressed per g fat, hence the concentrations in breast milk are calculated according to equation 2. For each congener the resulting concentration in milk was fitted to 21 different distribution functions (normal, lognormal, inverse Gaussian, etcetera). In this procedure the "best fit" function giving only positive values was selected based on the minimisation of χ^2. As a comparison the lognormal function was fitted as well. Note that for congeners with a high number of non-detects the characterisation of the distribution function is strongly influenced by attributing half of the detection limit as the concentration in non-detects. Figure 1 shows an example of the outcome of the fitting procedure for BDE #47. As can be seen the function which best fitted to the data, i.e. the inverse Gaussian function, closely resembled the fitting of the lognormal function. Similar results were obtained with the other 9 PBDEs (data not shown).
In the exposure calculations the "best fit" probability density functions were used.

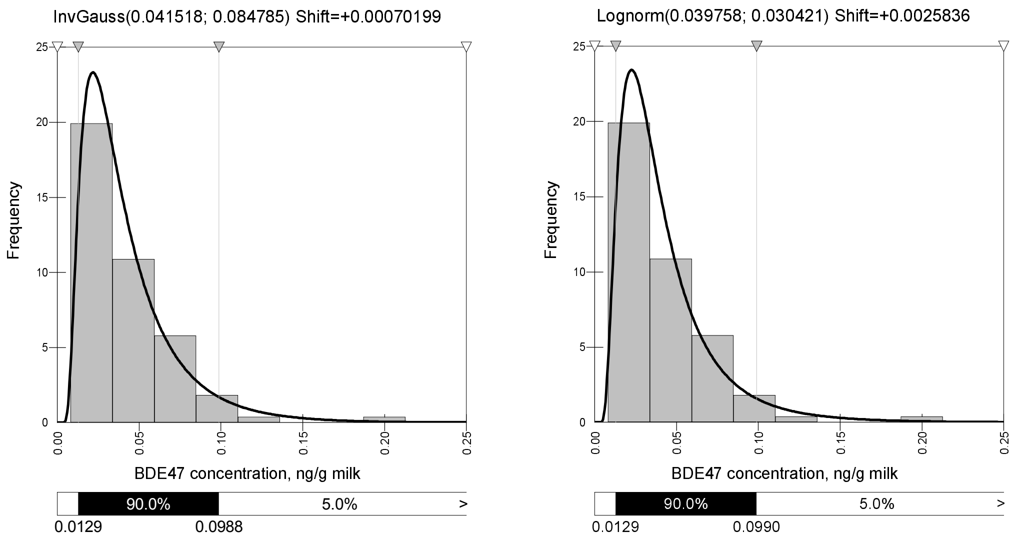

Figure 1. The" best fit" probability density function (inverse Gaussian) and the lognormal function as fitted to BDE #47 concentrations in Dutch breast milk.

2.2.2 Breast milk intake

Breast milk intake rates are determined as a function of age following the weighed (by the number of nursing infants studied) average approach used in the Exposure Factors Handbook (1997). The mean breast milk intake rates and standard deviations are determined using data from Neville (1988) for nursing infants younger than 1 month. For nursing infants aged 1 to 12 months data from Butte et al. (1984), Cox et al. (1996), Dewey et al. (1983 and 1991), Kent et al. (1999), Köhler et al. (1984), McCrory et al. (1999), Neville et al. (1988), Nommsen et al. (1991) and Pao et al. (1980) were used (Appendix 1). The breast milk intake rate by nursing infants increases in the first month of life and decreases after six month due to introduction of other food (Figure 2). Normal distributions truncated to positive values up to a maximum of 1200 g/day (Exposure Factors Handbook, 1997) with the determined means and standard deviations represent the probability density functions describing the breast milk intake by nursing infants.
In the calculation of the exposure doses a positive correlation between breast milk intake and body weight of 0.56 (Dewey et al., 1991) is taken into account.

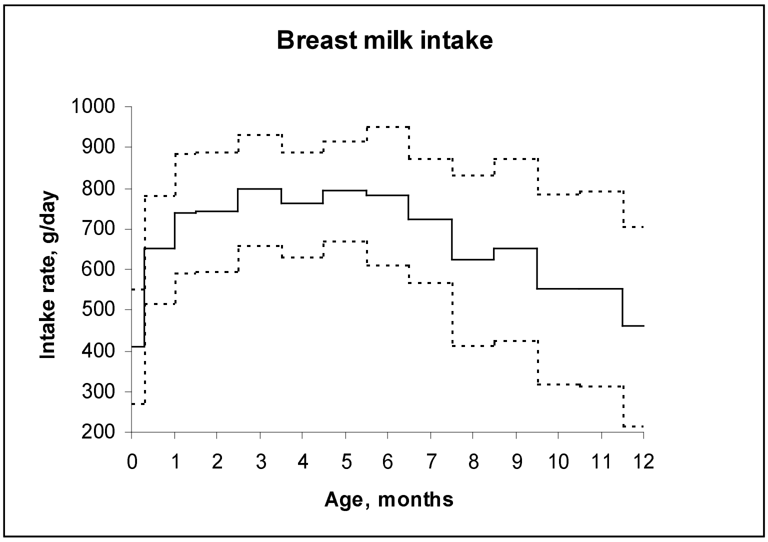

Figure 2. Breast milk intake (mean and ranges equal to one standard deviation) by nursing infants from birth to 1 year of age.

2.2.3 Nursing infant body weight

The body weights and standard deviations of neonates at the age of < 1 month are from ICRP (1974) and of infants aged 1 to 9 months are averaged weights and standard deviations for Dutch boys and girls from Burgmeijer et al. (1998), (Appendix 1). Normal distributions truncated to only positive values with these mean and standard deviation represent the probability density functions describing nursing infant weight.

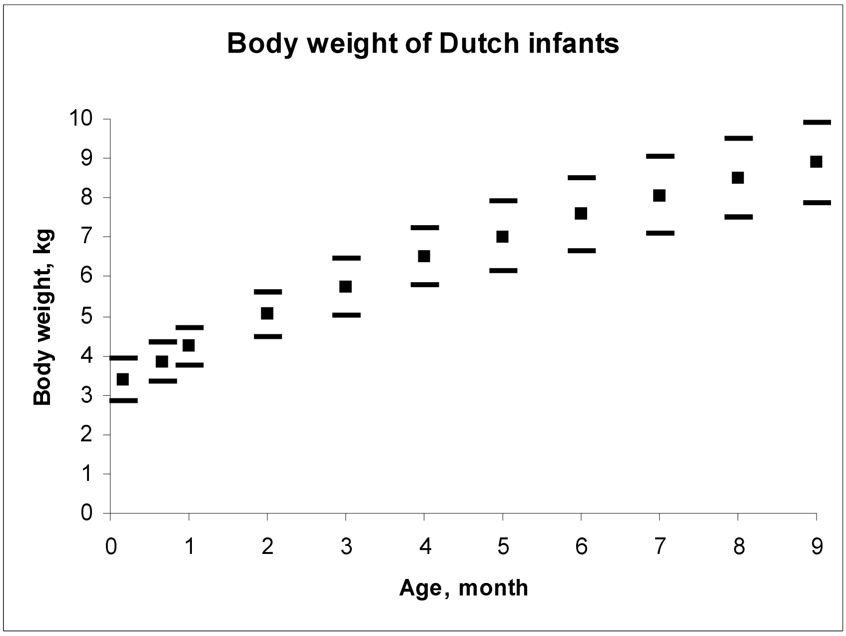

Figure 3. Body weights and standard deviations of Dutch infants from birth to 9 months of age.

2.2.4. Duration of breast-feeding for Dutch nursing infants

In a recent study (Lanting et al., 2002) the type of food consumed (breast milk fed, partially breast-fed or formula bottle-fed) was defined for 3346 Dutch infants of different ages. The percentage of Dutch nursing infants exclusively breast-fed and partially breast-fed for different ages from birth to 9 months from a 2000/2001 study (Lanting et al., 2002) and from a 1999 study (Hagen et al., 2000) are shown in Table 2 (the age of > 6 month was taken as 7.5 month, i.e. intermediate between 6 and 9 months). As shown, the percentage of nursing infants exclusively breast-fed has considerably increased from 1999 to 2000/2001, with an obvious increasing trend since 1996 (Lanting et al., 2002). Furthermore, with increasing age, the percentage of infants exclusively breast-fed decreases. However, there is still a small percentage (2.8 %) of infants exclusivily breast-fed at the age of 9 months (Hagen et al., 2000). In order to cover the period up to 9 months after birth, the exposure of the nursing infant via breast milk was calculated for the following feeding periods: 8 days, 1 month, 2, 3, 4, 5, 6, 7.5 and 9 months.
Finally, it should be mentioned that the mean intake of breast milk by partially breast-fed infants (Pao et al., 1980) is 1.5 times less than by exclusively breast-fed infants at the age of 1 month and up to 1.9 times less at the age of 6 months.

Table 2. The fraction of Dutch infants exclusively and partially breast-fed.

Age, complete days or months	**Dutch infants exclusively breast-fed in 2000/2001, %**	**Infants partially breast-fed in 2000/2001, %**	**Dutch infants exclusively breast-fed in 1999, %**
0 days	75.3	0	76.4
8 days	72.4	1.5	-
1	53.4	7.9	47.2
2	39.2	13.4	31.4
3	32.4	11.1	22.5
4	22.8	13.2	18.4
5	16.6	16.1	14.2
6	18.5	13.9	11.1
7.5 (> 6)	16.3	12.5	-
9	-	-	2.8

3. Results

The exposure of Dutch nursing infants via breast milk was calculated for 10 PBDE congeners and for breast feed duration periods of 8 days, 1 month, 2, 3, 4, 5, 6, 7.5 and 9 months. In general the following ranking of exposure was obtained: #47 > #153 > #99 ≅ #183 ≅ #100 > #28 > #66 ≅ #154 ≅ #85 > #17.

In the Netherlands a breast feeding period of 6 months is recommended (Lanting et al., 2002, with 18.5 % of Dutch infants exclusively being breast fed up to this period). In Table 3 the mean and 95th percentile of the cumulative exposure at 6 months to the six most abundant PBDEs is presented. A complete overview of the mean, standard deviation, minimum, maximum, 5th and 95th percentile of the exposure calculations at the different timepoints is given in Appendix 2.

Table 3. Cumulative exposure of nursing children (mean and 95th percentile) to PBDEs at 6 months

congener	mean ng/kg bw	95th percentile
BDE #28	92	189
BDE #47	1045	2454
BDE #99	391	977
BDE #100	252	557
BDE #153	688	1307
BDE #183	323	816

The probability distributions of the exposure to BDE #47, i.e. the congener with the highest concentration at six months is given in Figure 3. As can be seen the mean exposure to BDE #47 amounted 1045 ng/kg bw, equivalent to a mean daily intake rate during this period of 1045/180 = 5.8 ng/kg bw/day. Figure 4 also shows that a rather large inter-individual variation may be expected for the exposure of nursing children to BDE #47, the 5th and 95th percentiles of the exposure distribution being 316 and 2454 ng/kg bw.

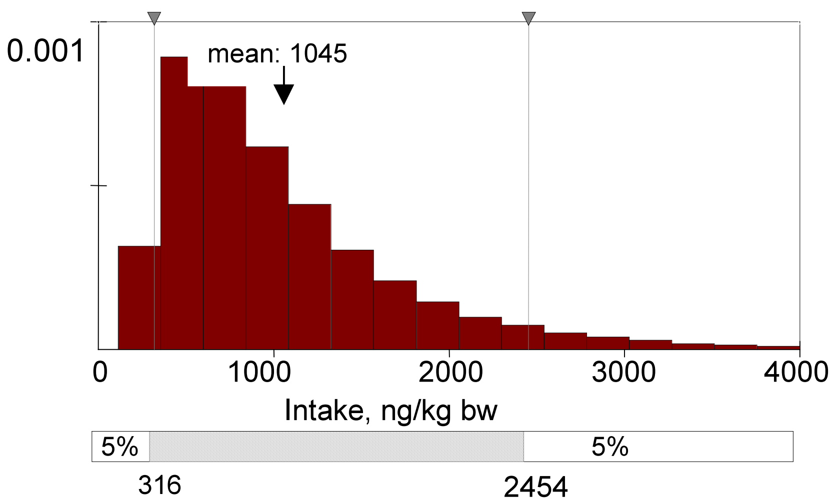

Figure 4. Probability distribution of exposure via breast milk to BDE #47 of Dutch infants exclusively breast-fed during 6 months (18.5 % of the infants).

A complete overview of the cumulative 6 month's exposure to all 10 congeners studied is presented in Figs. 1-12 of Appendix 3. As with BDE #47 a rather large inter-individual variation in exposure was found for all congeners. For example, when the ratio between the 5 and the 95 percentiles of the exposure distributions was taken as a measure for inter-individual variability the following variability was calculated: 4.6 (BDE #17), 5.7 (BDE #28), 7.8 (BDE #47), 10.9 (BDE #66), 4.6 (BDE #85), 9.2 (BDE #99), 7.3 (BDE #100), 5.1 (BDE #153), 9.0 (BDE #154) and 15.4 (BDE #183).
As expected, the exposure increases with increasing breastfeeding period. Figure 5 illustrates this principle for BDE #47. As can be seen the exposure to this congener almost linearly increases as the duration of breast feeding period increases. A complete overview of the distribution functions underlying Figure 5, i.e. BDE #47 specific exposure distribution functions after 8 days, 1, 2, 3, 4, 5, 6, 7.5 and 9 months of breast feeding, are presented in Figures 11-19 of Appendix 3.

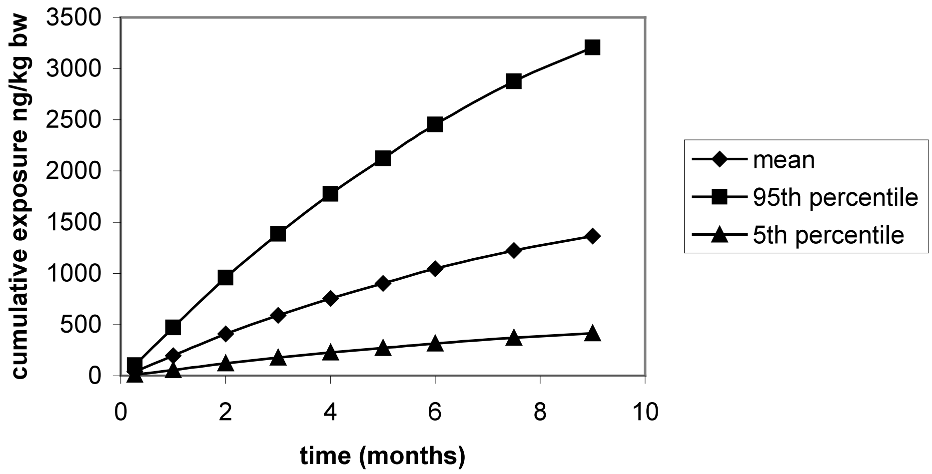

Figure 5. The cumulative exposure (mean, 5th percentile and 95th percentile) of Dutch nursing infants to BDE #47 via breast milk at increasing period of breast feeding

4. Discussion

In this report the results of an exposure assessment of Dutch nursing infants to 11 polybrominated biphenyl ethers (PBDEs) via breast milk are presented. The (probabilistic) exposure assessment was based on inter-individual variability in PBDE levels in Dutch breast milk which had been collected in 1998, in milk intake and in infant body weight. Although such an exposure assessment has been performed before for persistent polychlorinated organic contaminants by Hoover (1999), Hoover's assessment did not include PBDE's. So, to our knowledge no literature data which are comparable with the results presented in this report are available.

In interpreting the calculations presented here the following remarks should be made.

Although concentrations of polychlorinated contaminants do tend to decrease as the breast feeding period increases (La Kind et al., 2001) no data of such a decrease are available for PBDEs. For this reason a decrease was not incorporated in the exposure assessment presented in this report. It should be kept in mind that this might have led to an overestimation of exposure as the breast feeding period increases.

In calculating the exposure half of the level of detection was attributed to milk samples in which a specific PBDE congener was below the level of detection. Consequently the accuracy of the exposure assessment depends on the number of milk samples in which the congener could or could not be detected. Of the 11 congeners evaluated, 6 could be detected in more than 97 % of the samples (PBDEs #28, #100, #183, #99, #153, #47), in two cases in 33-47 % of the samples (PBDEs #66, #154) and in 3 in only 0-13 % of the samples (PBDEs #138, #17, #85). This undoubtedly has influenced the accuracy with which the exposure to PBDEs #66, #154, #138, #17 and #85 was assessed.

In a current report a positive correlation between breast milk intake and body weight of 0.56 (Dewey et al., 1991) for each nursing infant age is taken into account. A calculation was made where additionally correlations in time between the weights, between the breast milk intakes and between the breast milk intake and body weight based on Dewey et al. (1991) are taken into account. The results did not differ significantly from the ones presented here.

Restricting the exposure assessment to the 6 PBDE congeners which could be detected in almost all of the analysed milk samples and taking the mean cumulative exposure after a breast feeding period of 6 months as a reference, it appears that the exposure of nursing infants via breast milk is about 6 times higher than the exposure of adults via food (see Table 4).

Table 4. Mean daily PBDE intake of nursing children via breast milk during a breast feeding period of 6 months and daily PBDE intake of adults via food (De Winter et al., 2003)

Congener	**Nursing infants exposure** **ng/kg bw/day**	**Adults exposure** **ng/kg bw/day**
BDE #28	0.5	0.009
BDE #47	5.8	0.70
BDE #99	2.2	0.54
BDE #100	1.4	0.24
BDE #153	3.8	0.96
BDE #183	1.8	Not determined
Sum 6 PBDEs	15.5	2.45

The relative high exposure per kilogram body weight of nursing children to PBDEs via breast milk may also lead to a relative high body burden of these compounds in nursing children. For example, assuming the PBDE concentration in milk fat to reflect the "steady state" PBDE concentration in body fat and a 65 kg woman to contain 16 kg of adipose tissue (25 % body fat) the body burden of PBDEs in the maternal body can easily be calculated as the product of the PBDE concentration in milk fat and the amount of maternal adipose tissue. Table 5 shows a comparison of the outcome of such a calculation with the 6 month's cumulative exposure of nursing infants to PBDEs via breast milk.

Table 5. Mean cumulative 6 month's exposure of nursing infants to PBDEs via breast milk and estimated body burden of PBDEs in the maternal body.

Congener	**Nursing infants cumulative exposure (ng/kg bw)**	**Adults cumulative exposure (ng/kg bw)**
BDE #28	92	25
BDE #47	1045	300
BDE #99	391	100
BDE #100	252	75
BDE #153	688	225
BDE #183	323	100
Sum 6 PBDEs	2791	825

As can be seen in Table 5 the relative exposure of nursing children to PBDEs via breast milk may, within the assumptions made, lead to a higher body burden of these compounds in nursing children than in adults. The interpretation of a accumulation of PBDEs in nursing children when compared to adults in terms of risk assessment of course depends on the mode of action of these compounds. Although providing such an overview is beyond the scope of this report, it is crucial in interpreting the exposure calculations presented in this report.
The exposure assessment of adults to BFRs via food performed by De Winter et al. (2003) demonstrated that this exposure is not restricted to PBDEs (intake: 3.5 ng/kg bw/day for the sum of PBDEs) but also comprises hexabromocyclododecane (HBCD, intake: 2.9 ng/kg bw/day) and tetrabromobisphenol-A (TBBP-A, intake: 0.04 ng/kg bw/day). Given the intake and the accumulative properties of HBCD (EU draft human health risk assessment report, May 2003) it is expected that HBCD will be present in Dutch breast milk and, consequently, will contribute significantly to the exposure of nursing infants to BFRs via breast milk. TBBP-A is not expected to accumulate in humans (EU draft human health risk assesment report, February 2003). In this context the development of an analytic chemical methods to quantify HBCD in breast milk is therefore recommended.

5. Conclusions and recommendations

The present report indicates that nursing infants are exposed to considerable amounts of PBDEs via breast milk. This exposure, which is higher than the exposure of adults to PBDEs via food, may lead to a relatively high accumulation of PBDEs in nursing children.
The absence of measurements of HBCD in breast milk may lead to a significant underestimation of the exposure of nursing children to BFRs. The development of analytical chemical methods to quantify these compounds in breast milk is therefore recommended.
The exposure assessment described here incorporates a number of methodological assumptions. Regarding the accuracy of the calculations these assumptions include the negligence of the depuration of PBDEs in breast milk and the attribution of half of the detection limit to non-detects. It is recommended to perform an additional study on the effects of these assumptions on the outcome of the exposure calculations.
It is also recommended to assess the exposure to dioxins, furans and PCBs with the same methodology and to compare the levels of exposure to PBDEs, dioxins, furans and PCBs.

References

Baumann et al. (2002) Analyseresultaten van brandvertagers in moedermelk, RIVM letter report 476/02, LOC/RB.

Boon, J.P., Lewis, W.E., Tjoen-A-Choy, M.R., Allchin, C.R., Law, R.J., De Boer, J., Ten Hallers-Tjabbes, C.C., Zegers, B.N. (2002) Levels of ploybrominated diphenyl ether (PBDE) flame retardants in animals representing different trophic levels of the North Sea food web. Environ. Sci. Technol., 36: 4025-4032.

Burgmeijer, R.J.F. et al. (1998) Groeidiagrammen. Bohn Stafleu Van Loghum, Houten, the Netherlands.

Butte, N.F., Garza, C., O'Brian Smith, E., Nichols, B.L. (1984) Human milk intake and growth in exclusively breast-fed infants. J. Pediatr., 104: 187-195.

Cox, D.B., Owens, R.A. and Hartmann, P.E. (1996) Blood and milk prolactin and the rate of milk synthesis in women. Exp. Physiol., 81: 1007-1020.

Darnerud, P.O., Aune, M., Atuma, S., Becker, W., Bjerselius, R., Cnattingius, S. and Glynn, A. (2002) Time trend of polybrominated diphenyl ether (PBDE) levels in breast milk from Uppsala, Sweden, 1996-2001. Organohalogen Compounds, 58, 233-236.

Dewey, K.G. and Lönnerdal, B. (1983) Milk and nutrient intake of breast-fed infants from 1 to 6 months: relation to growth and fatness. Journal of Pediatric Gastroenterology and Nutrition 2: 497-506.

Dewey, K.G., Heinig, M.J., Nommsen, L.A., Lönnerdal, B. (1991) Maternal versus infant factors related to breast milk intake and residual milk volume: the DARLING study. Pediatrics, 87: 829-837.

Exposure Factors Handbook (1997) Chapter 14: Breast milk intake. National Center of Exposure Assessment, United States Environmental Protection Agency, EPA/600/P-95/002Fa.

EU Council Regulation on Existing Substances. Draft human health risk assessment report for hexabromocyclododecane, February 2003.

EU Council Regulation on Existing Substances. Draft human health risk assessment report for tetrabromobisphenol-A, May 2003.

ICRP (1974) Report of the task groep on reference man. ICRP publication no. 23, Pergamon Press, New York.

Hagen van, E.E, Wouwe van, J.P., Buuren van, S., Burgmeijer, R.J.F., Hirasing, R.A., Jonge de, G.A. (2000) Peiling Veilig Slapen 1999, Leiden, TNO-PG, publicatie nr. 2000/047.

Hoover, S.M. (1999) Exposure to persistent organochlorines in Canadian breast milk: a probabilistic assessment. Risk Analysis, 19: 527-545.

Kent, J.C., Mitoulas, L., Cox, D., Owens, R.A., Hartmann, P.E. (1999) Breast volume and milk production during extended lactation in women. Experimental Physiology 84: 435-447.

Köhler, L., Meeuwisse, G., Mortensson, W. (1984) Food intake and growth of infants between six and twenty-six weeks of age on breast milk, cow's milk formula and soy formula. Acta Paediatr. Scand. 73:40-48.

LaKind, J.S., Berlin, C.M., Naiman, D.Q. (2001) Infant exposure to chemicals in breast milk in the United States: what we need to learn from a breast milk monitoring program. Environmental Health Perspectives, 109: 75-88.

Lanting, C.I., Herschderfer, K., Van Wouwe, J.P., Reijneveld. S.A. (2002) Peiling melkvoeding van zuigelingen 2000/2001 en het effect van certificering op de borstvoedingscijfers. TNO Preventie en Gezondheid , TNO-report 2001.252, Leiden.

Leonards, P., Brandsma, S, Kruijt, A., Lohman, M., van Hesseling, J., de Boer, J. Achtergrondgehalten van gebromeerde vlamvertragers in voedingsproducten. RIVO report, 2002.

McCrory, M.A., Nommsen-Rivers, L.A., Molé, P.A., Lönnerdal, B., Dewey, K.G. (1999) Randomised trial of the short-term effects of dieting compared with dieting plus aerobic exercise on lactation performance. Am. J. Clin. Nutr., 69: 959-967.

Neville, M.C., Keller, R., Seacat, J., Lutes, V., Neifert, M., Casey, C., Allen, J., Archer, P. (1988) Studies in human lactation: milk volumes in lactating women during the onset of lactation and full lactation. Am. J. Clin. Nutr., 48: 1375-1386.

Nommsen, L.A., Lovelady, C.A., Heinig, M.J., Lönnerdal, B., Dewey, K. G. (1991) Determinants of energy, protein, lipid and lactose concentrations in human milk during the first 12 month of lactation: the DARLING study. Am. J. Clin. Nutr., 53: 457-465.

Norén, K., Meironyté, D. (2000) Certain organochlorine and organobromine contaminants in Swedish human milk in perspective of past 2-30 years. Chemosphere, 40: 1111-1123.

Pao, E.M., Hines, J.M., Roche, A.F. (1980) Milk intakes and feeding patterns of breast-fed infants. Journal of American Dietetic Association, 77:540-545.

Winter-Sorkina, R. de, Bakker, M.I., Donkersgoed, G. van, Klaveren, J.D. van (2003) The dietary intake of brominated flame retardants by the Dutch population, (to be published as RIVM report).

Zeilmaker, M.J., Houweling, D.A., Cuijpers, C.E.J., Hoogerbrugge, R., Baumann, R.A. (2002) Verontreiniging van moedermelk met gechloreerde koolwaterstoffen in Nederland: niveaus in 1998 en tijd-trends. RIVM report 529102012/2002.

Appendix 1 Breast milk intakes and infant body weights

Table A1.1 Mean breast milk intake rates and standard deviations.

Age, months	Mean breast milk intake, g/day	Standard deviation, g/day	Number of nursing infants
0-0.3	411	141	78
0.3-1	650	133	61
1	738	148	114
2	744	147	83
3	796	137	285
4	761	127	78
5	795	123	37
6	782	170	150
7	721	154	12
8	622	210	10
9	651	223	90
10	551	234	11
11	554	240	9
12	462	247	72

Table A1.2. Body weights and standard deviations of Dutch infants from birth to 9 months of age.

Age months	Mean weight kg	sd[1] kg
0-0.3	3.4	0.6
0.3-1	3.9	0.5
1	4.2	0.5
2	5.1	0.6
3	5.8	0.7
4	6.5	0.7
5	7.0	0.9
6	7.6	0.9
7	8.1	1.0
8	8.5	1.0
9	8.9	1.0

[1]sd: standard deviation

Appendix 2 Exposure to PBDE: data

Table A2.1 Mean, standard deviation, minimum, maximum, 5 and 95 percentiles of Dutch nursing infant exposure via breast milk to 10 PBDE congeners.

Breast feeding period	Congener	Minimum, ng/kg bw	Maximum, ng/kg bw	Mean, ng/kg bw	Standard Deviation, ng/kg bw	5%, ng/kg bw	95%, ng/kg bw
8 days	BDE #17	0.0	17.9	0.5	0.4	0.2	1.1
	BDE #28	0.0	24.4	3.6	2.3	1.0	7.9
	BDE #47	0.0	455.3	40.9	32.0	9.8	102.6
	BDE #66	0.0	556.3	1.8	5.1	0.4	5.0
	BDE #85	0.0	25.6	1.4	0.9	0.5	3.0
	BDE #99	0.0	1257.2	15.2	22.2	3.3	40.1
	BDE #100	0.0	109.1	9.8	7.2	2.3	23.2
	BDE #153	0.0	173.4	26.8	15.5	7.8	55.7
	BDE #154	0.0	14.7	1.4	1.2	0.3	3.8
	BDE #183	0.0	140.8	12.6	10.8	1.8	33.7
1 month	BDE #17	0.5	117.6	2.4	1.8	1.0	5.0
	BDE #28	1.9	102.0	17.3	9.8	6.1	36.3
	BDE #47	19.6	1907.9	197.9	141.1	57.2	472.6
	BDE #66	1.0	2880.4	8.8	24.8	2.1	24.2
	BDE #85	1.1	100.0	6.7	4.0	2.8	13.8
	BDE #99	5.7	10156.3	74.1	119.0	19.3	188.0
	BDE #100	2.3	461.2	47.8	31.7	13.8	107.9
	BDE #153	0.0	680.5	130.3	65.9	46.8	253.0
	BDE #154	0.7	62.5	6.9	5.5	1.8	17.7
	BDE #183	2.5	541.9	61.2	48.5	9.9	156.3
2 months	BDE #17	1.2	234.9	5.0	3.7	2.2	10.2
	BDE #28	6.3	198.2	35.8	19.8	12.9	73.7
	BDE #47	41.0	3761.9	408.4	285.5	122.0	959.5
	BDE #66	2.3	5389.1	18.1	48.4	4.4	49.3
	BDE #85	2.6	215.2	13.8	8.1	5.9	28.1
	BDE #99	18.8	21726.0	153.0	245.1	40.9	384.8
	BDE #100	3.9	863.5	98.6	63.9	29.4	219.4
	BDE #153	0.0	1349.9	268.9	131.3	99.7	512.8
	BDE #154	2.5	109.6	14.2	11.0	3.8	36.2
	BDE #183	5.7	1159.2	126.3	98.6	20.5	320.8
3 months	BDE #17	1.6	337.7	7.2	5.4	3.2	14.6
	BDE #28	9.4	281.9	51.7	28.5	18.7	106.6
	BDE #47	59.6	5116.9	589.5	410.5	177.8	1386.9
	BDE #66	3.3	7542.9	26.1	68.7	6.4	71.1
	BDE #85	3.9	312.1	19.9	11.6	8.6	40.5
	BDE #99	27.7	30546.4	220.8	350.8	59.5	554.8
	BDE #100	5.3	1235.0	142.3	91.9	42.6	316.7
	BDE #153	0.0	1884.2	388.2	188.4	144.9	738.5
	BDE #154	3.8	160.6	20.5	15.9	5.5	52.3
	BDE #183	9.0	1684.7	182.4	142.2	29.7	462.1
4 months	BDE #17	2.2	422.3	9.3	6.8	4.1	18.8
	BDE #28	12.6	357.4	66.4	36.5	24.0	137.1
	BDE #47	78.0	6363.0	757.1	525.5	228.5	1776.5
	BDE #66	4.4	9710.6	33.6	88.2	8.3	90.9
	BDE #85	4.9	393.8	25.5	14.9	11.1	52.1

	BDE #99	34.6	39107.9	283.6	450.7	76.6	710.3
	BDE #100	6.8	1681.0	182.7	117.7	55.0	405.1
	BDE #153	0.0	2407.2	498.5	240.8	186.5	947.6
	BDE #154	5.1	210.8	26.4	20.4	7.1	67.0
	BDE #183	11.6	2199.4	234.3	182.3	38.2	592.6
5 months	BDE #17	2.7	488.5	11.1	8.1	4.9	22.4
	BDE #28	16.0	421.9	79.2	43.5	28.7	163.2
	BDE #47	94.3	7471.4	903.3	626.0	273.2	2123.4
	BDE #66	5.4	11626.2	40.1	105.5	9.9	108.4
	BDE #85	5.6	472.3	30.4	17.7	13.3	62.1
	BDE #99	41.0	46595.1	338.3	537.4	91.8	845.6
	BDE #100	8.2	2063.9	218.0	140.1	65.6	482.2
	BDE #153	0.0	2924.0	594.7	286.3	222.0	1131.0
	BDE #154	6.1	250.1	31.5	24.3	8.5	80.0
	BDE #183	14.2	2629.6	279.6	217.3	45.6	705.9
6 months	BDE #17	3.2	551.1	12.8	9.4	5.7	25.9
	BDE #28	18.8	484.6	91.6	50.3	33.3	189.0
	BDE #47	111.9	8716.8	1044.8	723.2	316.3	2454.4
	BDE #66	6.2	13443.0	46.3	121.8	11.5	125.7
	BDE #85	6.4	560.0	35.2	20.5	15.4	71.6
	BDE #99	48.0	52679.1	391.3	616.6	106.1	977.3
	BDE #100	9.6	2450.6	252.1	161.9	75.9	557.0
	BDE #153	0.0	3538.8	687.8	330.5	257.3	1307.4
	BDE #154	7.1	291.7	36.4	28.0	9.9	92.1
	BDE #183	17.0	3003.7	323.4	251.1	53.1	816.2
7.5 months	BDE #17	3.7	632.7	15.1	10.9	6.7	30.3
	BDE #28	22.2	587.3	107.4	59.0	39.1	221.4
	BDE #47	127.5	10472.2	1224.6	846.6	372.0	2877.3
	BDE #66	7.1	15847.0	54.3	143.3	13.5	147.5
	BDE #85	7.4	682.9	41.3	24.0	18.1	83.7
	BDE #99	57.9	61404.1	458.6	720.7	124.4	1141.4
	BDE #100	11.3	2876.9	295.6	189.6	89.1	653.9
	BDE #153	0.0	4202.4	806.2	386.6	301.8	1533.1
	BDE #154	8.6	339.6	42.7	32.9	11.6	107.8
	BDE #183	20.2	3406.6	379.0	294.0	62.1	958.4
9 months	BDE #17	4.1	720.3	16.8	12.2	7.4	33.8
	BDE #28	25.0	649.3	119.6	65.7	43.5	246.4
	BDE #47	136.7	11671.7	1363.6	943.3	413.8	3207.3
	BDE #66	7.7	17711.7	60.5	159.9	15.1	164.9
	BDE #85	8.5	745.4	46.0	26.7	20.3	93.3
	BDE #99	66.6	65892.1	510.4	790.3	138.3	1270.9
	BDE #100	12.4	3202.2	329.1	211.2	99.0	727.5
	BDE #153	0.0	4559.2	897.7	430.3	336.4	1703.9
	BDE #154	9.7	387.7	47.5	36.6	12.9	120.3
	BDE #183	23.0	3721.5	422.2	327.6	69.4	1067.0

Appendix 3 Exposure to PBDE: graphs

Figs. A3.1-A3.10 6 month's probability functions of exposure, 18.5 % of babies breast-fed.

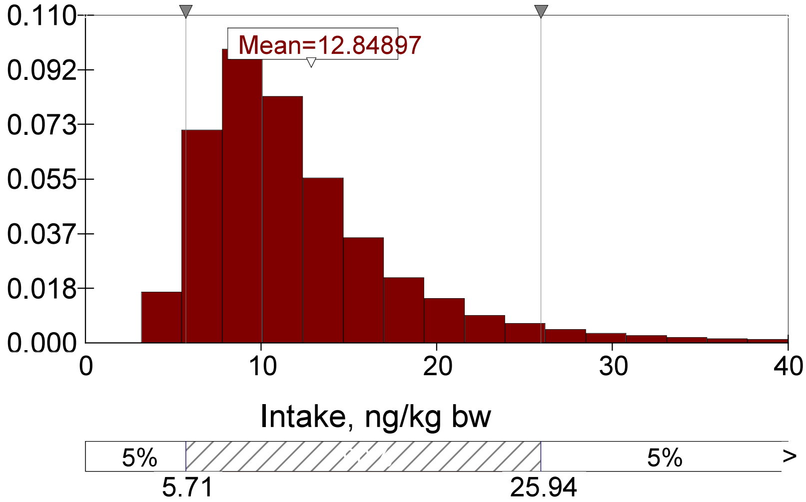

Figure A3.1. Probability distribution of exposure via breast milk to BDE #17 of Dutch infants exclusively breast-fed during 6 months.

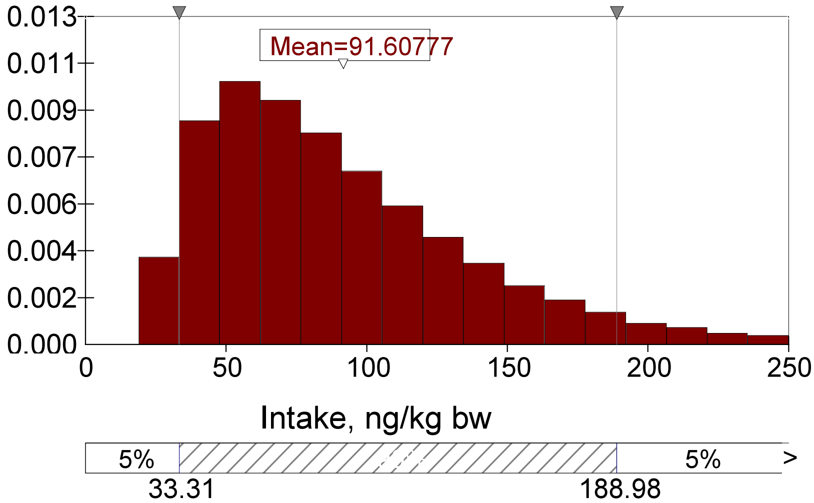

Figure A3.2. Probability distribution of exposure via breast milk to BDE #28 of Dutch infants exclusively breast-fed during 6 months.

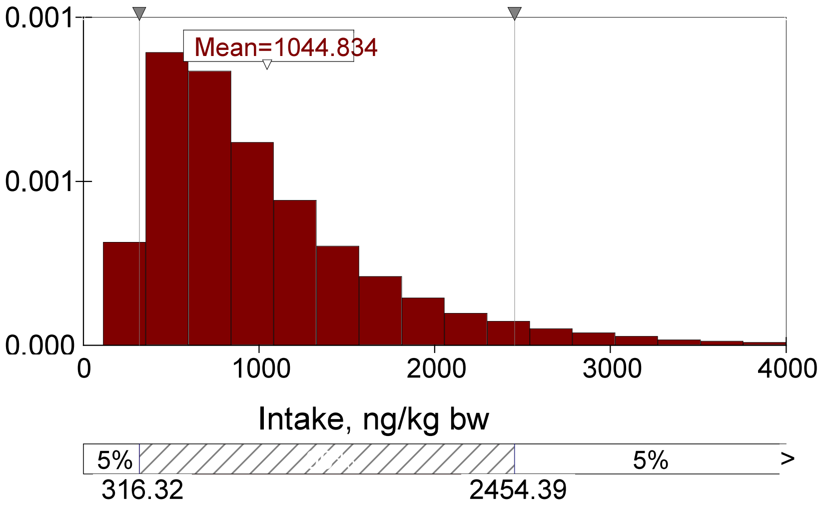

Figure A3.3. Probability distribution of exposure via breast milk to BDE #47 of Dutch infants exclusively breast-fed during 6 months.

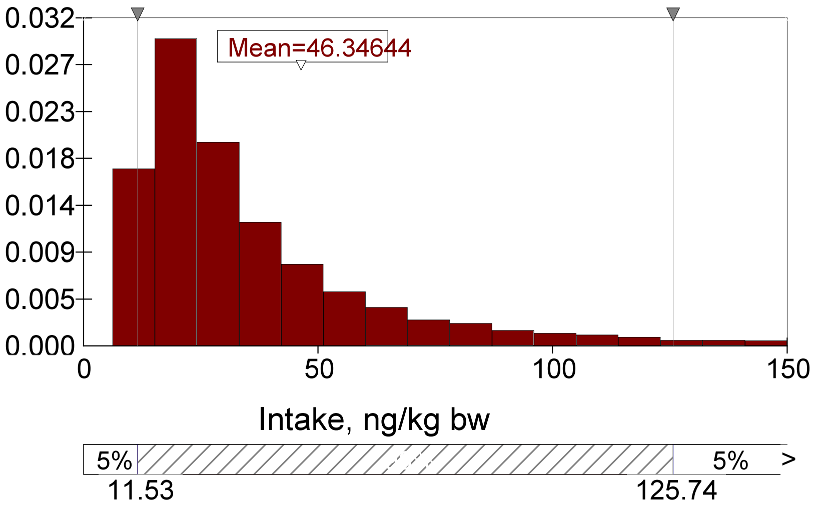

Figure A3.4. Probability distribution of exposure via breast milk to BDE #66 of Dutch infants exclusively breast-fed during 6 months.

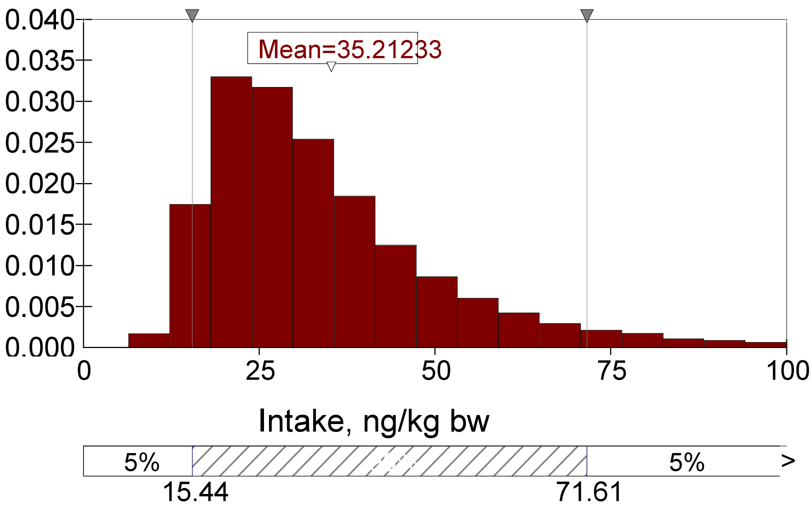

Figure A3.5. Probability distribution of exposure via breast milk to BDE #85 of Dutch infants exclusively breast-fed during 6 months.

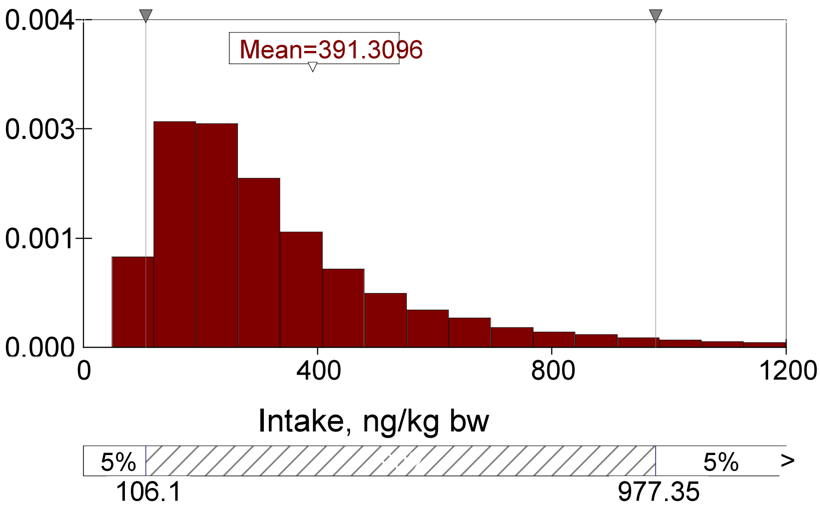

Figure A3.6. Probability distribution of exposure via breast milk to BDE #99 of Dutch infants exclusively breast-fed during 6 months.

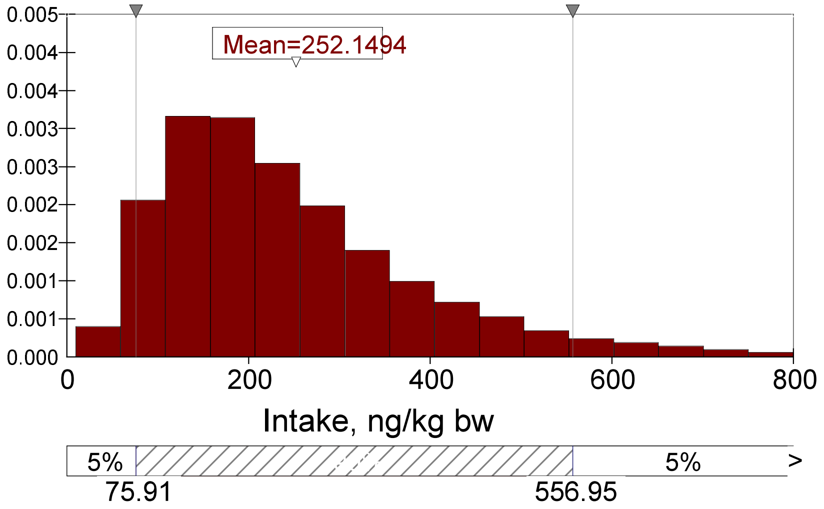

Figure A3.7. Probability distribution of exposure via breast milk to BDE #100 of Dutch infants exclusively breast-fed during 6 months.

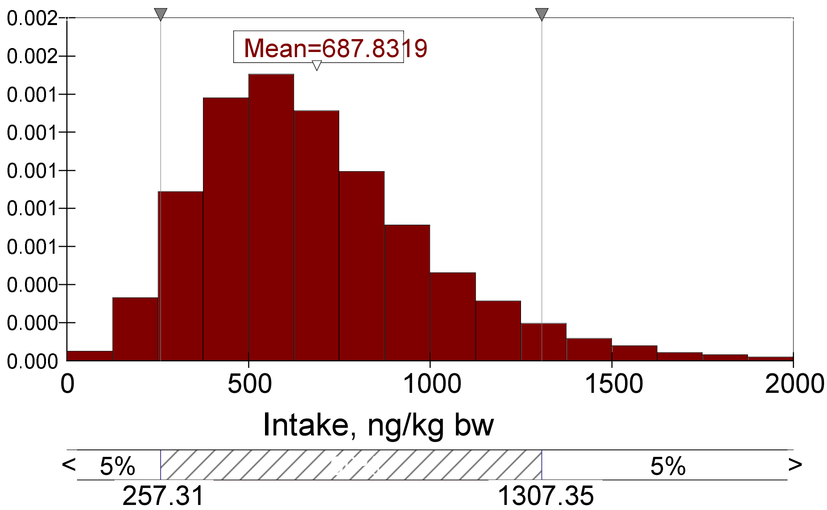

Figure A3.8. Probability distribution of exposure via breast milk to BDE #153 of Dutch infants exclusively breast-fed during 6 months.

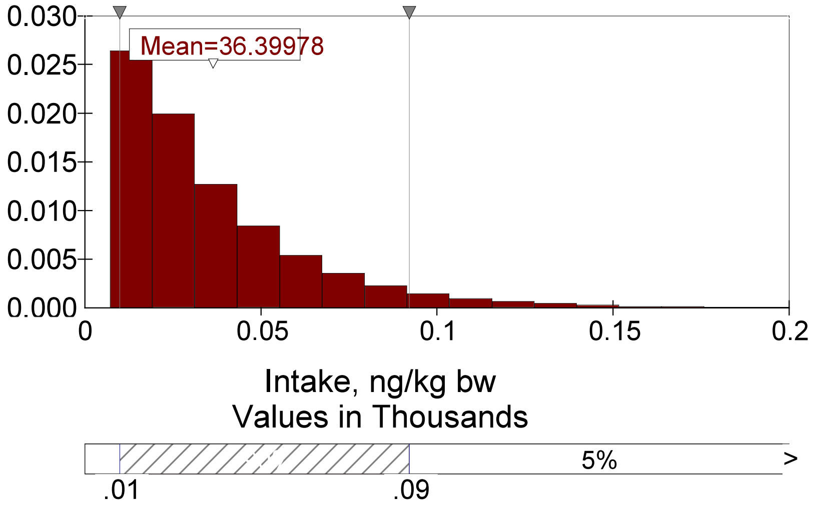

Figure A3.9. *Probability distribution of exposure via breast milk to BDE #154 of Dutch infants exclusively breast-fed during 6 months.*

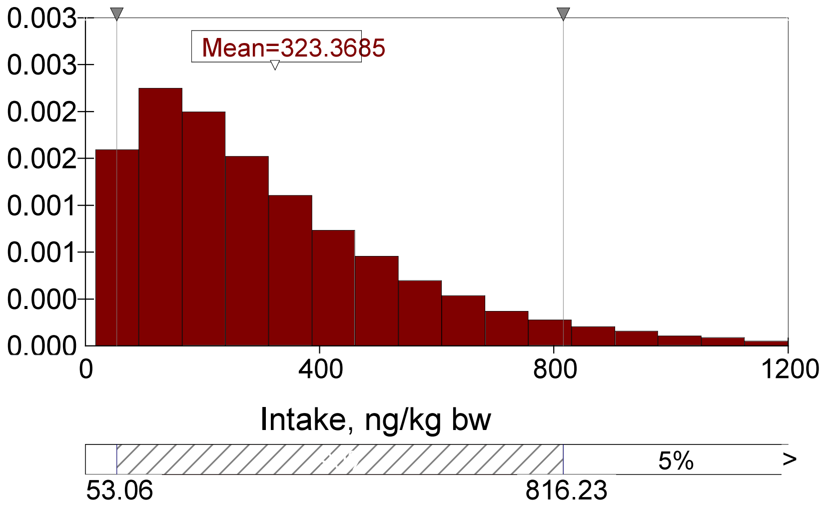

Figure A3.10. *Probability distribution of exposure via breast milk to BDE #183 of Dutch infants exclusively breast-fed during 6 months.*

Figures A3.11-A3.19 Probability distributions of 8 days to 9 months exposure to BDE #47

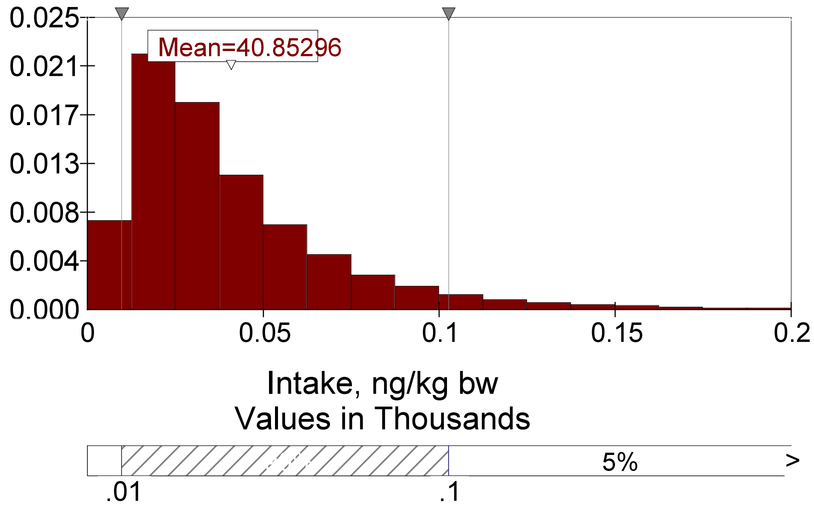

Figure A3.11. Probability distribution of exposure via breast milk to BDE #47 of Dutch infants exclusively breast-fed during 8 days.

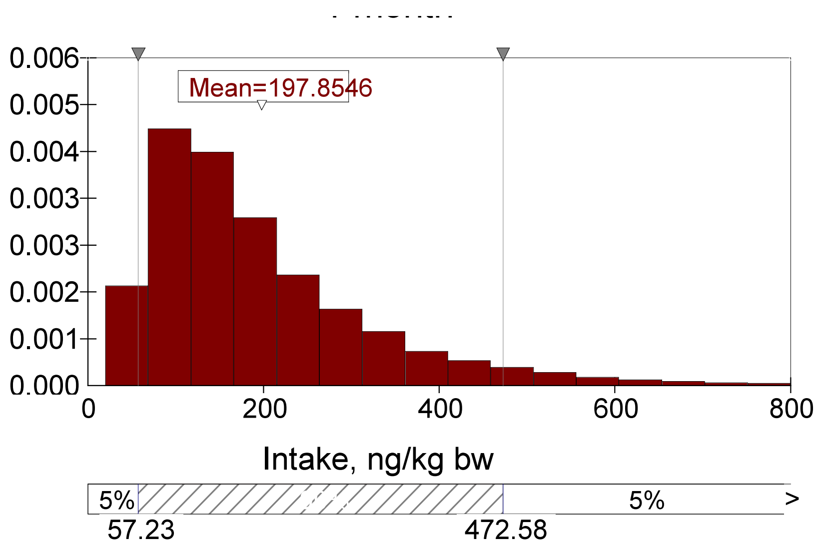

Figure A3.12. Probability distribution of exposure via breast milk to BDE #47 of Dutch infants exclusively breast-fed during 1 month.

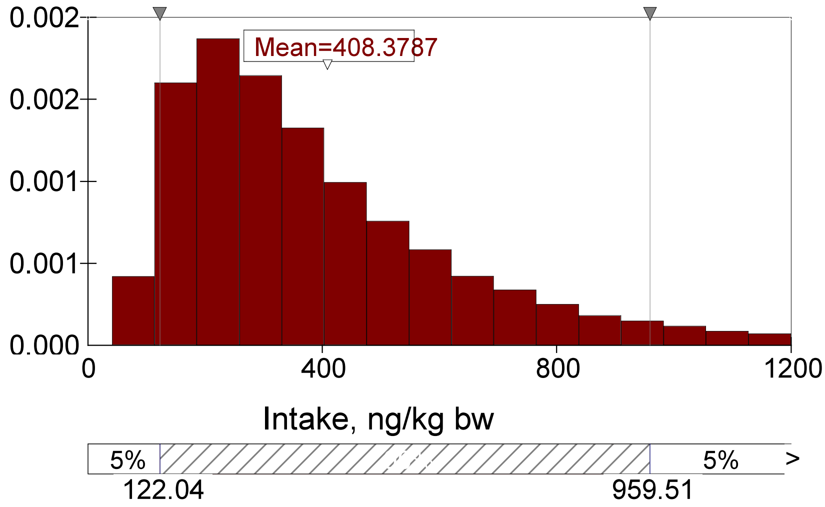

Figure A3.13. Probability distribution of exposure via breast milk to BDE #47 of Dutch infants exclusively breast-fed during 2 months.

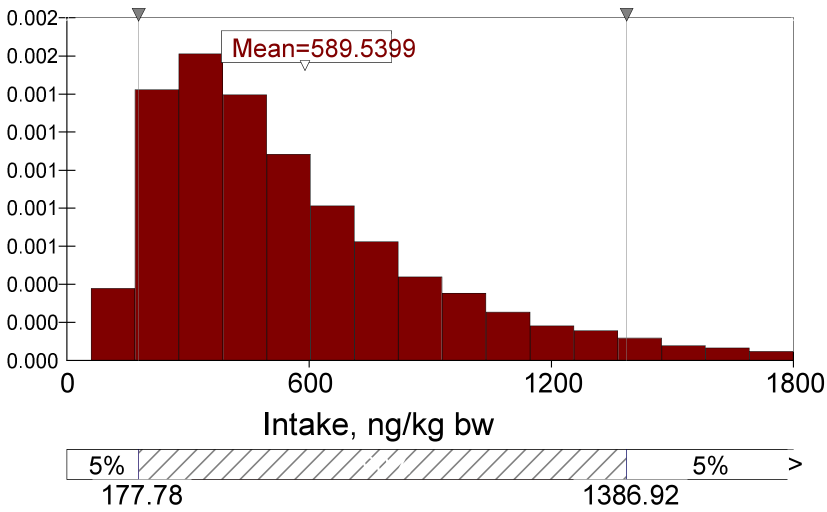

Figure A3.14. Probability distribution of exposure via breast milk to BDE #47 of Dutch infants exclusively breast-fed during 3 months.

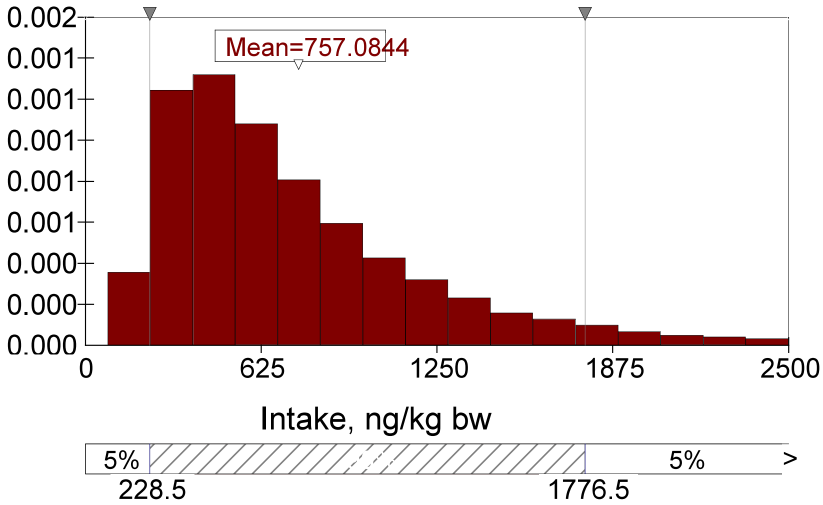

Figure A3.15. *Probability distribution of exposure via breast milk to BDE #47 of Dutch infants exclusively breast-fed during 4 months.*

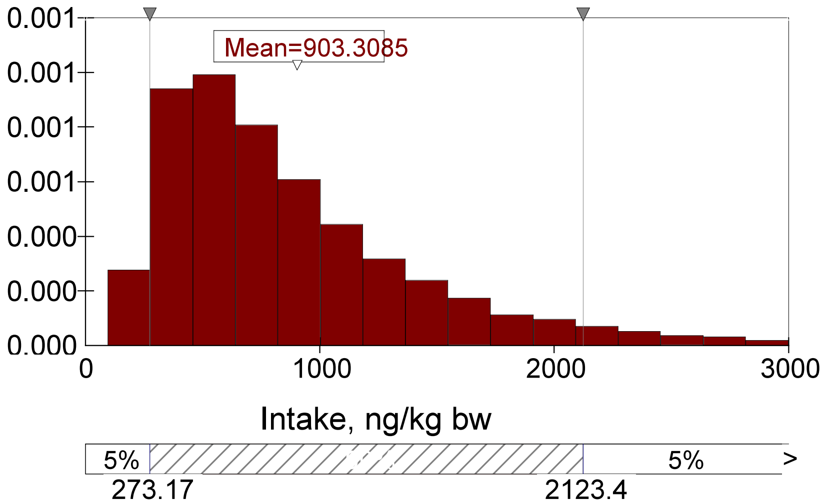

Figure A3.16. *Probability distribution of exposure via breast milk to BDE #47 of Dutch infants exclusively breast-fed during 5 months.*

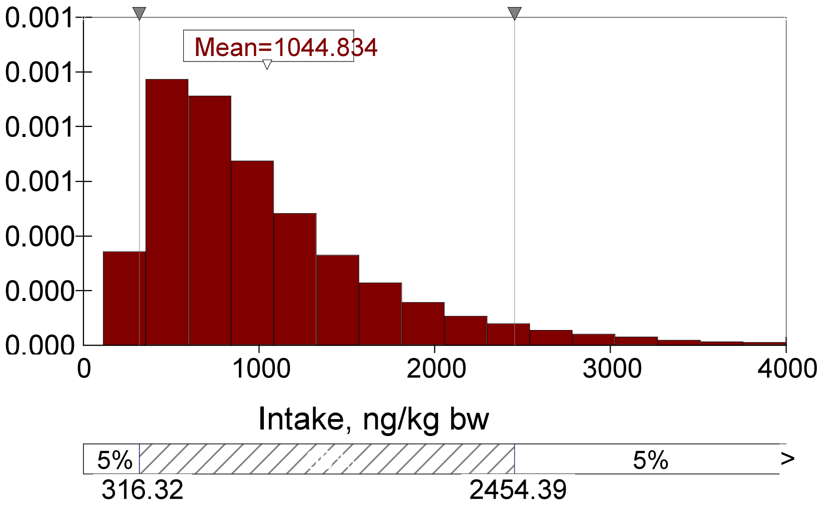

Figure A3.17. *Probability distribution of exposure via breast milk to BDE #47 of Dutch infants exclusively breast-fed during 6 months.*

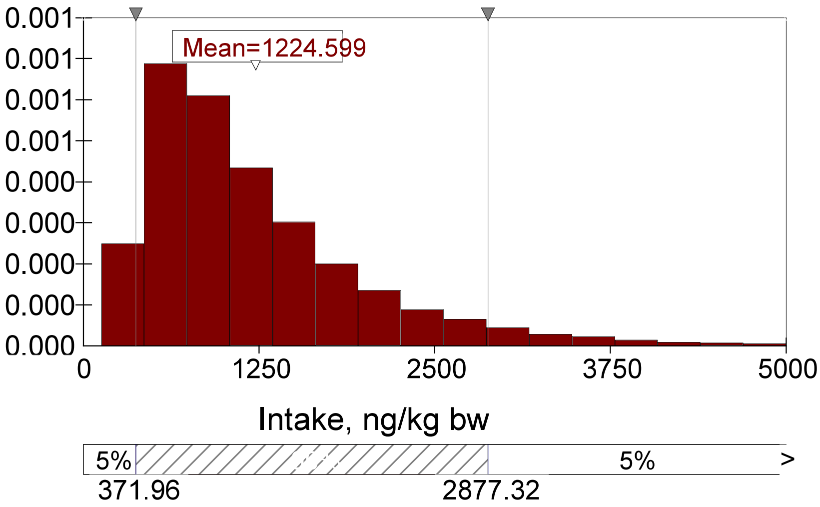

Figure A3.18. *Probability distribution of exposure via breast milk to BDE #47 of Dutch infants exclusively breast-fed during 7.5 months.*

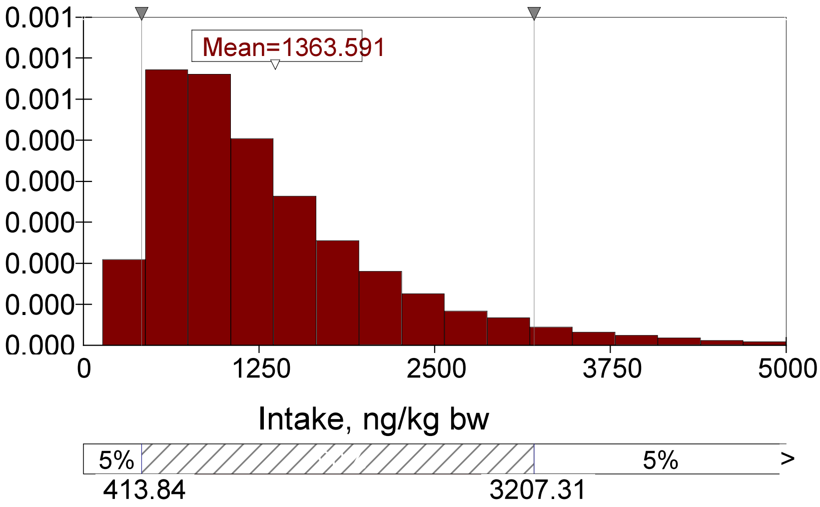

Figure A3.19. *Probability distribution of exposure via breast milk to BDE #47 of Dutch infants exclusively breast-fed during 9 months.*

Appendix 4 Mailing list

1 Prof. P. Peters, VWA
2 Ir. H. de Goeij, VWS
3 Dr. ir. G. Kleter, KvW
4 Dr. J.M.de Stoppelaar, VGB, VWS
5 Drs. B.W. Ooms, VWA
6 Dr. ir. W. de Wit, VWA
7 Dr. W.F. Passchier, Gezondheidsraad
8 Dr. G. Ellen, NIZO, Ede
9 Dr. P.O. Darnerud, National Food Administration, Uppsala
10 Dr. G. Becher, Norwegian Instiute of Public Health, Norway
11 Dr. R. Malisch, State Institute for Chemical and Veterinary Analysis of Food, Germany
12 Dr. J.S. LaKind, LaKind Associates, USA
13 Dr. S. Harrad, University of Birmingham, UK
14 Dr. L.S. Birnbaum, US EPA, USA
15-25 Werkgroep dioxinen
26 Depot Nederlandse Publikaties en Nederlandse Bibliografie
27 Directie RIVM
28 Prof. dr. ir. D. Kromhout
29 Dr. ir. M.N. Pieters
30 Dr. L.A. van Ginkel
31 Dr. E.A. Hogendoorn
32 Dr. F.X.R. van Leeuwen
33 Dr. A.G. Oomen
34 Dr. ir. A.J.A.M. Sips
35 Dr. C.H.M. Versantvoort
36 Prof. dr. J.G. Vos
37 Ir. H.J. van de Wiel
38-42 authors
43 SBC/afdeling Communicatie
44 Bureau Rapportenregistratie
45 Bibliotheek RIVM
46 Archief SIR
47-51 Bureau Rapportenbeheer