

Maisons-Alfort, 5 March 2010

**OPINION**  
**of the French Food Safety Agency**  
**on interpreting the health impact of PCB concentration levels in the French population**

THE DIRECTOR GENERAL

**1- Review of the request and questions asked**

A national study of PCB concentration levels was implemented by the French Food Safety Agency (AFSSA) in partnership with the French Institute for Public Health Surveillance (InVS) to: i) clarify the existence of high blood PCB levels in fishermen who are consumers of river fish, ii) contribute to the development of management measures, and iii) compare PCB concentration levels in France with those observed in other countries. The findings of this study are expected in early 2011.

AFSSA received a request from the Directorate General for Health, on 20 February 2008, for an opinion on interpreting the health impact of PCB concentration levels in the French population.

After analysing the data available in the literature, and data collected as part of the study of dioxin levels in populations living around MSWIs<sup>1</sup>, the GECU<sup>2</sup> on assessment of risks related to PCBs in food and feed and the Scientific panel on Chemical and physical residues and contaminants are issuing the following opinion.

**2. Reviews on PCBs (see previous requests)**

As indicated in AFSSA's Opinion of 23 October 2007<sup>3</sup>, the term PCB refers to polychlorinated biphenyls, which are chlorinated aromatic compounds constituting a family of 209 compounds or congeners<sup>4</sup>. In the past, these 209 congeners were added, in highly variable concentrations, to the composition of commercial mixtures<sup>5</sup> used for their insulating properties (electrical transformers) and their chemical and physical stability (cutting oils, inks, and paints). These uses were restricted to closed systems (transformers and capacitors) during the 1970s, and the production and use of PCBs was then banned in France in 1987. PCBs, chemically stable and relatively non-biodegradable, are classified as persistent organic pollutants (POP). They are lipophilic substances that become concentrated in food chains and are mainly found in animal fats.

In humans, contamination occurs mainly through food consumption and the PCBs then accumulate in the body, particularly in adipose tissue; they can be found at significant levels in maternal milk and blood lipids.

<sup>1</sup> *Etude d'imprégnation par les dioxines des populations vivant à proximité d'usines d'incinérations d'ordures ménagères* [Study of dioxin levels in populations living around municipal solid waste incinerators], InVS/AFSSA, November 2006.

<sup>2</sup> GECU: Emergency collective expert assessment group

<sup>3</sup> For more information, refer to the AFSSA Opinion of 23 October 2007 on the establishment of relevant maximum levels for non dioxin-like polychlorinated biphenyls (NDL-PCBs) in some foodstuffs

<sup>4</sup> For more information, consult: i) the AFSSA Opinion of 8 April 2003 on the possible existence of a significant correlation between levels of different PCB congeners and ii) the report cited in the Opinion entitled "*Données récentes sur l'évaluation des dangers liés à la présence de PCB dans l'alimentation.*" [Recent data on the assessment of hazards related to the presence of PCB in food], J.P. Cravedi and J.F. Narbonne, December 2002, available at [www.afssa.fr](http://www.afssa.fr)

<sup>5</sup> Commercial mixtures: products sold in the past, consisting of several PCB congeners that are subject to brand names or registered trademarks (for example, Aroclor registered by Monsanto (USA), Phenochlor and Pyralene by Prodelec (France). In the Aroclor line of compounds (for example, Aroclor 1254), the first two digits in the name indicate the mass number of carbon atoms present in the molecule (here 12) and the last two digits indicate the weight percentage of chlorine in the mixture (here 54%).

Chronic PCB toxicity (dioxin-like :‘DL-PCBs’ or non dioxin-like :‘NDL-PCBs’) is primarily correlated with cumulative tissue burden (see PCB levels in the body) and not directly with the amount consumed at a given time.

The toxicity of PCBs varies considerably according to species and different congeners within the same species, with the number and position of the chlorine atoms on the phenyl rings determining their toxicity. The persistence of PCBs in the environment and the body increases with the number of chlorine atoms. The higher the number of chlorine atoms of a congener (see *ortho*-substituted NDL-PCBs), the slower its elimination and the longer its persistence in the body (Brown 1994).

### Toxicological Reference Values and main toxic effects of PCBs

The main toxic effects of dioxin-like PCBs (DL-PCBs) and non dioxin-like PCBs (NDL-PCBs) observed in animals were broadly described in AFSSA’s November 2005<sup>6</sup> report and Opinions of 23 October 2007<sup>7</sup> and 28 March 2008<sup>8</sup>.

DL-PCBs have similar mechanisms of action to those of dioxins because of their ability to bind to the Ah receptor. A toxicological reference value (provisional tolerable monthly intake, PTMI) of 70 pg TEQ<sup>9</sup>/kg bw/month (i.e. **2.33 pg TEQ/kg bw/day**) was established in 2001 by JECFA [Joint FAO/WHO Expert Committee on Food Additives] for all dioxins/furans and dioxin-like PCBs (PCDD/Fs + DL-PCBs) based on the alteration of sexual maturation observed in young male rats exposed to the so-called Seveso dioxin (2,3,7,8-TCDD [tetrachlorodibenzo-p-dioxin])<sup>10</sup>.

Regarding NDL-PCBs, thyroid and hepatotoxic effects are the main critical effects reported in adult animals (weaned rats) exposed to individual congeners. The no observed adverse effect level (NOAEL [!]) observed in a 90-day study in rats ranged from 30 to 40 µg/kg bw/day depending on the nature of the congeners tested (PCB 28, 128 and 153).

Toxicological studies conducted in monkeys with mixtures of representative congeners in PCB profiles found in the environment and in human milk have shown, however, that brain development of the foetus may be altered at doses below those leading to toxicity in the adult animal. These data have therefore been accepted as being the most relevant for establishing the toxicological reference value (TRV) **of 20 ng/kg bw/day** which is applied to all 209 PCB congeners (see value adopted by the RIVM<sup>11</sup> (The Netherlands) in 2001).

Moreover, considering that the sum of the six PCB congeners most frequently found in food matrices (PCB-28, 52, 101, 138, 153 and 180) represents up to 50% of all congeners present (EFSA, 2005), a **TDI [tolerable daily intake] of 10 ng/kg bw/day** was selected by AFSSA for this group of congeners.

The assessment of dietary exposure of the French population to these six NDL-PCBs in connection with consumption of six categories of foods (seafood, eggs, vegetables, dairy products, meat and fish) showed levels exceeding this TDI of 10 ng/kg bw/day in children and adults who are high consumers (Annex 1).

<sup>6</sup> *Dioxines, furanes et PCB de type dioxine: Evaluation de l'exposition de la population française* [Dioxins, furans and dioxin-like PCBs: Assessment of exposure in the French population]

<sup>7</sup> *Avis de l'afssa du 23 octobre 2007 relatif à l'établissement de teneurs maximales pertinentes en polychlorobiphényles qui ne sont pas de type dioxine (PCB « non dioxin-like », PCB-NDL) dans divers aliments* [AFSSA Opinion of 23 October 2007 on the establishment of maximum relevant levels for non dioxin-like polychlorinated biphenyls (NDL-PCBs) in some foodstuffs]

<sup>8</sup> *Avis de l'afssa du 28 mars 2008 relatif à l'imprégnation corporelle en dioxines des forts consommateurs de produits animaux d'origine locale* [AFSSA Opinion of 28 March 2008 on body impregnation by dioxins in high consumers of animal products from local sources] as part of the INVS-AFSSA study of November 2006.

<sup>9</sup> TEQ: toxic equivalency, for a mixture of congeners, in order to account for their relative toxicity (by weighting their individual concentrations by a toxic equivalency factor or TEF).

<sup>10</sup> The toxic equivalency factors (TEF) considered in this opinion are themselves derived from the WHO in 1998 (TEF 98), with new TEF being proposed by the WHO in 2005.

<sup>11</sup> RIVM : Rijksinstituut voor Volksgezondheid en Milieu (National Institute of Public Health and the Environment) of the Netherlands) (2001), Baars AJ, Theelen RMC, Janssen PJ, Hesse JM, van Apeldoorn ME, Meijerink MC, Verdam L, Zeilmaker MJ. Re-evaluation of human toxicological maximum permissible risk levels. Report 711701025

### 3. Updating the toxic mechanisms of action of PCBs

The latest scientific data made public in May 2008 at the 5<sup>th</sup> PCB Workshop (<http://www.pcbworkshop.org>) indicate that:

- interference with thyroid homeostasis is the most critical endocrine effect of PCBs, in both humans and animals. It results from the interaction of PCBs and their metabolites (OH-PCBs) with the thyroxin transporting protein transthyretin (TTR) and to a lesser extent with thyroid hormone (TR) cell receptors. A reduction in total thyroxin (T4) circulating levels has been observed repeatedly in animals. Since *in utero* development is very sensitive to thyroid disturbances (Miller *et al.*, 2009), fluctuations in maternal circulating T4 levels could be associated with impaired cognitive development in children.  
Furthermore, recent experimental studies conducted with commercial mixtures of PCBs show thymimetic-like effects, particularly the increased expression of genes regulated by thyroid hormones.
- hearing loss has been observed in rodents exposed to PCBs *in utero* (Powers *et al.* 2006; Kenet *et al.* 2007). These effects have also been reported in humans (see the PCB RISK Project).  
However, additional studies on pure congeners are needed for a better understanding of the mechanisms of action of PCBs on the cognitive development of children (Royland J-E *et al.*, 2008).
- effects of DL-PCBs on the cardiovascular system have been observed in rodents after long-term exposure. These effects are specific to DL-PCBs and involve Ah receptor binding (Hennig *et al.*, 2002).
- PCBs may be involved in the development of atherosclerosis through the induction of oxidative stress and inflammatory process (Helyar *et al.* 2009, Goncharov *et al.* 2008).

### 4- Review of the literature on effects observed in humans

#### 4.1 Health impact of PCBs

##### 4.1.1 Review of INSPQ literature

The impact of PCBs on human health has been investigated in various studies conducted in the United States, Canada and Europe.

In 2007, the National Public Health Institute of Quebec conducted a critical review of epidemiological studies published since 1997 (INSPQ, 2007) to analyse the causal relationships between exposure to PCBs (assessed in terms of levels in the body, which are estimated in most of these studies, by measuring the PCBs in plasma lipids and in maternal milk) and the incidence of health problems in exposed subjects.

Dose-response relationships have been researched by correlating markers of exposure with markers of effects. Analysis of the available studies has shown:

- variability in the sources and history of contamination depending on the regions studied, which may be the source of variations in the profiles of PCB congeners and the contamination levels observed,
- significant differences in the number of congeners measured (from 3 to 40) and in the way the results are expressed (see PCB concentration per unit of volume of plasma or plasma lipids, noting that the methods for determining fat constitute an additional factor of variability) according to the studies,
- strong heterogeneity in the effects observed according to the biomarkers used and biological specimens studied,

- variability in the exposures and effects based on the populations studied (i.e., general population, high consumers of fish, individuals living in contaminated areas, etc.).

This review of the literature thus highlights great variability in the results observed from one study to another and/or in the same cohort, and in particular:

- inconsistencies regarding causal relationships between perinatal exposure to PCBs and the disruption of immune parameters in children,
- lack of a relationship between perinatal exposure to PCBs and the incidence of upper airway infections in children aged under five years,
- lack of a relationship between exposure to PCBs and female fertility,
- the existence of contradictory relationships between exposure to PCBs and male fertility (see changes in sperm parameters) making it impossible to establish a maximum biological level without effect on humans, to date,
- lack of any effect of PCBs on neurological function (manual stability and/or mnemonic functions) of subjects aged 50 to 90 years (consumers or non-consumers of fish) whose PCB concentration levels are lower than 1900 ng of total PCB/g of plasma lipids.

However, from this analysis it is apparent that the critical<sup>12</sup> health effects most often reported in humans are:

- effects on mental and motor development in children exposed *in utero*,
- effects on the endocrine system (particularly the thyroid).

#### 4.1.2 Results of the PCBRISK Project

In Europe, Eastern Slovakia is particularly contaminated with PCBs due to historical pollution related to the presence (particularly in the Michalovce District) of a chemical factory releasing large quantities of PCBs into nearby rivers for 25 years (1959-1984). The Slovak PCBRISK Project (<http://www.pcbrisk.sk>) is the most comprehensive European epidemiological study so far, in terms of range of exposure and PCB concentration levels, for establishing relationships between PCB levels in the body and the occurrence of health effects after chronic exposure to low doses in both adults (2047 individuals) and children aged 8-9 years (434 individuals) (Cerna M *et al.*, 2008; Park J.S. *et al.*, 2007 and 2008; Petrik *et al.*, 2006; Jursa S *et al.*, 2006; Pavuk M. *et al.*, 2004).

In this cohort, 15 PCB congeners were measured: PCB 28, 52, 101, 105, 114, 118, 123, 138, 153, 156, 157, 167, 170, 180, and 189. The results indicate:

- in adults, average concentration levels of approximately 2000 ng PCB / g of plasma lipids and levels of up to 3500 ng PCB <sub>(15 cong.)</sub> /g of plasma lipids in those most exposed (90<sup>th</sup> percentile). The maximum value observed was approximately 100,000 ng PCB <sub>(15 cong.)</sub> /g of plasma lipids,
- in children aged 8-9 years, average concentration levels of approximately 570 ng PCB <sub>(15 cong.)</sub> /g of plasma lipids, reaching 1200 ng PCB <sub>(15 cong.)</sub> /g in those most exposed (90<sup>th</sup> percentile). The maximum value observed was approximately 6500 ng PCB <sub>(15 cong.)</sub> /g of plasma lipids.

In the most heavily exposed adults, the observed effects consist of:

- changes in the parameters for functional exploration of the thyroid: thyroid volume, elevated anti-thyroperoxidase antibodies, change in level of thyroid hormones and thyrotropin (Langer *et al.* 2009),
- disturbances of glucose metabolism (Langer *et al.* 2007),

<sup>12</sup> Effects appearing at the lowest doses

In children (particularly vulnerable during the prenatal period and lactation) the effects observed were:

- impairment of mental and motor development (hyperactivity, sensorimotor abilities and memory, etc.),
- hearing problems (measured by different functional screening tests appropriate for children),
- defective dental enamel formation.

## 4.2 Reference values reported in humans

### 4.2.1 INSPQ

The critical PCB concentration level estimated by the INSPQ (**900 ng total PCB /g of maternal plasma lipids**) corresponds to the level of **prenatal** PCB body burden (see plasma concentration in women during pregnancy) below which the probability of effects on the mental and motor development on the child has been estimated as negligible.

It should be noted that other health effects and metabolic disturbances reported by the authors (effects on fertility, immune effects, neurological effects in adults, etc.) have been observed for levels in the body always higher than 1000 ng PCB total /g of plasma lipids.

### 4.2.2 PCBRISK

Based on results from the PCBRISK study, different BMDLs (Benchmark Dose Lower confidence Limit, see definition in Annex 2) were proposed by Trnovec T., at the 5<sup>th</sup> PCB Workshop (Iowa City, 2008):

- a **BMDL of 673 ng PCB<sub>(15 cong.)</sub>/g of plasma lipids** estimated from the observation of reduced hearing ability in children, exposed during the prenatal phase and during lactation (BMD in the mother of 1013 ng PCB/ g of plasma lipids;  $P_o=0.05$  and BMR [Benchmark Response]=0.05)<sup>13</sup>.

- a **BMDL of 10,000 ng PCB<sub>(15 cong.)</sub> / g of plasma lipids** (BMD of 14,000 ng PCB<sub>(15 cong.)</sub> / g of plasma lipids;  $P_o=0.05$  and BMR =0.05) estimated from thyroid effects observed in individuals with the highest exposure (see changes in thyroid volume and change in the level of free thyroxin or FT4).

### 4.2.3 EFSA

Two other BMDLs of 630-710 ng total PCB /g of lipids and 1200-3000 ng total PCB /g of lipids respectively, established on the basis of cognitive and immunotoxic effects observed in children exposed to PCBs *in utero*, have also been reported in the literature (Jacobson *et al.* 2002). This led EFSA, in its Opinion of 8 November 2005, to suggest a BMDL of approximately **1000 ng total PCB / g of plasma lipids** ( $P_o=0.05$  and BMR=0.05) for the entire population.

<sup>13</sup> The potential changes in neurological development in children were assessed using several criteria to measure hearing ability that were considered to be more objectifiable and less dependent on socioeconomic factors than the sole measurement of intelligence quotient (IQ).

## 5- Choosing a critical concentration level

### 5.1 Discussion

The effects considered to be critical in humans, both through a review of the epidemiological studies conducted by the National Public Health Institute of Quebec (INSPQ, 2007), as well as the European PCB RISK Project and EFSA Opinion of 8 November 2005, are comparable.

**Regarding, pregnant women or women of childbearing age, as well as lactating women,** the three reports converge to accept a critical concentration level of **700 to 1000 ng total PCB /g of maternal plasma lipids**<sup>14</sup>. This value corresponds to the level of prenatal PCB body burden (see plasma concentration in pregnant women) above which the occurrence of significant effects on the mental and motor development of children exposed *in utero* cannot be ruled out.

**Regarding the other population categories,** various relationships have been described between exposure to PCBs (in terms of levels in the body) and changes in the physiological parameters related to reproductive, endocrine and immune function. However, the **heterogeneity of the results across the different studies failed to clearly establish a causal relationship.**

In the PCB RISK cohort, various changes in the parameters of thyroid function have been observed in particular (Langer *et al.* 2003 and 2009), such as an increase in thyroid volume associated with an increase in free thyroxin (FT4), particularly in men with the highest exposure.

On the basis of these critical effects, Trnovec *et al.* have proposed a BMDL of approximately 10,000 ng PCB (15 cong.) /g of plasma lipids ( $P_0=0.05$  and  $BMR=0.05$ ) which corresponds to the concentration level associated with a thyroid volume of 16 mL and a free thyroxin (FT4) blood level of 21 pmol/L (New Knowledge Gained From Old Pollutants 5<sup>th</sup> PCB Workshop, 18-22 May 2008). This BMDL is consistent with i) concentration levels involving a significant difference in thyroid volume in populations in the Michalovce District exposed to PCBs compared with control individuals and ii) no-effect levels on the increase of thyroid volume described in the INSPQ report (Langer *et al.* 2003).

Furthermore, the detailed analysis of data on the PCB RISK adult cohort shows a significant correlation between PCB concentration levels and blood levels of thyroid hormones (FT4 and TT3) and of thyrotropin (TSH) ( $p>0.001$ ), particularly a significant increase in FT4 and TT3 levels for average PCB concentration levels of approximately 5800 ng/g of lipids (minimum value 2349 ng/g of lipids). With regard to TSH, an increase was also noted in the percentage of individuals with values lower than 0.5 mU/L (a sign of hyperthyroidism) from 2349 ng PCB/g of lipids.

In light of these observations, the critical concentration threshold for adults and children over three years of age could thus be estimated at 2300 ng/g of lipids. Nevertheless, the clinical significance of these biological indicators is difficult to establish since the measured values remain within the confidence interval of the physiological values and many confounding factors (circadian rhythm, seasons, and intra- and inter-individual differences) can explain them.

### 5.2 Conclusions

According to current knowledge, the effects of PCBs on the mental and motor development of the child exposed *in utero* represent the best documented critical effect for establishing a critical concentration level in humans. AFSSA thus proposes a value of **700 ng total PCB /g of plasma lipids** as the **critical concentration threshold for pregnant women, women of childbearing age, lactating women, and children under three years of age.**

<sup>14</sup> In its Opinion of 8 November 2005, EFSA accepted a BMDL of 1000 ng/g of plasma lipids based on the neuro-developmental and immunotoxic effects observed in humans after perinatal exposure to PCBs.

Due to the persistence of PCBs in the body and thus the gradual increase in concentration levels with age, this threshold value also applies to young and adolescent girls.

In boys over three years of age, adult men, and women past childbearing age, the data are fragmentary and even contradictory, making clinical interpretation difficult.

Given that,

- variations in thyroid hormones reported in the PCB RISK study occur in individuals with PCB levels in the body higher than 2300 ng total PCB /g of plasma lipids, and that
- the results reported by Schantz *et al.* (1999), in subjects aged 50 to 90 years (consumers or non-consumers of fish) indicate that below 1890 ng total PCB /g of plasma lipids, the effect of PCBs on neurological function (manual stability and/or mnemonic functions) can be excluded,

**AFSSA suggests, for information purposes, the value of 1800 ng total PCB /g of plasma lipids as the critical concentration level for the rest of the population** (boys over three years of age, adult men, and women over 45 years).

	Women < 45 years	Women > 45 years	Men < 45 years	Men > 45 years
<b>Critical concentration levels in humans</b> (ng total PCB / g of plasma lipids)	<b>700</b>	<i>1800*</i>	<i>1800*</i>	<i>1800*</i>

*\*Value given for information purposes regarding results available in adults*

**These critical values make it possible to position the concentration levels observed in populations compared to health criteria. They aim to provide benchmarks to guide public policy for the purpose of protecting the entire population from health effects linked to exposure to PCBs. They do not comprise screening threshold values at the individual level.**

## 6- Interpretation of PCB concentration data for the French population

### 6.1 PCB concentration levels measured in humans between 1980 and 2005.

The first French data regarding PCB concentration levels in the general population date from the **late 1980s**.

The study conducted at that time, at the request of the Ministry of Health, on 600 individuals had shown an average concentration level in adults (aged from 18 to 60 years) of 4.92 µg PCB/L of blood or around **1800 ng total PCB /g of lipids**<sup>15</sup> (Dewailly *et al.* 1988). The individuals with the highest concentrations (97.5 percentile) showed concentration levels of approximately 3600 ng total PCB /g of lipids with a maximum of 7200 ng total PCB/g of lipids.

**In 2005**, a national study was undertaken by the InVS and AFSSA<sup>16</sup> with the objective of:

- i) comparing levels of exposure to dioxins and PCBs in populations living around municipal solid waste incinerators (MSWI) with those of the general population, and
- ii) clearly identifying the determinants of this exposure (dietary or other).

This study has contributed new information about dioxin and PCB levels in the (mainland) French adult population.

It does not show any statistically significant difference between PCB concentrations in people exposed to an incinerator plume and the general population.

The entire population group studied (exposed and unexposed individuals) consisted of 1030 men and women aged from 30 to 65 years (average age = 52 years).

Lacking more recent data on PCB concentrations and given that no difference was found between individuals exposed and unexposed to the incinerator plume, this population group was considered, at that stage, as representative of the French population. Other research programmes, including in particular the national human biomonitoring programme in France<sup>17</sup> being developed by the InVS, should help to consolidate and refine these initial observations.

A total of four PCB congeners were measured (PCB 118, 138, 153 and 180) in this study. The PCB concentration levels were expressed as ng PCB /g of plasma lipids.

In order to compare the results obtained to critical concentration levels defined in the literature based on total PCBs, a multiplier of 1.7<sup>18</sup> was applied to the results obtained for the sum (PCB 138+153+180) considering, on the one hand, that these three congeners are the most abundant and the most representative of overall exposure and formulating, on the other hand, the hypothesis of a similarity of PCB contamination profiles between the PCB-RISK study population group and the InVS/AFSSA study population group.

The results obtained after applying the weighting factor are presented in Table 1.

<sup>15</sup> The PCBs representing most exposure were PCBs 20, 28, 52, 101, 138, 153 and 180.

<sup>16</sup> InVS/AFSSA: *Etude d'imprégnation par les dioxines des populations vivant à proximité d'usines d'incinération d'ordures ménagères* [Study of dioxin levels in populations living around municipal solid waste incinerators]. 2006. [http://www.invs.sante.fr/publications/2006/etude\\_impregnation\\_dioxine/index.html](http://www.invs.sante.fr/publications/2006/etude_impregnation_dioxine/index.html)

<sup>17</sup> <http://www.invs.sante.fr/beh/2009/hs/160609/index.htm>

<sup>18</sup> Correlation factor defined and used for interpreting data from the Slovakia cohort (see PCB-RISK Project study report)



**Table 1:** Total PCB levels in plasma lipids (ng/g of fat) estimated after applying a multiplier of 1.7 to the sum of PCBs 138, 153 and 180, taken from French data from the MSWI study (February – June 2005)

Total PCB (ng/g plasma lipid)													
MSWI study population	n	Average	SD	min	p25	p50	p75	p90	p95	p97.5	p99	p99.5	max
Total	1029	630	317	7	424	581	743	1017	1162	1370	1713	2276	4036
Adults under 45 years	228	442	235	142	303	377	547	667	778	930	1265	1265	2957
Adults over 45 years	801	686	317	7	485	624	810	1050	1213	1455	1753	2335	4036
Women under 45 years	110	481	204	162	331	461	597	699	814	996	1265	1265	1457
Women over 45 years	466	650	281	7	485	601	730	952	1193	1421	1678	1857	2677
Men under 45 years	118	407	255	142	293	351	472	623	745	926	1161	2957	2957
Men over 45 years	335	736	354	98	509	696	911	1092	1303	1501	2104	2396	4036

Average PCB concentration levels measured for this study ranged between **400 and 740 ng PCB<sub>(total)</sub> /g of plasma lipids**.

Without jeopardising the development of methods for analysing PCBs, these results suggest a reduction in PCB concentration levels in the French population since the 1980s (Dewailly *et al.* 1988).

These results are consistent with observations reported in Europe and internationally (Brucker-Davis F. *et al.* 2008, Annex 3), and highlight:

- a gradual reduction in PCB concentration levels over time,
- concentration levels in France that are comparable to those that can be observed in the general population in other European countries for equivalent periods,
- higher concentration levels in regions of Europe historically contaminated by PCBs (Slovakia, the Czech Republic),
- PCB concentration levels that are higher overall in Europe than in North America.

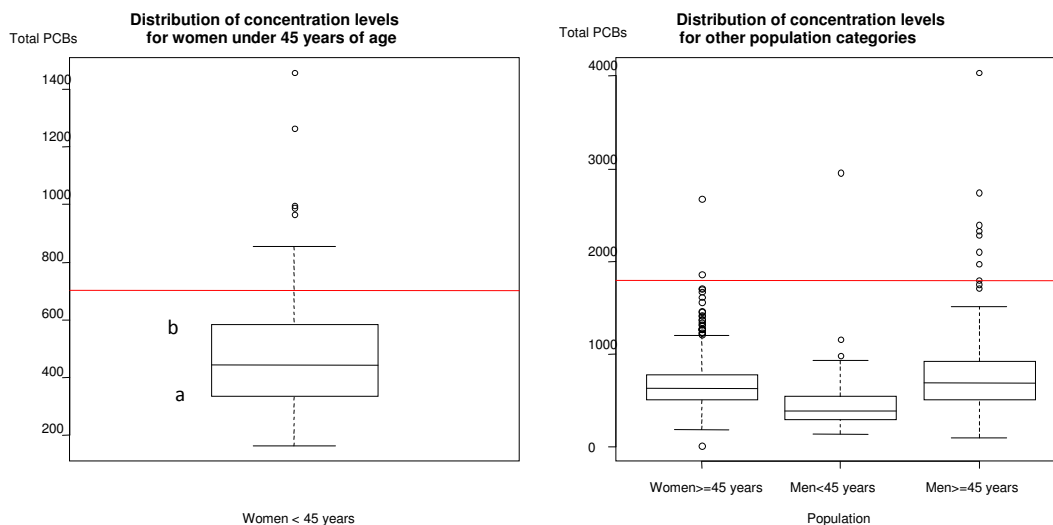
Furthermore, these results have confirmed that sociodemographic factors (age, build, gender, weight change, and smoking), as well as food consumption, are key determinants of PCB levels.

## 6.2 Comparison of French concentration data with critical concentration levels

If the concentration levels measured in the MSWI study are compared with the critical concentration levels adopted for different population categories (Annex 4), it appears that:

- approximately 90% of women under 45 years of age (i.e. women of childbearing age) showed PCB concentration levels below the critical threshold of 700 ng total PCB/g of plasma lipids (see Figure 1 and Annex 4).
- more than 98% of the rest of the population studied showed total PCB levels below the concentration level of 1800 ng total PCB /g of plasma lipids, with the highest concentration levels being observed in men over 45 years of age (Annex 4).

**Figure 1: Distribution of total PCB concentration levels (ng /g of plasma lipids) in adults from the MSWI study.**



*Caption: These box-plots represent total PCB concentration levels, with a thick black solid line indicating the median, "a" (lower boundary of the box) indicating the value at the 25<sup>th</sup> percentile, and "b" (upper boundary of the box), indicating the value at the 75<sup>th</sup> percentile. The points beyond represent the maximum values.*

## 7- General conclusion

The current body of knowledge acquired both in humans and animals (Annex 5) shows that the neurological development of foetuses and young children is the most critical effect of exposure to PCBs.

Based on the analysis of available epidemiological data, a critical concentration value of approximately 700 ng total PCB /g of plasma lipids could be estimated for women who are pregnant or of childbearing potential (women and girls under 45 years), lactating women and children under three years of age. This level corresponds to the level of prenatal PCB body burden below which the probability of adverse effects for the foetus or young child has been estimated as negligible.

In adults (men and women past the age of procreation), certain health effects have been associated with PCB concentrations higher than 1800 ng total PCB /g of plasma lipids, but no causal relationship with pre- or postnatal exposure to PCBs has been established.

In France, analysis of the available data and, in particular, the results of the InVS/AFSSA study on MSWIs indicates that around 90% of women under 45 years would exhibit concentration levels below the critical concentration level of 700 ng total PCB /g of plasma lipids, and that the highest concentration levels are observed in men over 45 years, most likely due to the peak exposure to PCBs observed in the 1970s and the bio-accumulative nature of these contaminants.

These concentration levels are in decline compared to those found in the general population during the 1980s<sup>19</sup> and are of the same magnitude as those reported today in most of the populations of the European Union (Annex 3).

Nevertheless, they show that special attention should be given to monitoring the exposure of women who are pregnant (or likely to become pregnant) and lactating due to the particular vulnerability of the developing central nervous system to the effects of PCBs. For this category of the population, it is particularly recommended to improve identification of the food and non-

<sup>19</sup> These factors are to be considered without jeopardising the development of methods for analysing PCBs

food determinants likely to lead to excessively high PCB concentrations, in order to implement specific management measures as needed.

Fishery products from the sea, and fish in particular, are considered to be the main vectors of dietary PCB intake. By early 2011, the study of PCB levels implemented by AFSSA, in partnership with the InVS, in regular consumers of river fish caught in areas contaminated by PCBs should provide more comprehensive information on concentration levels in high consumers of river products, shedding additional light on dietary factors that could lead to excessively high PCB concentrations.

More generally, the French national human biomonitoring programme<sup>20</sup> that is being developed by the InVS will provide, in the coming years, new perspectives on concentration levels of different environmental contaminants, including PCBs.

The Director General of the  
French Food Safety Agency

**Marc MORTUREUX**

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<sup>20</sup> <http://www.invs.sante.fr/beh/2009/hs/160609/index.htm>

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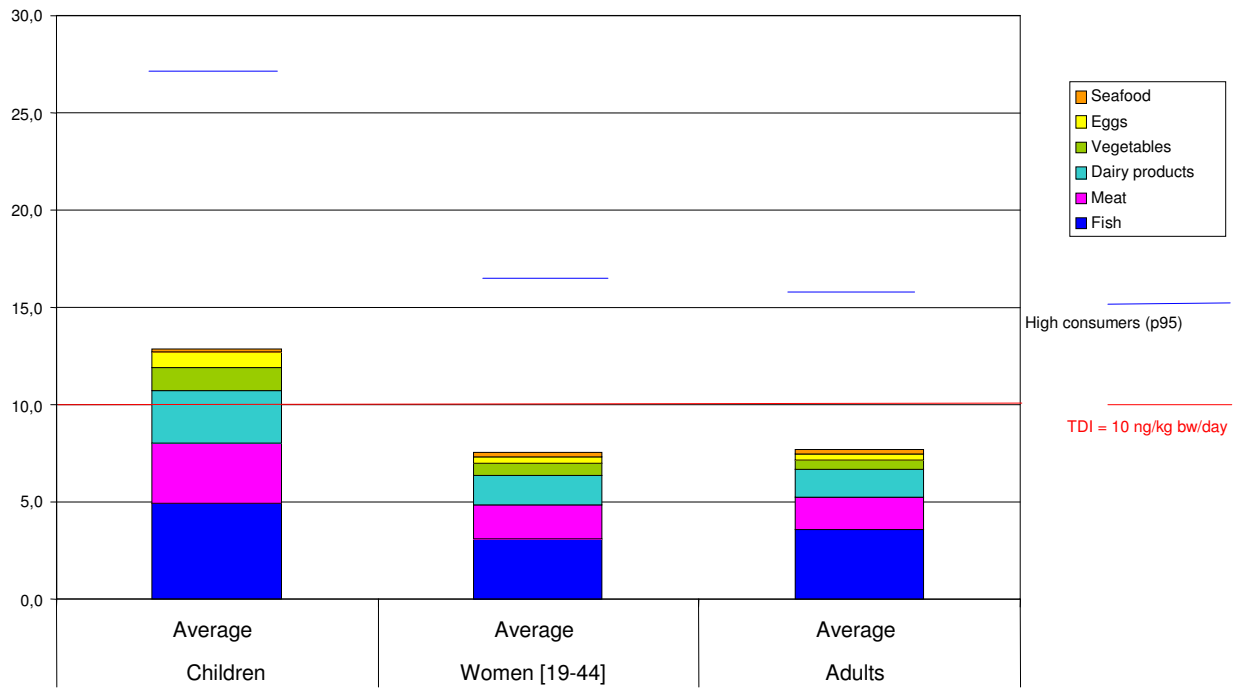
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**ANNEX 1**  
**Assessment of dietary exposure to the six NDL-PCBs (ng/kg bw/day) by comparison with the TDI of 10 ng/kg bw/day**



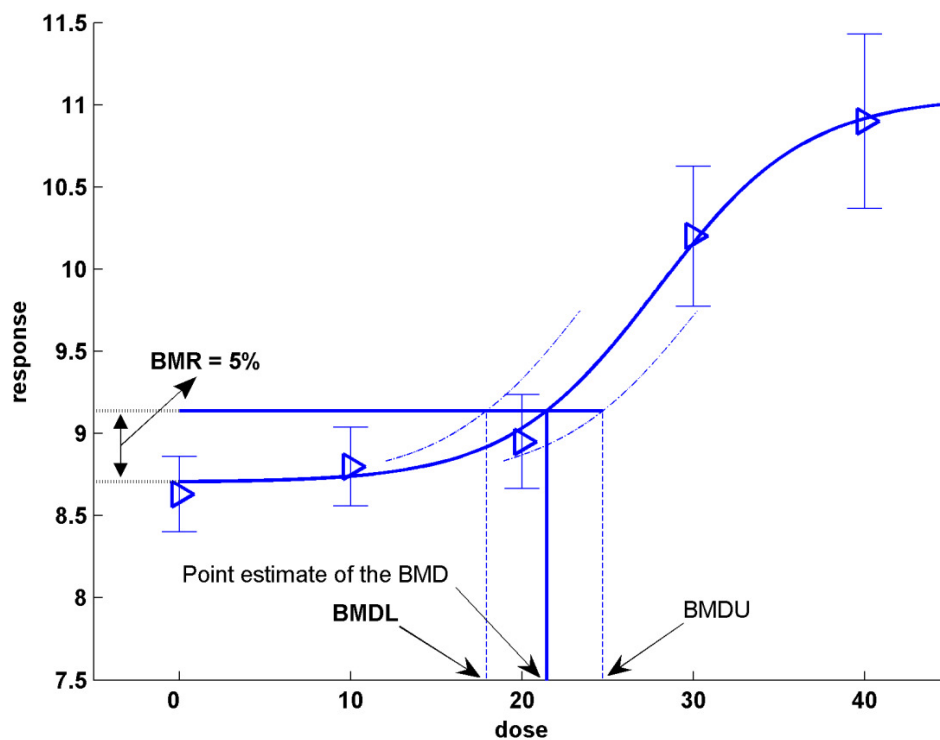
## ANNEX 2 The Benchmark Dose Approach

Conventional risk assessment is based on the comparison of an estimated dietary exposure value in humans using a toxicological reference value (ADI or Acceptable Daily Intake) determined from an experimental NOAEL<sup>21</sup> established in animals.

Recent years have witnessed the development of the benchmark dose (BMD) method of calculation, which represents an alternative quantitative approach used especially for analysing dose-response data from various experimental animal studies or observational epidemiological studies (see Figure below and EFSA Opinion of 26 May 2009).

The BMD corresponds to the dose inducing an excess risk level (Benchmark Response or BMR) set at 5 or 10% of the critical effect selected.

The Benchmark Dose Lower confidence Limit (BMDL) is the lower limit of the confidence interval at 95% of the BMD.



<sup>21</sup> NOAEL: No Observed Adverse Effect Level

## ANNEX 3

## Summaries of PCB concentration levels measured in the blood of different populations in Europe and internationally (ng PCB /g of lipids)

Table 1 shows the PCB concentration levels collected in the literature for the countries of North America and Europe (general population).

Only the plasma levels of PCB 153 were used in order to facilitate comparison between study results.

Table 2 shows the PCB concentration levels measured as part of various surveys conducted by the WWF in the European population.

Figure 1 shows the average NDL-PCB and (dioxin + DL-PCB) concentration levels reported in fish eaters in the American Great Lakes.

**Table 1: PCB 153 concentration level reported in the literature for different population categories in Europe and North America**

Country	Year collected	Number	Population	Age	PCB 153 (median ng/g of fat)	References
<b>North America</b>						
United States – population of Lake Michigan fishermen (control population)	1973-1974	27	Men – controls	42.9	285.7	*estimated values from original levels in ppb or ng/g of blood by Aroclor 1016, 1254 and 1260 equivalent with the following scenarios: 1) lipid level of 7g/L of blood, 2) PCB 153 represents around 20% of total PCBs <b>He et al. 2001</b>
		52	Women – controls	57.1	142.9*	
United States	2005	1074	General population – men	>20	31.5	<b>CDC 2006 – National Health and Nutrition Examination Survey (NHANES)</b>
		1232	General population - women	>20	29.1	
<b>Europe</b>						
France	1986	569	General population	18-60	281.1*	*geometric average estimated from original levels of 7 PCB congeners in µg/L of blood with the following scenarios: 1) lipid level of 7g/L of blood, 2) the 7 PCBs and PCB 153 represent respectively 50% and 20% of total PCBs – <b>Dewally et al. 1998</b>
Spain	1992-1996	953	General population (5 regions)	35-64	182.6	<b>Agudo et al. 2009</b>
Germany	1998	2818	General population	18-69	102.9	<b>German Environmental Survey (GerES III)</b>
Belgium	1999	200	Women in general population – Flanders Environmental and Health Study (FLEHS)	50-65	158 (47 pools)	<b>Koppen et al. 2002</b>
Slovakia	2001	1009	Population in contaminated area (Michalovce)	47	578	<b>Petrik et al. 2006</b>
		1038	Population in control area (Svidnik)		232	
Sweden	2002-2004	189	Fishermen	48	190	<b>Jonsson et al. 2005</b>
		544	Spouses of fishermen	50	84	
United Kingdom	2003	154	General population (13 regions)	40.5	41	<b>Thomas et al. 2006</b>
France	2004	1030	Populations living around MSWIs	52	123.4	<b>Fréry et al. 2009</b>
Czech	2006	202	General population	33	438	<b>Cerna et al. 2008</b>



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**Table 2: Total PCB concentration levels reported by the WWF in different population categories in Europe**

Studies	M / W / age	N=	Max	Min	Mean/Median*
Bad Blood - Ministers (WWF) EU 2004	10 M / 4 W	14	911.8	78.8	337 / 199.7*
Chemical Check Up (WWF) EU 2004	24 M / 23 W  (35 to 66 years; median age 52 years)	47	1373.3	26.7	471.66*
Generations X (WWF) EU 2005* /Next generation (WWF) UK 2004	<b>Total</b>		<b>1176</b>	<b>13</b>	<b>274.5*</b>
	<b>Grandmother</b> (58 to 92 years; median age = 70 years)		1176	125	398*
	<b>Mother</b> (38 to 59 years; median age = 45 years)		417.7	47.5	300.6*
	<b>Children</b> (12 to 28 years; median age = 16 years)		129.5	13	75.83*

*The WWF Generations X Survey screened for the presence of 107 different chemical products including PCBs in European citizens aged from 12 to 92 years spanning three generations (grandmothers, mothers, and children). This study was conducted in Germany, Belgium (2 families), Denmark, Finland, France, Greece, Hungary, Italy, Latvia, Luxembourg, Poland, and Sweden.*

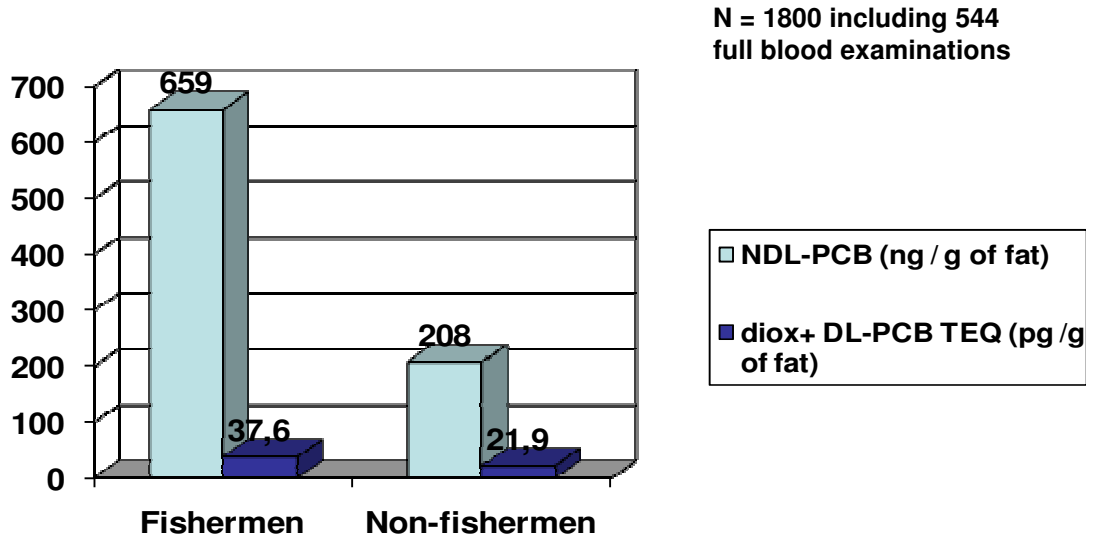
*The survey was carried out with the support of the EEN (EPHA Environment Network) and Eurocoop (European Community of Consumer Cooperatives).*

*The WWF Chemical Check Up survey screened for the presence of 101 different chemical products including PCBs in 47 volunteers from 17 European countries, including 39 members of the European Parliament.*

*Although no scientific conclusion could be drawn because of the low number of individuals analysed, the results have made it possible to indicate that the levels of contamination varied significantly by the volunteer's country of origin and that the PCBs accumulated with age.*

*The WWF 'Bad Blood' survey conducted an exploratory investigation into the presence of 103 different chemical products including PCBs in 14 Ministers from 13 European countries.*

Figure 1: Average NDL- PCB and (dioxin + DL-PCB) concentration levels in fish eaters from the American Great Lakes (Michigan, Erie, and Huron (University of Chicago and the Great Lakes Consortium) - (Turyk M *et al*, 2006)



## ANNEX 4

**Comparison of PCB concentration levels observed in the MSWI study compared with the critical concentration levels of 700 and 1800 ng total PCB /g of plasma lipids**

**Percentage of the population of the French MSWI study showing PCB concentration levels higher than critical concentration values:**

	% > CCL*	CI
Women <45 years	10.9	[0-28.5]
Women >=45 years	0.4	[0-9.5]
Men <45 years	0.8	[0-18.8]
Men >=45 years	2.4	[0-13.0]

*\*CCL: PCB Critical Concentration Level: 700 ng/g of plasma lipids for women under 45 years and indicative value of 1800 ng/g for others.*

**ANNEX 5****Comparison of no-effect levels in animals and estimated critical concentration thresholds in humans**

The critical effects of PCBs identified in animals are respectively neurotoxic effects (effects observed in young monkeys exposed *in utero*) as well as thyroid, liver and immunotoxic effects (effects observed in weaned rats).

The estimated no-effect levels are respectively 2.5 µg/kg bw/day for neurological effects in foetuses and from 30 to 40 µg/kg bw/day for other effects.

The appearance of effects in adult animals is thus observed for levels of exposure to PCBs more than ten times higher than those inducing an effect in young monkeys exposed *in utero*.

The critical effects reported in humans are of a similar nature to those observed in animals: i) effects on the mental and motor development of children exposed *in utero* and ii) thyroid effects.

As for animals, the data available for humans show that the central nervous system of the foetus exhibits increased sensitivity to the effects of PCBs because the estimated critical concentration level in the mother is 700 ng total PCB/g of plasma lipids whereas the critical concentration level used for the rest of the population is close to 1800 ng total PCB /g of plasma lipids.

The data on average exposure to the 6 NDL-PCBs indicates the probability of exceeding 20% of the ADI of 10 ng/kg bw/day (established on the basis of experimental data in animals) for women of childbearing age (<45 years). The concentration data measured in the MSWI study confirm these predictions since around 10% of them exceed the critical concentration level of 700 ng total PCB /g of maternal plasma lipids established on the basis of available epidemiological data.