NON DIOXIN-LIKE PCBs (NDL-PCBs): OVERVIEW OF THE FRENCH FOOD RISK ASSESSMENT

Arnich Nathalie[1], Tard Alexandra[1], Jean-Charles Leblanc[1], Bruno Le Bizec[2], Jean-François Narbonne[3], Remi Maximilien[4]

[1]AFSSA, Maisons-Alfort; [2]LABERCA, Nantes; [3]Université Bordeaux I; [4]CEA, Fontenay-aux-Rose - France

Introduction

The term PCB refers to a family of polychlorinated biphenyl compounds including 209 congeners which were found in variable amounts among commercial mixtures used for insulation (electrical transformers) or chemical and physical properties (cutting oils, inks, and paints). PCBs are chemically stable, slowly biodegradable and lipophilic substances which are to be considered as persistent organic pollutants (POPs) concentrating in food chains and therefore found predominantly in animal fat. In France, production and uses of PCB were restricted during the 1970s to closed systems such as transformers and capacitors and were banned in 1987. European Regulation (EC) No 1881/2006 establishes maximum levels for the sum of dioxins and DL-PCBs in some foodstuffs. Discussions are still in progress within Europe for regulating NDL-PCBs in the same foodstuffs, through the sum of 6 congeners. In this paper we report the dietary exposure to NDL-PCBs of the French population and thereafter analyse the relevance of maximum NDL-PCBs levels in some foodstuffs, taking into account the maximum levels proposed in the European draft regulation (2006) and alternative hypothesis on maximum levels suitable for NDL-PCBs tolerable daily intake.

Methodology

The exposure model

A deterministic approach was used, as a more appropriate and more efficient method when disaggregated food level is considered. Dietary exposure was estimated by combining the individual food consumption data for each food item with the mean contamination level of each food item and divided by the actual body weight of the consumer. Consumption data were obtained from the French ''INCA'' survey[1] (individual and national survey of dietary intake in France) carried out from August 1998 to June 1999, to incorporate seasonal effects. Consumption data were recorded during one week. The final sample included 1474 adult (≥ 15 years) and 1018 children (3–14 years). Food contamination data concerning PCB-28, 52, 101, 138, 153 and 180 were assayed in 1665 samples of foodstuffs available on the French market and were generated by accredited laboratories from official national surveys performed between 2002 to 2006. Contamination data from other sources were also included for cow's milk, plant products, foodstuffs not analysed in monitoring plans (some types of shellfish) and for processed foods such as tinned fish (tuna, mackerel, sardine, anchovy, crab)[2,3].

Impact of maximum NDL-PCBs levels in foodstuffs contributing to exposure

Maximum levels (MLs) for the sum of 6 NDL-PCBs in various foodstuffs have been tested in different risk management scenarios going from proposed European Commission (EC) regulation (last draft update in 2006) actually under consideration to levels proposed by AFSSA scientific panel on Contaminants. ML proposals from EC are based on the ALARA ("as low as reasonably achievable") approach from contamination data issued by the European Member States (Table I), aiming to discard highly contaminated products from the market and are not based on toxicology consideration. ML proposals from AFSSA namely, 50, 25 and 10 ng/g of fresh weight or fat, similar for all products targeted, are based on toxicology consideration in order to adequately protect all consumers and particularly sensitive groups.

Results and discussion

Tolerable daily intake

Based on the studies of Tryphonas *et al.*[4-6] and Arnold *et al.*[7, 8], a daily reference dose of 20 ng/kg b.w./d was proposed for the commercial mixture Aroclor 1254 by the US-EPA in 1996 and for all 209 PCB congeners by the ATSDR in 2000, considering the immunological effects observed in monkeys. This assessment was validated by an international group of experts during the Meeting of the CICAD Final Review Board held in Ottawa in

2001 (Canada, 29 october-1 November 2001) and adopted by the IPCS in 2003. Human data corroborate this reference dose as shown by the study of Tilson *et al*.[9] analysing the relationship between the concentration of PCBs in the mother's milk and the neurological development of the child, following contamination events in Asia[10]. A non-effect dose of 0.093 µg/kg b.w./d was identified and the daily reference dose would be 20 ng/kg b.w./d after applying a safety factor of 6 for allowing uncertainties and intra-species variation. Considering the whole spectrum of data and the convergence of different types of toxicological studies towards the same reference value[4-8, 9, 11-14], a reference dose of 20 ng/kg b.w./d for all 209 PCB congeners was proposed by WHO at the "2nd PCB workshop" in Brno (Czech Republic, May 2002). This reference dose, expressed as a tolerable daily intake (TDI) was adopted by the RIVM[15, 16] (Netherlands) in 2001 and by AFSSA (France) in 2003 and 2007. Agreeing with IPCS which concludes that immunological effects observed at low doses should be considered as variations of biological parameters of unclear significance for human health, AFSSA considers that the TDI of 20 ng/kg b.w./d for all PCB should be derived from neurological effects observed in monkeys[13, 14]. In addition, since the sum of 6 PCB congeners most commonly found in food matrices (PCB-28, 52, 101, 138, 153, 180) accounts for approximately 50% (49 to 57%) of total NDL-PCBs (sum of 19 NDL-PCB congeners[17]), a TDI of 10 ng/kg b.w./d can be adopted for this group of 6 congeners (RIVM[15] initiative to estimate the risk associated with dietary exposure to NDL-PCBs).

Dietary exposure to NDL-PCBs

For the sum of 6 congeners of NDL-PCBs (PCB 28, 52, 101, 138, 153, 180), the mean intake of children is 12.9 ng/kg b.w./d (p95: 27.3 ng/kg b.w./d), exceeding the TDI of 10 ng/kg b.w./d. For women of childbearing age and adults, the average intake is 7.6 and 7.7 ng/kg b.w./d respectively, not exceeding the TDI; however, values at p95 are close to 16 ng/kg b.w./d for both groups.

In Europe, four studies of dietary exposure to NDL-PCBs are available[17]. The averages/medians estimated are from 5.6 ng/kg b.w./d (for Netherlands, sum of 7 congeners) to 15.3 ng/kg b.w./d (for Germany, sum of 3 congeners). In 2005, EFSA proposed an estimation of European dietary exposure for NDL-PCBs "averaging" 15 ng/kg b.w./d, increasing to 20 ng/kg b.w./d for high consumers of meat and 35 ng/kg b.w./d for high consumers of fishery products. The French estimation of average exposure to the 6 NDL-PCBs of 7.7 ng/kg b.w./d in adults falls within these available European estimations.

Impact of maximum NDL-PCBs levels in foodstuffs contributing to exposure

Under the current situation, in which no maximum NDL-PCB limits are established, this study shows that the French exposure to 6 NDL-PCBs exceeds the TDI (10 ng/kg b.w./d) for 58.4% of children and 20% of women of childbearing age and adults. Exposure scenario using European draft MLs for NDL-PCBs would have a very limited impact on the dietary exposure of the French population compared with the current situation (Table II). Simulation of exposures using MLs of 50, 25 or 10 ng/g in targeted foodstuffs shows that a ML of 25 ng/g would significantly reduce exposure for children and adults. But only a ML of 10 ng/g for all foodstuffs would have a significant impact on the overall exposure of all population subgroups. Such a scenario would reduce average exposure of children by around 65%, compared with the current situation without ML. It is noteworthy that a ML of 10 ng/g in foodstuff does not guarantee that the TDI is not exceeded for almost 30% of children, 4% of women of childbearing age and adults. However, such a ML would lead to the rejection of 21.4% of the targeted products from the market compared with 1.3% according to the European draft regulation. The food groups that would be the most targeted by this ML are fish and meat products with a rejection percentage of around 33 and 37% respectively, compared with 2% for fish only with the European draft regulation.

Assessment of the health risks associated with exceeding the TDI

For adults and children over 3 years of age, the critical endpoint to be considered from experimental studies is hepatotoxicity induced by the most toxic PCB congener (PCB-153) in a 90-day rat study[18] and observed at doses greater (34 µg/kg b.w./d,) than those inducing neurotoxicity in monkey. Therefore the key study which pertains the PCBs' TDI (20 ng/kg p.c./j) was not taken into account for calculating Margins of exposure (MOEs) for dietary exposure in this group of the population, which were quite large in adults (**4400** on average and **2000** at P95) and in children **(2600** and **1200).** Women of childbearing age are of particular concern, because foetal exposure to PCBs is not directly connected to dietary contamination, but to the PCBs level of the umbilical cord blood, which in turn depends on the mother's body burden as a result of the accumulation of PCBs since birth and of the number of previous pregnancies. In such a case, the Margin of boby burden (MOBB) approach would be more appropriate, by comparing human and animal body burdens for the most toxic PCB congener (PCB-153); in the same 90-day rat study[18]. The body burden corresponding to the NOAEL was 1200 µg/kg b.w. As no consolidated data on the body burden of women of childbearing age are available in France, the risk assessment was performed with the average and maximal value measured in European populations[17] (sum of 6 PCBs), 176 ng/g fat (or 35 µg/kg body weight) and 1009 ng/g fat (or 202 µg/kg b.w.) respectively. A correction factor of 2 was applied, corresponding to the body fat content differences between rat and human. The MOBB values are around **69** for average and **12** for the maximal value. It is well accepted that maternal milk contributes to 5-10% of the body burden observed in adult age. Considering that a significant proportion of children under 3 years of age are breastfed, they should be placed in the same group as women of childbearing age.

Conclusion

For the group of adults and children over 3 years of age, the MOEs exceed 1000, based on estimated daily intakes and critical liver effects. However, for women of childbearing age and children under 3 years of age, the MOBBs which are found to be less than 100, would be considered as not acceptable. As a result of this food risk assessment for the general population and of other assessments in relation with high levels of PCBs in French rivers, a national survey of occurrence of PCBs (DL- and NDL-PCBs) in blood is under development and should start in 2008. Although this survey would focus on high consumers of freshwater fishes, women of childbearing age would be included. Results should be available in spring 2011. Considering nutritional benefits, it should be recommended to consume various fish species originating from different fishing areas in order to minimize PCBs intake from oily fish of the most contaminated areas. It should be pointed out that, unlike dioxins, reduction of PCBs contamination cannot be readily achieved, since it results predominantly from environmental pollution associated with past uses. As a result, the risks associated with PCBs are to be managed distinctly from dioxins. The relevance of maximum levels for the sum of dioxins and DL-PCBs in foodstuffs is to be debated. More efforts should be allocated to determine whether PCBs in food should be managed considering DL- and NDL-PCBs, as it currently envisaged by European regulation, or one group including all the PCBs.

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Table I: Maximum levels proposed by the European draft regulation (2006)

Foodstuffs	**Maximum levels proposed Sum of PCB 28, 52, 101, 138, 153, 180**
Meat (in ng/g fat)	
ruminants	50
poultry and game	50
pork	50
Livers (in ng/g fat)	200
Fish and fish-based products except * (in ng/g fresh weight)	100
*eel (en ng/g fresh weight)	200
Milk and dairy produce (in ng/g fat)	50
Eggs (in ng/g fat)	50
Oils and fats (in ng/g fat)	
animal	50
vegetable	50
fish	200

Table II: Exposure to 6 NDL-PCBs depending on the different scenarios (ng/kg b.w./d),

Exposure scenarios	**Children (3 to 14 years old)**			
	average	**p95**	**% person > TDI [CI]**	
No maximum level	12.9	27.3	58.4	[55.4-61.5]
European draft maximum levels	12.6	25.8	56.8	[53.7-59.8]
Maximum levels at 50 ng/g	12.4	25.8	56.4	[53.3-59.4]
Maximum levels at 25 ng/g	**11.6***	**23.5***	**52.0***	**[48.9-55.0]***
Maximum levels at 10 ng/g	**8.4***	**16.3***	**27.9***	**[25.1-30.7]***
	Women of childbearing age [19-44 years old]			
	average	**p95**	**% person > TDI [CI]**	
No maximum level	7.6	16.5	19.5	[15.6-23.5]
European draft maximum levels	7.4	16.3	18.3	[14.4-22.1]
Maximum levels at 50 ng/g	7.3	16.0	15.9	[12.3-19.6]
Maximum levels at 25 ng/g	6.8	14.1	12.6	[9.3-15.9]
Maximum levels at 10 ng/g	**4.9***	**9.6***	**3.9***	**[1.9-5.8]***
	Adults (>15 years old. excluding women of childbearing age)			
	average	**p95**	**% person > TDI [CI]**	
No maximum level	7.7	15.8	20.0	[17.6-22.4]
European draft maximum levels	7.5	15.4	19.2	[16.8-21.5]
Maximum levels at 50 ng/g	7.3	14.9	17.8	[15.5-20.1]
Maximum levels at 25 ng/g	**6.7***	**13.3***	**13.8***	**[11.8-15.9]***
Maximum levels at 10 ng/g	**4.8**	**9.0**	**3.3**	**[2.3-4.4]**

CI : Confidence interval, * significantly different from exposure with no maximum level