# Opinion of the European Food Safety Authority on non dioxin-like polychlorinated biphenyls (PCB) in feed and food

Heppner C[1], Fürst P[2], Larsen JC[3], Schrenk D[4], van Leeuwen FXR[5]

[1]European Food Safety Authority, Largo N. Palli 5/A, 43100 Parma, Italy; [2]Chemisches Landes- und Staatliches Veterinäruntersuchungsamt, Joseph-König-Strasse 40, 48147 Münster, Germany; [3]Danmarks Fødevare- og Veterinærforskning, Department for Toxicology and Riskassessment, Mørkhøj Bygade 19, 2860 Søborg, Denmark; [4]University of Kaiserslautern, Food Chemistry & Environmental Toxicology, Erwin-Schroedinger-Strasse 52, 67663 Kaiserslautern, Germany; [5]National Institute of Public Health and the Environment, Antonie van Leeuwenhoeklaan 9, P.O. Box 1, 3720 BA Bilthoven; The Netherlands

**Introduction**

Polychlorinated biphenyls (PCB) cover a group of theoretically 209 different PCB congeners, which based on their biochemical and toxicological properties, can be divided into two different groups, dioxin-like PCB (DL-PCB) and non dioxin-like PCB (NDL-PCB). Although production and use of PCB has been discontinued in most countries since the 1980s, large amounts remain in electrical equipment, plastic products, and building materials. PCB are persistent and can still be found even though they were released into the environment in the past. Once, released into the environment, NDL-PCB accumulate along the food chain as they are stored in adipose tissue and show long elimination half-lives. Both groups of PCB, NDL-PCB as well as DL-PCB, can be found in food and feed. The European Food Safety Authority´s (EFSA) Panel on Contaminants in the Food chain (CONTAM Panel) was asked by the European Commission (EC) to carry out this risk assessment of NDL-PCB in food and feed. Before EFSA was established, earlier EC Scientific Committees [1,2,3] carried out risk assessments on the presence of dioxins and dioxin-like PCBs in the food and animal feed chain.

**Challenges in the risk assessment**

Depending on the chlorine content and the production process the composition of technical PCB mixtures such as Arochlor, Clophen, Phenochlor, Kanechlor, Pyralene, Fenclor, and Delor differed significantly in the numbers of individual PCB congeners. Moreover, technical PCB mixtures may have contained other chlorinated compounds as impurities, such as polychlorinated naphthalenes (PCN) and polychlorinated dibenzofurans (PCDF). For example, the concentration of DL-PCB and PCDF, expressed as WHO-TEQ, of two different Aroclor 1254 lots differed by more than one order of magnitude[4]. The different composition, as well as the presence of toxicologically relevant impurities may have had a significant impact on the results of toxicological studies with technical PCB mixtures. Therefore, the presence of DL-PCB and PCDF in different technical PCB mixtures and/or batches must be considered when interpreting toxicological animal studies aimed at assessing the toxic effects of NDL-PCB.

Once released into the environment, individual PCB congeners undergo bio- or photodegradation, which results in a different congener pattern compared to the original technical mixture. Such changes are even more pronounced when PCB mixtures are taken up by animals: mammals including humans. Several NDL-PCB congeners are metabolised to hydroxy-PCB and/or methylsulfonyl-PCB. In general, lower chlorinated congeners are metabolised rather quickly, whereas higher chlorinated congeners are more stable and can accumulate in the food chain.

**Occurrence and exposure**

Data on the occurrence of NDL-PCB in food and feed have been reported in the literature in different ways, for example as the sum of three PCB congeners (PCB 138, 153 and 180), as the sum of six PCB congeners (PCB 28, 52, 101, 138, 153, 180) often referred to as indicator PCB or as the sum of seven (sum of six indicator PCB plus PCB 118). This lack of consistency often hampers a direct comparison of occurrence data. The Panel decided to use the sum of the six indicator PCB as the basis for the evaluation in their opinion, because these congeners are appropriate indicators for different PCB patterns in various sample matrices and are most suitable for a risk assessment of NDL-PCB on the basis of the available data. The Panel noted that the sum of the six indicator PCB represents about 50% of total NDL-PCB in food.

Occurrence data were taken from the EC recommended monitoring programme for dioxins and PCB from up to 12 countries within Europe. However, selection criteria (e.g. analysis between 1997 and 2004, limit of quantification) were applied to overcome the variations within the reported data. Although a vast number of data were originally submitted to the EC, only 171 data points for feed and 4,183 data points for food were considered in the opinion.

The following data, unless stated otherwise, are reported as the sum of the six NDL-PCB (PCB 28, 52, 101, 138, 153, 180). Feed categories *fish oil* as well as *fish and fishery products* revealed the highest mean levels of 54.7 and 25.6 ng/g product, respectively. The congener profile in different food groups of animal origin was quite similar, PCB 138 and 153 being the most predominant congeners. Although only based on a limited number of samples, low background contamination of up to 0.1 ng/g fresh weight for food samples of plant origin were found. Considerably higher levels were found in food samples of animal origin, ranging from 2.6 to 12.7 ng/g fat, excluding fish products. The highest mean levels were found in *fish oil* (70.2 ng/g fat) and *fishery products* (12.7 ng/g fresh weight), whereas fish samples from the Baltic Sea contained higher levels of NDL-PCB.

Occurrence data of NDL-PCB in human milk was taken from the third round of the WHO human milk field study[5]. These data included 58 samples from 18 European countries. PCB 153, 138 and 180 were the predominant congeners determined in human milk, making up on average 65% of all PCB congeners. A mean level of total NDL-PCB of 335 ng/g fat was calculated for the European countries. In most of the European countries that implemented measures at an early stage, a decline in PCB levels of approximately 30 to 70% was observed in human milk samples between 1998 and 2001.

The main route of human exposure to NDL-PCB - more than 90% - is via food. Average daily dietary intake of total NDL-PCB can be estimated to be in the range of 10 - 45 ng/kg body weight (b.w.) per day. Limited exposure data for young children of up to 6 years of age, indicate that the average intake (breastfeeding excluded) of total NDL-PCB is about 27 - 50 ng/kg b.w. per day. However, where data on both adults and children within a specific population were available, in general, children had exposure levels 2.5 fold higher than adults. In specific subpopulations with high dietary PCB exposure, such as Baltic Sea fishermen, the daily intake from fish of the sum of the six NDL-PCB could be about 40 ng/kg b.w., corresponding to an intake of total NDL-PCB of 80 ng/kg b.w. per day before taking into account the rest of the diet. Breastfed infants are a group of high NDL-PCB intake which might be two orders of magnitude higher than adult exposure.

Other routes of exposure such as ambient and indoor air, dust and soil, usually do not contribute significantly to the body burden of the general population. However, there are situations in which the contribution from contaminated indoor air could be considerable.

**Relationships between NDL-PCB and other DL compounds**
Due to the different sources of contamination and different origins of feed and of food commodities, there is generally no correlation between the concentrations of NDL-PCB and DL-PCB Toxic Equivalents (TEQ) or the total TEQ (polychlorinated dibenzo-p-dioxins (PCDD), PCDF and DL-PCB) with the exception of specific well-defined contamination cases or in geographically defined sampling areas. However, samples that normally contain high levels of NDL-PCB will also contain high levels of DL-PCB and PCDD and PCDF. In these circumstances, risk management measures to reduce DL-PCB TEQ and total TEQ levels will probably also protect consumers from elevated NDL-PCB exposure. In specific situations, such as contamination with lower chlorinated technical PCB mixtures, where levels of NDL-PCB could be high but TEQ levels could be low, measures to reduce total TEQ will not guarantee protection of the population against products with high levels of NDL-PCB.

**Toxicology**
Technical PCB mixtures used in toxicity studies contain both NDL-PCB and dioxin-like compounds such as DL-PCB. These mixtures exert a variety of toxicological effects such as effects on liver, thyroid, immune function, reproduction and behaviour as well as carcinogenicity. The adverse effects reported in laboratory animals following exposure to individual NDL-PCB were on the thyroid, liver and brain, as well as immunotoxicity,

oestrogenicity, reproductive and neurodevelopmental effects. The latter effects are found particularly in the offspring of rodents following *in utero* exposure. However, since several PCDD, PCDF and PCB 126 were shown to be about three orders of magnitude more potent as liver or thyroid toxicants than the NDL-PCB tested, contamination of NDL-PCB with 0.1% or less of potent dioxin-like contaminants would be sufficient to explain the observed adverse effects.

Results of *in vitro* and *in vivo* genotoxicity studies indicate that PCB are not mutagenic at the gene or chromosome level. Some NDL-PCB, in particular the lower chlorinated congeners, caused DNA damage, probably resulting from the formation of reactive oxygen species. IARC classified PCB in Group 2A (probably carcinogenic to humans), based on limited evidence in humans and sufficient evidence in animals. Evaluation of the cancer studies in rats with technical PCB mixtures, and comparison with data obtained with TCDD, indicate that the dioxin-like components in technical PCB mixtures are likely to be responsible for the carcinogenic response of these mixtures. No peer reviewed data are available on the carcinogenicity of individual NDL-PCB congeners.

Occupational exposures to PCB have been reported to be associated with an increased risk of cancer of the digestive system and possibly other sites. Some studies suggest that environmental PCB exposure may be linked to the development of breast cancer, although perhaps only in certain vulnerable sub-groups. Among non-cancer effects reported to be associated with environmental PCB exposure, adverse reproductive outcomes, delayed neurodevelopment and impairment of the immune system during development are considered to be the most important. The epidemiological studies however, do not allow for an estimation of the toxicity that may specifically be attributed to the NDL-PCB.

**Risk characterisation for domestic animal health**
The CONTAM Panel compared the effect concentrations in the experimental diet with the NDL-PCB concentration in animal feed. Following a conservative approach, the 90$^{th}$ percentile of the sum of six NDL-PCB in *compound feedstuff*, 0.02 mg/kg feed was taken as the point of comparison. This figure corresponds to about 0.04 mg total NDL-PCB, which is more than two orders of magnitude below the concentrations causing effects in most domestic animals studied. The 90$^{th}$ percentile of the sum of the six NDL-PCB in *fish and fish products* was 0.067 mg/kg corresponding to 0.13 mg/kg total NDL-PCB. This is only about five times below the concentration of PCB in feed that produced pronounced effects on reproduction in mink. The CONTAM Panel concluded therefore, that current background levels of NDL-PCB in animal feed are of no health concern for most domestic animals, with the possible exception of mink.

**Risk characterisation for human health**
Although the absence of mutagenicity indicates that a threshold approach is appropriate for hazard characterisation, the toxicological database was considered to be too limited to allow for the establishment of a health based guidance value for NDL-PCB. The CONTAM Panel therefore decided to perform its health risk characterisation on the basis of a margin of exposure approach. The most sensitive effects seen in studies with individual NDL-PCB congeners in experimental animals are liver and thyroid toxicity. The No Observed Adverse Effect Levels (NOAELs) for these effects in 90-day rat studies with the individual NDL-PCB congeners PCB 28, 128, and 153 were in the range of 30 - 40 µg/kg b.w. per day. The CONTAM Panel compared estimated body burdens at the either the NOAEL or Lowest Observed Adverse Effect Levels (LOAEL) for different effects in animals, with the estimated median human body burden derived from the most recent analyses of human milk. NOAEL or LOAEL "margin of body burdens" (MoBB) were calculated by dividing the estimated animal body burdens by the estimated median human body burden. Based on the most sensitive effects (e.g. effects on liver and/or thyroid) in the rats the CONTAM Panel chose an overall body burden of 500 µg /kg b.w. as a representative, conservative NOAEL BB (body burden at the NOAEL) for all individual NDL-PCB and for the sum of NDL-PCB that occurred in human tissue. Comparison with an estimated median human body burden for NDL-PCB of about 50 µg/kg b.w. resulted in a NOAEL MoBB of about 10.

The CONTAM Panel noted that thyroid and liver toxicity in rats can also be observed after treatment with PCDD, PCDF, or DL-PCB. Thus, the estimation of a NOAEL for NDL-PCB is hampered by the uncertainty to

what extent NDL-congeners were contaminated with potent PCDF and/or DL-PCB exhibiting the same effect. Therefore, the "true" NOAEL MoBB for NDL-PCB might be larger. On the other hand, the MoBB was calculated on the basis of the median concentrations of NDL-PCB in human milk, and some populations in Europe may have considerably higher body burdens.

During the nursing period, breastfed infants may have daily intakes, on a body weight basis, of NDL-PCB estimated to be about two orders of magnitude higher than the average adult intake. This elevated intake by infants is related to the mother's long-term intake of NDL-PCB with food. However, the subtle neurodevelopmental effects that were reported in some studies of human infants were mainly associated with exposure to a mixture of NDL-PCB, DL-PCB, and PCDD/PCDF, and any causal role of NDL-PCB is unclear. The CONTAM Panel noted that in many other studies of infants, breastfeeding was associated with beneficial effects, in spite of the contaminants present in human milk.

**Conclusions**

No health based guidance value for humans could be established for NDL-PCB because simultaneous exposure to NDL-PCB and dioxin-like compounds hampers interpretation of the results of the toxicological and epidemiological studies. Also the database on effects of individual NDL-PCB congeners is rather limited. There are however indications that subtle developmental effects being caused by NDL-PCB, DL-PCB, or by PCDD/PCDF alone or in combination, may occur at maternal body burdens that are only slightly higher than those expected from the average daily intake in European countries. Because some individuals and some European (sub)-populations may be exposed to considerably higher average intakes, a continuous effort to lower the levels of NDL-PCB in food is warranted.

**Acknowledgements**

We would like to thank the following additional members of the working group Aksel Bernhoft, Ake Bergman, Alessandro Di Domenico, Roberto Fanelli, Philippe Grandjean, Ron Hoogenboom, Niklas Johansson, Andrew Renwick, Greet Schoeters, Gerhard Winneke for preparing the draft opinion, as well as Elena Dellatte, Elena Fattore, Barbara Gallani, Stefanie Knerr, and Deborah Rice for the preparation of the background documents.

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