Toxic organic compounds in human milk, 2017

The study targeted the presence of polychlorinated biphenyls (PCBs), organochlorine pesticides (OCPs), perfluorinated compounds (PFCs) and brominated flame retardants (BFRs) and their derivatives, including NBFRs. The content of trans-fatty acids in part of the human milk samples was analysed as well.

In 2017, the national Human biomonitoring was carried out in four localities – Prague, Liberec, Ostrava and the Vysočina Region (Žďár nad Sázavou and Jihlava). The study was focused on analysis of selected groups of substances in human milk, involving a total of 232 primiparas.

The study targeted the presence of polychlorinated biphenyls (PCBs), organochlorine pesticides (OCPs), per- and polyfluorinated compounds (PFAS) and brominated flame retardants (BFR) and their derivatives. High-performance liquid chromatography (UHPLC) with tandem mass spectrometry (MS/MS) and capillary gas chromatography (GC) with mass spectrometry were used for analytical purposes. The content of trans-fatty acids in part of the samples was analysed using gas chromatography with a flame ionization detector (FID).

Some of the monitored substances are listed in the Stockholm Convention on Persistent Organic Pollutants as suspected of developmental, reproductive and systemic toxicity, carcinogenic effects and disruption of hormonal equilibrium with serious outcomes for the general population.

Polychlorinated biphenyls

PCBs are a family of 209 congeners with differing physical/chemical properties and toxicity. Health-relevant PCBs have chlorine atoms on benzene rings in positions 2, 3, 7 and 8. PCBs were first manufactured in the 1920s with wide-scale industrial application occurring mainly in the 1950s. As a result of intensive commercial use and inherent persistence PCB concentrations in the environment, and particularly the food chain, increased. In time, the negative effects of PCBs became apparent: disruption of hormonal balance, carcinogenicity, neurotoxicity etc. This resulted in a European ban on PCBs in the latter half of the 1970s; in former Czechoslovakia they were banned in 1984. The main exposure route is dietary.

A summary of PCB concentrations in human milk for 2017 is presented in Tab. 1.

Tab. 1 Levels of PCBs (ng/g fat) in human milk, 2017

	PCB 28	PCB 118	PCB 138	PCB 153	PCB 170	PCB 180	Sum of PCBs*
N	232	232	232	232	232	232	232
LOQ	0.3	0.3	0.3	0.3	0.3	0.3	
Geomean	0.4	2.0	14.4	28.8	9.6	19.1	107.9
Median	0.4	2.1	14.3	29.8	10.0	19.7	110.5

95thPerc	1.6	5.8	40.2	81.2	31.9	66.6	316.6

*Sum of PCBs = (PCB 138 + PCB 153 + PCB 180)x1,7

Some PCBs have highly toxic effects, similar to those of dioxins (dioxin-like PCBs). From these, PCB 118 was monitored; median concentration was 2.1 ng/g of fat.

Organochlorine pesticides

This group consists of a wide range of persistent lipophilic substances previously used as insecticides in the 1940s – 1960s. They comprise DDT derivatives (o,p' and p,p' DDT, DDD and DDE), α-, β-, γ-, δ-HCH (hexachlorocyclohexane), HCB (hexachlorobenzene), heptachlor, endosulfan, methoxychlor, aldrin, dieldrin, endrin, mirex and toxaphene. The general population is exposed to these substances via the dietary route in most cases. Negative effects are usually associated with the nervous and reproductive systems, with suspected carcinogenicity. For instance, lindane, DDT and HCB have been classified by IARC as category 2B potential human carcinogens on the basis of animal experiments. Although use of these substances has been banned in this country since the 1970s they are still detectable in the human organism several decades later. Long term biological monitoring has been conducted of DDT, HCB and α-, β-, γ- HCH derivatives.

Concentrations in human milk for 2017 are shown in Tab. 2. DDT levels, expressed as the sum of DDT isomers (with prevalence of p,p'-DDE) confirms a declining trend associated with the gradual decrease of load documented since the 1980s and repeatedly confirmed by previous years of biological monitoring. In 2017, the median concentration of the sum of DDT derivates in human milk was 76.5 ng/g fat. The hexachlorobenzene content in human milk (median concentration 11.5 ng/g fat) reflects a gradual decline observed over the years of monitoring. Concentrations of hexachlorocyclohexane β-HCH in human milk have also been declining since 2005 (2005 - 18 ng/g fat, 2017 - 6 ng/g fat).

Tab. 2 Levels of organic pesticides (ng/g fat) in human milk, 2017

	p,p'-DDT	p,p'-DDE	Sum of DDTs+	HCB	β-HCH
N	232	232	232	232	232
LOQ	0.3	0.3		0.3	0.3
Geomean	4.5	70.5	76.3	11.6	6.2
Median	4.3	72.0	76.5	11.5	6.2
95thPerc	19.6	283.9	302.2	24.5	18.3

+Sum of DDTs = p,p'-DDT + p,p'-DDE

Perfluorinated compounds and their derivatives

Perfluorinated compounds (PFAS) is a collective term for a group of synthetic fluorinated compounds, with perfluorooctanesulfonic acid (PFOA) and perfluorooctanesulfonate (PFOS) as the most important representatives. They are persistent organic environmental pollutants with bioaccumulative potential. Animal studies have revealed their developmental, reproductive and systemic toxicity, carcinogenic effects and disruption of hormonal balance with serious consequences. PFCs are used as finishes or

coatings on carpeting, leather, textiles, paper, upholstery, food packaging or are contained in cleaning products and paints. PFOA serves as an emulsifier in the manufacture of polytetrafluoroethylene (Teflon). Exposure routes are through house dust ingestion and inhalation, drinking water and food. These compounds can be released into foods from their packaging during storage.

In 2017, a total of 19 PFAS were analysed. Concentrations exceeding the limit of quantification (LOQ) in over 50% of samples were detected for PFOA (100% samples exceeding LOQ), PFNA (perfluorononanoic acid, 98.7% samples exceeding LOQ), PFOS: Br-PFOS (98.3% samples exceeding LOQ) and L-PFOS (99.6% samples exceeding LOQ).

The results are summarised in Tab. 3. In contrast to 2006, 2010/2011 and 2014, for the first time ever almost all samples of human milk were positive for PFNA. Conversely, there is a continuing decline in PFOA and PFOS content. The content of other monitored PFCs mainly ranged below the LOQ (0.003 – 0.006 ng/ml) and positive findings were sporadic (0-1.3% samples).

Tab. 3 Levels of PFAS (ng/ml) in human milk, 2017

	PFOA	PFNA	Br-PFOS	L-PFOS	Sum PFOS*
N	232	232	232	232	232
LOQ	0.003	0.003	0.001	0.002	-
Geomean	0.024	0.007	0.007	0.014	0.022
Median	0.023	0.007	0.007	0.013	0.020
^{95th}Perc	0.058	0.012	0.040	0.041	0.078

*Sum of PFOS = Br-PFOS + L-PFOS

Brominated flame retardants and their derivatives

Flame retardants and self-extinguishing additives are a diverse group of brominated organic compounds that are added to flammable materials (plastics, textiles, electronic equipment etc.) to retard or limit their flammability and improve fire safety. Polybrominated biphenyl ethers (PBDE) are amongst the best known BFRs, with a total of 209 congeners. Other associated substances include hexabromocylododecane (HBCD), polybrominated biphenyls (PBB) and brominated bisphenols such as tetrabromobisphenol A (TBBPA). At present, the above-mentioned BFRs are frequently being replaced with ‘new’ brominated flame retardants which are a structurally variable group of substances comprising aromatic, cyclic and cycloaliphatic compounds.

The most probable exposure route is inhalation of dust in indoor air, largely originating from building materials and electronic devices. The hazard posed by BFRs is primarily given by their high stability and bioaccumulation. BFRs persist in the body, particularly in fatty tissue and organs. They are endocrine disruptors, negatively affecting hormonal balance in the organism. Animal studies have shown their potential as neurotoxins and carcinogens.

In 2017, a total of 19 PBDE congeners were analysed. As in previous years, congeners predominated in over 50% of human milk samples at amounts below the LOQ (0.1 – 1.0 ng/g fat). Identification of

these congeners ranged 0% - 42% of individual samples, with the exception of congener BDE 206 which in 2017 was quantified in human milk for the first time (61% samples in excess of LOQ).

As in previous years, values of hydroxylated BDE metabolites did not exceed the LOQ of the method used (0.006 ng/ml fat).

HBCD isomers (α-, β- and γ- HBCDD) are relatively easily released into the environment from commercial products. This substance is listed on the List of Substances of Very High Concern under the REACH and on the list of substances to be eliminated from production and use in Annex A of the Stockholm Convention. α-HBCDD was detected in a quarter of human milk samples (25%), the other two isomers were rare (up to 3% of the samples).

Tetrabrombisphenol A (TBBPA) was found in only two samples of human milk from a total of 232 samples.

As an alternative to flame retardants regulated by legislation so-called new flame retardants have been introduced. Important representatives of this group are decabromdiphenyl ethane (DBDPE) or 1,2-bis(2,4,6-tribrom-phenoxy)ethane (BTBPE). However, some of these compounds have also been found to have bioaccumulative, toxic and potentially carcinogenic effects. Concentrations of the new flame retardants over LOQ were detected sporadically.

Trans fatty acids content

Trans isomers of fatty acids (TFA) are unsaturated fatty acids with one or more double bonds in -*trans* geometric configuration. They are present in food only and do not occur naturally in the organism. The main sources of TFAs are partially hydrogenated fat and foods that contain such fat (margarine, edible fats, long-life bakery products, fast food etc.). In small amounts they occur naturally in the fat of ruminants (and so in meat and dairy products). TFAs may increase the risk of cardiovascular disease and diabetes. They have damaging effects on blood lipoproteins (increasing LDL and decreasing HDL cholesterol). High intake of TFA affects the immune system and endothelium, and excessive intake in pregnancy may disrupt essential fatty acid metabolism and foetal development.

Human milk serves as a suitable matrix for monitoring TFA levels in the body and is the basis for evaluating infant TFA intake.

Trans fatty acids were monitored for the first time in 2017 as part of human biomonitoring in the form of a pilot study involving 50 samples of human milk from Prague. Results are shown in Tab. 4. TFA content in human milk was not evaluated individually but by using sum of TFA[1] and sum of octadecenoic acid isomers C18:1t[2].

The median value of the sum of TFA in 2017 was 0.9 g/100g fat. The range of monitored values in 2017 (0.3 – 1.6 g/100g fat) corresponds to results from a study assigned by the Chief Public Health Officer [1] (0.5 – 1.9 g/100g fat, median 0.8/100g), but is also many times lower than results from a 2002 study of Prague-resident women [2] (1.84 – 9.78 g/100g fat) and a 2008 study [3] (1.51 – 7.84 g/100g fat). With caution, knowing the uncertainties of comparing the results of various studies, it can be concluded that the burden of the population by the *trans* fatty acids is gradually decreasing due to the changes in the production of hardened fats.

Some EU states have introduced limit values for TFA content in foods; such limits have not been set in the Czech Republic yet, although the sale of foods containing TFAs from partially hydrogenated fats in

schools and school facilities is forbidden. Nonetheless, major producers have voluntarily reformulated their products and the majority of margarines on the Czech market have a low TFA content [1].

Tab. 4 Levels of trans-fatty acids (g/100g fat) in human milk, 2017

	Sum TFA *	Sum C18:1t **
N	50	50
Geomean	0.86	0.53
Median	0.92	0.54
^{95th}Perc	1.33	0.79

*sum TFA = C18:1t + C14:1n-5t, C16:1n-7t, C18:2tt, C18:2ct, C18:2tc, C18:3n-3ttt, C18:3n-3ttc, C18:3n-3ctt, C18:3n-3cct, C18:3n-3ctc, C18:3n-3tcc

**sum C18:1t = *trans* izomers with double bond on carbons 6-13

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