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MEETING REPORTS

Perfluorinated compounds (PFC) hit the headlines

Meeting report on a satellite symposium of the annual meeting of the German Society of Toxicology

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Recently, agricultural land in the rural area Sauerland in North Rhine-Westphalia, Germany, has been contaminated with perfluorinated compounds (PFC) (Kraft et al. 2007). Industrial waste containing mainly perfluorooctanoic acid (PFOA) has been illegally manufactured into a so-called "soil improver" by a recycling company and disseminated by farmers, leading to increased levels of PFOA after leaching into surface raw water for drinking water production (Fig. 1). Irrespective of this headline-catching incident PFC represent a group of emerging chemicals of concern (Table 1). An increasing number of studies show that humans are exposed to a large number of PFCs (Kärrman et al. 2007; So et al. 2007). PFOA and PFOS, the two most important PFCs in the environment, are auxiliary substances for the industrial production of perfluorinated polymers. These are widely used for non-stick coatings for instance on cooking pans and stain repellent coatings on items such as fast-food packaging, furniture and carpets. The major source of PFOA and PFOS in the environment seems to be their dissemination with waste water and their release in traces from consumer products.

In order to achieve a realistic risk assessment an expert panel met during the Annual Meeting of the German Society of Toxicology. Detlef Wölfle (Federal Institute for Risk Assessment, BfR, Berlin) reported on the persistence and toxicology of PFCs. Some compounds, e.g. PFOA and PFOS, are resistant to biotransformation and were ubiquitously found in human blood with half-lives of several years. Oral toxicity studies in rats and monkeys showed that liver is the primary target organ. While PFCs were not considered to be genotoxic, PFOA and PFOS are tumor promoters in rats (COT 2006a, b). Following in utero exposure in rodents PFOA (Hernderson and Smith 2007; Wolf et al. 2007) and PFOS produced reduced viability, body weights deficits and other postnatal effect on pups (Fig. 2).

Jürgen Angerer (University of Erlangen) presented epidemiological data. Several studies have reported an increase in PFC concentrations in humans up to the late 1990s. Recent efforts have not yet resulted in declining environmental concentrations. In two independent studies, median values of blood plasma concentrations of PFOS and PFOA were determined. They amount to 12–22 µg/l and 5–7 µg/l, respectively. Blood levels did not correlate with age. Interestingly, the levels were higher in male compared to female individuals. Importantly, lactation is a considerable source of exposure for infants (Kärrman et al. 2007). Furthermore, PFCs undergo trans-placental transfer (Midasch et al. 2007). The total amount of PFCs transferred to a breast fed infant is approximately 200 ng/day. Michael Wilhelm (University of Bochum) presented brand-new data

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Fig. 1 The Möhne Lake: recreation area and drinking water source highly contaminated by perfluorinated compounds

on individuals exposed to PFOA-contaminated drinking water as a consequence of the "Sauerland-soil-improver scandal". Compared to controls 4–8-fold increased levels of PFOA in plasma have been observed in children, women and men. In contrast to PFOA, plasma concentrations of PFOS did not differ from controls. Therefore, individuals exposed to PFOA- contaminated drinking water could be clearly identified by an increased PFOA/PFOS ratio. Additionally, there was a clear positive association between consumption of drinking water and PFOA concentrations in plasma. Hermann Dieter (Federal Environmental Agency, Berlin) addressed regulatory aspects of PFCs. Recently, criteria have been proposed that allow differentiation between specific and non-specific genotoxicity (Dorn et al. 2007). Based on this classification PFCs can be categorized as weakly non-specific genotoxic. The Federal Environmental

Table 1 Perfluorinated compounds (PFCs): facts and terminology

Biochemical and general toxicology—selected aspects: PFCs

– are highly lipophobic, but only moderately soluble in water
– are persistent and bioaccumulative in non-adipose tissues
– are largely resistent to degradation in the environment and in mammalian metabolism
– are subject to entero-hepatic circulation
– are transferred trans-placentally
– delay development, growth lags and increase liver weights in rodents and monkeys
– are tumour promoters in rats at high concentrations (>1.4 mg/kg per day)
– are not primarily genotoxic
– inhibit intercellular communication via gap junctions
– interact with peroxisome proliferator-activated receptor α
– inhibit ß-oxidation of long chain fatty acids in peroxisomes (Borges et al. 1990, 1992; Wilson et al. 1995)

Epidemiology

Basal blood plasma concentrations in European populations (median values of two independent studies)

– PFOS: 12 µg/l and 22 µg/l
– PFOA: 5 µg/l and 7 µg/l
– Based on Fromme et al. (2007) and data presented at the symposium

Regulatory toxicology

– ≤0.10 µg PFC/l in drinking water (precautionary value recommended by the Umweltbundesamt/German Federal Environment Agency)
– 0.30 µg PFOA + PFOS/l in drinking water (long term toxicological threshold value recommended provisionally by the Umweltbundesamt/German Federal Environment Agency)
– 0.10 µg/(kg/day) as TDI (Tolerable Daily Intake recommended provisionally by the Umweltbundesamt/German Federal Environment Agency)

Terminology

PFC	Perfluorinated compounds	Family name of a large group of chemicals consisting of six to 16 C-atoms and entirely fluorine-substituted alkyl chains
PFT	Perfluorinated tensides	Used for PFC in German-speaking countries
PFCA	Perfluorinated carboxylic acids	Subgroup of PFCs
PFAS	Perfluorinated alkyl sulfonates	Subgroup of PFCs
PFOA	Perfluorooctanoic acid	Example of a PFCA; widely used for the production of stain repellents and of non-stick coatings
PFOS	Perfluorooctane sulfonate	Example of a PFAS; widely used for the production of stain repellent coatings (Fig. 2)
FTOH	Fluortelomer alcohol	In contrast to PFCs, fluortelomers contain also non-fluor substituted carbon atoms due to a specific procedure of their chemical synthesis

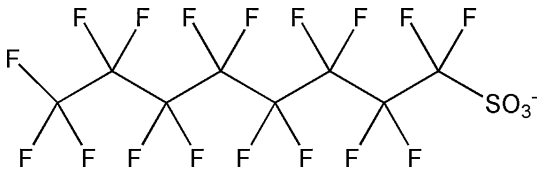

Fig. 2 Chemical structure of perfluorooctane sulfonate (PFOS) as an example of a PFC

Agency recommends for drinking water a precautionary value of 0.10 µg/l and a long-term toxicological threshold value of 0.30 µg/l. A tolerable daily intake (TDI) of 0.10 µg PFT/(kg/day) was proposed (Dieter 2007).

Finally, the expert panel addressed regulatory consequences of the "Sauerland-soil-improver scandal" in Germany. Further placement of PFC contaminated soil improver must be prohibited. Fortunately, PFOA plasma concentrations were considered to be too low to cause overt adverse health effects in the exposed population.

References

Borges T, Glauert HP, Chen LC, Chow CK, Robertson LW (1990) Effect of the peroxisome proliferator perfluorodecanoic acid on growth and lipid metabolism in Sprague Dawley rats fed three dietary levels of selenium. Arch Toxicol 64:26–30

Borges T, Robertson LW, Peterson RE, Glauert HP (1992) Dose-related effects of perfluorodecanoic acid on growth, feed intake and hepatic peroxisomal beta-oxidation. Arch Toxicol 66:18–22

Committee on toxicity of chemicals in food, consumer products and the environment, COT statement on the tolerable daily intake for perfluorooctanoic acid (2006a) http://www.food.gov.uk/multimedia/pdfs/cotstatementpfoa200610.pdf

Committee on toxicity of chemicals in food, consumer products and the environment, COT statement on the tolerable daily intake for perfluorooctane sulfonate (2006b) http://www.food.gov.uk/multimedia/pdfs/cotstatementpfos200609.pdf

Dieter HH (2007) Human toxicology evaluation of perfluorinated tensides (PFT) using Perfluorooctanoate (PFOA) and Perfluorosulfonate (PFOS) as examples (in German with abstract in English). Umweltmed Forsch Prax 12(2):95–104

Dorn SB, Degen GH, Muller T, Bonacker D, Joosten HF, van der Louw J, van Acker FA, Bolt HM (2007) Proposed criteria for specific and non-specific chromosomal genotoxicity based on hydrophobic interactions. Mutat Res 628:67–75

Fromme H, Midasch O, Twardella D, Angerer J, Boehmer S, Liebl B (2007) Occurrence of perfluorinated substances in an adult German population in southern Bavaria. Int Arch Occup Environ Health 80:313–319

Henderson WM, Smith MA (2007) Perfluorooctanoic acid and perfluorononanoic acid in fetal and neonatal mice following in utero exposure to 8–2 fluorotelomer alcohol. Toxicol Sci 95:452–461

Kärrman A, Ericson I, van Bavel B, Darnerud PO, Aune M, Glynn A, Lignell S, Lindstrom G (2007) Exposure of perfluorinated chemicals through lactation: levels of matched human milk and serum and a temporal trend, 1996–2004, in Sweden. Environ Health Perspect 115:226–230

Kraft M, Bernsmann T, Hölzer J, Just P, Krüger C, Quabeck G, Rauchfuss K, Wilhelm M (2007) The PFC case in the region Sauerland, Germany, from an environmental medical view —assessment and management (in German with abstract in English). Umweltmed Forsch Prax 12:79–86

Midasch O, Drexler H, Hart N, Beckmann MW, Angerer J (2007) Transplacental exposure of neonates to perfluorooctanesulfonate and perfluorooctanoate: a pilot study. Int Arch Occup Environ Health 80:643–648

So MK, Miyake Y, Yeung WY, Ho YM, Taniyasu S, Rostkowski P, Yamashita N, Zhou BS, Shi XJ, Wang JX, Giesy JP, Yu H, Lam PK (2007) Perfluorinated compounds in the Pearl River and Yangtze River of China. Chemosphere. DOI10.1016/j.chemosphere.2007.02.008

Wilson MW, Lay LT, Chow CK, Tai HH, Robertson LW, Glauert HP (1995) Altered hepatic eicosanoid concentrations in rats treated with the peroxisome proliferators ciprofibrate and perfluorodecanoic acid. Arch Toxicol 69:491–497

Wolf JC, Fenton SE, Schmid JE, Calafat AM, Kuklenyik Z, Bryant XA, Thibodeaux J, Das KP, White SS, Lau CS, Abott BD (2007) Developmental toxicity of perfluorooctacoic acid in the CD-1 mouse after cross-foster and restricted gestational exposures. Toxicol Sci 95:462–473