

Provisional evaluation of PFT in drinking water with the guide substances perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS) as examples

Statement by the Drinking Water Commission (Trinkwasserkommission) of the German Ministry of Health at the Federal Environment Agency

June 21, 2006 (revised July 13, 2006)

1. Introduction

In a May 2006 study of persistent substances in water by the University of Bonn's Department of Hygiene and Public Health Studies (*Institut für Hygiene und Öffentliche Gesundheit der Universität Bonn*), elevated concentrations of perfluorinated chemicals consisting of 50-80 percent perfluorooctanoic acid (PFOA) were detected in surface water and drinking water of Germany's *Hochsauerland* district (Skutlarek et al. 2006). The district's drinking water was found to contain PFOA concentrations ranging up to 0.56 µg/L, as well as substantially lower concentrations of perfluorooctane sulfonate (PFOS).

In view of the fact that no national legislation (including Germany's 2001 Drinking Water Ordinance (*Trinkwasserverordnung*)) currently defines specific limit values for PFOA, PFOS or any other perfluorocarbons, the *Hochsauerland* Public Health Department (*Gesundheitsamt des Hochsauerlandkreises*) asked the Drinking Water Commission (*Trinkwasserkommission, TWK*) of the German Ministry of Health (BMG) at the Federal Environment Agency (*Umweltbundesamt, UBA*) to determine the maximum tolerable concentrations of PFOA, PFOS and other PFTs in drinking water.

The present assessment was based on (a) an experts report by Prof. Dr. Ulrich Ewers of the Hygiene Institute of the Ruhr Area in the city of Gelsenkirchen that was conducted for the *Hochsauerland* District's Public Health Department (Ewers 2006); and (b) the minutes of a conference call that Dr. Ewers held with the members of the Drinking Water Commission (including its chairman Dr. Exner) and the Federal Environment Agency toxicologists Drs. H. H. Dieter and H.J. Grummt. Both the report and conference were realized between June 16 and 21 and revised on July 13, 2006.

2. Basis for the assessment of PFOA¹ and perfluorocarbons in drinking water

2.1 Health based precautionary value HPV

PFOA and PFOS are both partially assessable toxic substances, but little data are available on any other perfluorocarbons. However, perfluorocarbons are unlikely to have any direct and potent genotoxic effect stemming from factors such as reactive metabolites.

The Federal Environment Agency's (UBA) guidance published in 2003 (*Umweltbundesamt* 2003a; hereinafter referred to as "2003a Federal guidance") defines in its section 3.1 an admissible health based precautionary value HPV₁ (also referred to as Health based parametric value) of 0.1 µg/L for non- or low potency genotoxic substances that also applies to PFOA, PFOS and other perfluorocarbons.

2.2 Admissibility of substance concentrations exceeding the HPV₁

According to section 3.1 of the 2003a Federal guidance, the presence in drinking water of non-assessable or only partially assessable substances exceeding the HPV₁ is admissible for substances that are neither directly nor indirectly genotoxic. The admissible concentrations are defined in accordance with the quality of the available data base (*Umweltbundesamt* 2003a).

The main criterion for the admissibility of *any* substance concentration exceeding the lifelong precautionary value is its potential direct and/or indirect genotoxicity. Under certain circumstances, a HPV exceeding the HPV₁ can be defined for an indirectly genotoxic substance, but never for a directly genotoxic substance. Where indicated the HPV₁ = 0,10 µg/L should be replaced by HPV₂ = 0.01 µg/L for highly genotoxic substances.

According to *Hazard Assessment of Perfluorooctane Sulfonate and its Salts* (OECD, November 2002) and *Draft Risk Assessment* (EPA, January 2005), neither PFOS nor PFOA have a direct genotoxic potential, which means they lack the capacity to act directly on DNA either with or without metabolization. According to the aforementioned OECD and EPA studies, PFOA induces indirect genotoxicity in the form of chromosome aberrations and polyploids only if substance test concentrations also have a cytotoxic effect. However, (only) one recent study found a relatively high *indirect* genotoxic potential for *non*-cytotoxic concentrations of PFOA (Yao and Zhong 2005). The mechanism of action of this genotoxicity is similar to that of phthalate or bromate and is controlled by peroxisome proliferation accompanied by the release of oxygen radicals.

According to one recent study (Guruge et al. 2006), other indirect genotoxic effects of PFOA are the induction and suppression of a broad range of genes that control fat, carbohydrate, protein metabolism, cell adhesion, cell communication, hormone regulation, growth, immunity

¹ Inasmuch as PFOS and PFOA have comparable toxicity, the concentrations of the two substances were aggregated (see last item in box, section 2.3).

and apoptosis. This study also found that PFOA and perfluorocarbons can also inhibit the release of fat metabolism enzymes.

Consequently, it **cannot** be completely ruled out that PFOA and/or PFOS are potentially genotoxic (and hence carcinogenic) for humans, although this risk cannot be quantified at present. *Hence, until further notice the Federal Environment Agency's HPV₁ should be used to assess the presence of composite concentrations of PFOA, PFOS and any other perfluorocarbons in drinking water.*

However, in certain settings – and in light of the proportional amount of exposure attributable to other pollutants – the HPV₁ may be too conservative from a purely toxicological standpoint. This could turn out to be the case if, for example, envisaged Federal Environment Agency studies support the assumption that there is virtually no risk of indirect PFOA and/or PFOS genotoxicity in drinking water or that the population-based additional life expectancy risk from lifelong exposure to 0.1 µg/L of co-occurring PFOA and PFOS is less than 10⁻⁶.

2.3 Short and medium term acceptability of contaminant levels exceeding the HPV₁

The HPV₁ relates on **lifelong** exposure situations. Hence this value provides an additional measure of safety in cases of **less than lifelong** exposure (for the same toxicological end point), thus rendering brief exceedance periods (up to “precautionary action values”, see below) tolerable from a health and hygiene standpoint.

The following rounded-off precautionary action values PAV for composite PFOA and PFOS levels apply by using the interpolation factors IF₃ and IF₁₀ in implementing precautionary action values for non-threshold (primary genotoxic) substances pursuant to the Federal Environment Agency's *Maßnahmewert-Empfehlung* (Action value guidance) of August 2003 (*Umweltbundesamt 2003b*):

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| ▪ | >0.1-0.6 µg/L | PAV ₁₀ , tolerable for a maximum of ten years (VMW ₁₀) ² |
| ▪ | >0.6-1.5 µg/L | PAV ₃ , tolerable for a maximum of three years (VMW ₃) |
| ▪ | >1.5-5.0 µg/L | PAV ₁ , tolerable for a maximum of one year (VMW ₁) |
| ▪ | 5.0 µg/L | PAV ₀ , value requiring immediate action to reduce adults' intake of PFOA and PFOS in drinking water (VMW ₀) |
| ▪ | If PFOA and PFOS are present concurrently, the addition rule for “similar joint action” applies. In accordance with this rule, the total of the quotients of the various substance specific measurement values and the applicable precautionary value is not to exceed 1. | |

² Translator's note: The German acronym for “*Vorsorgemaßnahmewert* = precautionary action value (PAV) is *VMW*.”

The PAVs indicated here are *pragmatic* health orientation values that take into account the lack of data, as well as *the possibility that some toxic risks attributable to additional perfluorocarbons with shorter or longer chains than PFOA and PFOS have yet to be identified*. Consequently, these PAV are also lower than is justified from a strictly toxicological standpoint. Despite the shortage of data, current findings indicate that in all likelihood the health of the populations affected (within the meaning of § 6(1) of the 2001 Drinking Water Ordinance (TrinkwV 2001)) is adequately protected by these PAV. They should also be used to assess water used in the food processing industry.

In addition, pursuant to § 6(3) (minimization requirements) of the Drinking Water Ordinance (TrinkwV), efforts are to be made, as expeditiously as possible and insofar as financial resources and the local circumstances allow, to reduce composite perfluorocarbon levels to less than the HPV₁ of 0.1 µg/L.

In addition, the Drinking Water Commission of the German Ministry of Health recommends that human biomonitoring be realized for the blood samples of population groups exposed to drinking water that is found to contain perfluorocarbons. Human biomonitoring is an extremely useful tool for assessing risks incurred by specific populations. It can also be used to assess quantitatively the appropriateness of the provisional and strictly health based drinking water guide value for lifelong exposure recommended herein (see section 3).

Human biomonitoring data from a number of industrialized countries shows that PFOA and PFOS are ubiquitous in human blood serum, which means that human exposure to these substances must be equally commonplace. The proportion of overall exposure attributable to drinking water in specific settings (including in the *Hochsauerland* District) is currently unknown. HBM investigations could also shed a great deal of light on this issue.

2.4 Guidance relating to pregnancy and to preparation of infants formula

Infants need five to 10 times more fluid per day and kilogram of body mass compared to adults and children.

If the PAV₀ of 5 µg/L mentioned in section 2.3 (and for which immediate measures to reduce PFOA and PFOS intake in drinking water must be taken if these values are exceeded) is divided by the maximum factor of 10, this results in a PAV_i of 0.5 µg/L for infants. This PAV_i also applies to pregnant women since PFOA and PFOS also pass through the placenta.

Hence the Drinking Water Commission of the German Ministry of Health recommends that drinking water containing a composite PFOA and PFOS concentration exceeding 0.5 µg/L should not be used for baby food. In addition, pregnant women should avoid regular intake of such water alone or in beverage products.

3. Provisional toxicological assessment of PFOA³ and PFOS in drinking water

According to the *Draft Risk Assessment* of EPA (EPA January 2005), there are several LOAELs (lowest observed adverse effect levels) and NOAELs (no observed adverse effect levels) for **PFOA** at various toxic end points. A two-year study mentioned there with male and female Sprague-Dawley rats detected a LOAEL of approximately 15 mg/kg/day and a NOAEL of approximately 1.5 mg/kg/day. A LOAEL for toxicity on reproduction as measured in F0 and F1 rat generations is considered to be 1 mg/kg/day. Adverse effects amounting to 3 mg/day were detected in rhesus and cynomolgus monkeys that were exposed to drinking water containing PFOA and PFOS for only three and six months respectively. Therefore the **lowest** NOAEL for PFOA in animal studies is considered to be in the range **0.1 < 1.0 mg/kg/day**. If the lower range limit is used as the point of departure (PoD) for a preliminary PFOA toxicity assessment, using an extrapolation factor⁴ EF_{cd} of $10 \times 10 = 100$ and an additional uncertainty factor of 10 (to compensate for the extremely long halflife of PFOA in humans compared to rats), a tolerable daily intake of 0.1 µg/kg/day is obtained for all risk groups, which of course include infants and pregnant women.

A two-year study (OECD 2002) of rats documented NOAEL of 0.025 mg/kg for **PFOS**, whereas Seacat et al. (2002) observed NOAEL of 0.15 mg/kg for PFOS in cynomolgus monkeys after 26 weeks of exposure. Using the lower of these two NOAELs as a point of departure, Thayer and Houlihan (2002) derived a tolerable daily PFOS intake of 0.083 µg/kg (rounded off to 0.10 µg/kg) that allows for the substantial accumulations of PFOS in humans as well as inter- and intraspecies biological variability.

Each of these provisional and substance specific tolerable daily intake values, if assuming 10 percent exposure allocation to drinking water, and drinking water consumption of two liters daily for a 70 kilogram adult, results in a lifelong health based guide value of 0.3 µg/L (rounded figure), which therefore also applies to toxicity risk assessments of composite PFOA and PFOS concentrations in drinking water. This strictly health based guide value is identical to the lifelong precautionary value pursuant to the Federal guidance of March 2003 (*Umweltbundesamt* 2003a) for substances with demonstrably indirect genotoxic effects (the indirect effect of PFOA and PFOS is also substantiated by the available data). Hence this value also demonstrates its scientific appropriateness for statutory toxicity regulations even in the case of highly toxic substances with a tolerable daily intake of substantially less than 1 µg/kg and lacking an adequate data base

An Action Value AV (*Maßnahmewert, MW*) pursuant to the Drinking Water Commission's action value guidance of August 2003b may be derived from the aforementioned lifelong exposure guide value on the basis of the respective interpolation factor IF (*Umweltbundesamt*

³ See note 1.

⁴ Extrapolation factor EF_c applies to interspecies extrapolations whereas EF_d applies to intraspecies extrapolations.

2003b). A strictly health based AV_{10} of 5 $\mu\text{g/L}$ for an exposure period of up to 10 years can be calculated according to this guidance. This AV_{10} is numerically identical with the *precautionary* AV_0 (see section 2.3).

The PAVs recommended in section 2.3 are higher than the health based guide value for lifelong exposure (0,3 $\mu\text{g/l}$) as derived using the aforementioned method. If practically applied they would therefore have to be phased out within at latest ten years. Hence these values lie in a composite substance concentration range that does not pose any danger or risk to public (see § 6 (1) of the Drinking Water Ordinance (*TrinkwV* 2001)).

Note:

The derivation method for the toxicity of a composite lifelong exposure guide value for PFOA and PFOS in drinking water provides adequate safeguards against genotoxic, carcinogenic and other health hazards.

However, according to the current state of knowledge, this risk assessment method is **not** applicable to direct genotoxic effects or the consequent (possible) carcinogenic effects. This in turn means that risk regarding tolerable intake levels for these substances cannot be assessed at present owing to a lack of data.

However, there is currently no evidence that PFOA, PFOS or any other perfluorinated chemical might pose a **direct** (non-threshold) genotoxic risk.

4. Overall status assessment

Elucidation of the presence, production, application, removal and relevance of persistent, non-degradable, and difficult to eliminate substances such as perfluorocarbons is a highly complex process.

Hence risk assessment for some of these substances is currently either unrealizable or incomplete. Neither the German Drinking Water Ordinance nor the EU Water Framework Directive currently regulates concentrations or exposure levels for these substances, which accumulate in human blood, kidneys and liver if ingested in food or drinking water over an extended period.

Hence, in the interest of avoiding health risks and in keeping with WHO's Framework for Water Safety Plans, independent scientific studies of the concentrations of these substances in surface water and drinking water should be fostered and realized so that risk assessments can be conducted with a view to safeguarding users.

Such studies could also potentially provide insight into production and use related issues, as well as information that would be useful to the general public, which is entitled to an investigation process that is conducted independently and that methodically applies the relevant risk

assessment criteria. This also means that the relevant expertise in this field must be acquired and ensured by government and academic institutions.

5. Overview of the key maximum value guidance in the present report for composite PFOA and PFOS concentrations

Type of max. value	English (German) abbreviation	Relevant value	Relevant section in the present report
Health based <i>precautionary</i> value (long term minimum quality goal) for non-genotoxic substances	HPV ₁ (<i>GOW₁ = Gesundheitlicher Orientierungswert</i>)	0.1 µg/L	Section 2.1: lifelong precautionary value, e.g. in case additional perfluorocarbons would be present
Strictly <i>health based</i> guide value for safe lifelong exposure of all population groups	GV (<i>LW = Leitwert</i>)	0.3 µg/L	<u>Section 3</u> : Composite concentrations of PFOA and PFOS are (still) tolerable for an entire lifetime up to this concentration
Precautionary <i>action</i> value for infants	PAV _i (<i>VMW_s = Vorsorge-Maßnahmewert für Säuglinge</i>)	0.5 µg/L	Section 2.4: precautionary protection of infants, e.g. against the presence of additional perfluorocarbons
Precautionary <i>action</i> value for adults	PAV ₀ (<i>VMW₀ = Vorsorge-Maßnahmewert für Erwachsene</i>)	5.0 µg/L	<u>Section 2.3 (PAV₀) and section 3 (AV₁₀)</u> in conjunction with the action value guidance: drinking water inadmissible for food processing and preparation

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