Environ. Sci. Technol. **2005**, *39,* 3904−3910

Exposure Assessment and Risk Characterization for Perfluorooctanoate in Selected Consumer Articles

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An exposure assessment and risk characterization was conducted to better understand the potential human health significance of trace levels of perfluorooctanoate (PFO) detected in certain consumer articles. PFO is the anion of perfluorooctanoic acid (PFOA). Concentrations of PFO in the consumer articles were determined from extraction tests and product formulation information. Potential exposures during consumer use of the articles were quantified based on an assessment of behavior patterns and regulatory guidance. Health benchmarks were developed and then compared to the exposure estimates to yield margins of exposure (MOEs). A simple one-compartment model was also developed to estimate contributions of potential consumer exposures to PFO concentrations in serum. While there are considerable uncertainties in this assessment, it indicates that exposures to PFO during consumer use of the articles evaluated in this study are not expected to cause adverse human health effects in infants, children, adolescents, adult residents, or professionals nor result in quantifiable levels of PFO in human serum.

Introduction

An exposure assessment and risk characterization was conducted to better understand the potential human health significance of trace levels of perfluorooctanoate (PFO, $C_8F_{15}O_2^-$) in consumer articles. PFO, the anion of perfluorooctanoic acid (PFOA, $C_8HF_{15}O_2$), has been detected at low parts-per-billion (ppb) levels in blood of the general population (*1*−*6*). The United States Environmental Protection Agency (U.S. EPA) has identified direct industrial use (*7*) and products used in various consumer goods (*8*) as possible contributors to these levels (*9*). Further, the U.S. EPA has issued a preliminary risk assessment for total human exposure to PFO based on biomonitoring studies (*10*) and has initiated a public process to identify and generate additional information to strengthen its risk assessment (*9*).

This study evaluates certain consumer articles manufactured with either fluorotelomers or fluoropolymers. Fluorotelomer-based products are typically manufactured through telomerization of tetrafluoroethylene (TFE, $CF_2{=}CF_2$) with perfluoroethyl iodide (CF_3CF_2I) to create a linear, even-carbon chain length perfluoroalkyl iodide mixture (*11*, *12*). Trace amounts of PFO may be generated during this process as an unintended byproduct (*13*−*17*). Fluorotelomer-based products are used to treat a variety of consumer articles (e.g., apparel and carpeting), primarily to impart stain and soil resistance.

Fluoropolymers are films (e.g., on nonstick cookware) or membranes (e.g., in outerwear) and are distinguished from traditional hydrocarbon polymers by a repeating fluorocarbon chain (-CF_2-) within the polymer backbone (*18*, *19*). The ammonium salt of PFO (ammonium perfluorooctanoate, APFO) is an essential processing aid in the formulation of such fluoropolymers. Thus, residual PFO may be present in fluoropolymer films and membranes used in manufacturing certain consumer articles. For more information, see the Supporting Information for the chemical properties of the PFO compounds.

The primary goal of this study was to understand the magnitude of exposures to PFO that may occur through consumer use of certain articles. Other possible sources of PFO in the environment were beyond the scope of this investigation. A secondary goal was to provide a context for the calculated exposures through a risk characterization. This study was based on the methods described in regulatory guidance and risk assessments.

Analytical Testing Program

Analysis of PFO. The exposure assessment was based on data from two types of tests: (a) the analysis of PFO in fluorotelomer-based product formulations (products) and (b) the extraction of finished consumer articles manufactured with fluoropolymers or fluorotelomer-based products. The analytical methods used in these tests have been described (*20*−*22*) and are based on the detection of PFO by high-performance liquid chromatography with tandem mass spectrometry (LC/MS/MS).

PFO concentrations detected in the fluorotelomer-based products (expressed as a mass of PFO per volume of fluorotelomer product) were used to estimate the total PFO concentrations in the consumer articles (expressed as a mass of PFO per mass of treated article). The extraction test results relate to the PFO mass that is extractable from a given surface area of the treated article (expressed as mass per area).

Table 1 presents the range of PFO concentrations detected in the fluorotelomer-based products and the corresponding total concentrations in the fluorotelomer-containing articles. Application rates and dilutions used in estimating the total PFO concentrations in the consumer articles based on the range of PFO concentrations detected in the fluorotelomer-based products are provided in the Supporting Information. Total PFO concentrations were calculated for the treated portion of the article only (e.g., for carpet fibers, excluding the backing).

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10.1021/es048353b CCC: $30.25

Published on Web 04/20/2005

TABLE 1. Analytical Test Results

article group	concentration in fluorotelomer product formulation (mg of PFO/L)	calculated total concn in finished consumer article[a] (mg of PFO/kg of article)	extraction test result for finished consumer article (ng of PFO/cm^2 article)	*N*[b]
Fluorotelomer-Containing Articles				
mill-treated carpeting	30−80	0.2−0.6	ND[c] (<0.2) to 23	>60
carpet-care solution-treated carpeting	1−50	0.2−2	28−50	14
treated apparel	ND (<1) to 40	ND (<0.02) to 1.4	ND (<0.01) to 12	>100
treated upholstery	ND (<1)	ND (<0.034)	0.4−4	3
treated home textiles	ND (<1) to 40	ND (<0.02) to 1.4	NT[d]	NT
treated technical textiles	ND (<1)	ND (<0.034)	NT	NT
treated nonwoven medical garments	ND (<1)	ND (<0.034)	ND (<0.02)	6
stone, tile, and wood sealants	ND (<1)	ND (<0.1)	NT	NT
industrial floor waxes and wax removers	5−120	0.0005−0.06	NT	NT
latex paint	50−150	0.02−0.08	NT	NT
home and office cleaners	50−150	0.005−0.05	NT	NT
Fluoropolymer-Containing Articles				
membranes for apparel	NA[e]	NA	0.008−0.07	20
nonstick cookware	NA	NA	ND (<0.1)	>40
thread seal tape	NA	NA	0.02−0.08	20

[a] Total concentration in article calculated based on PFO concentration in fluorotelomer product, product dilution, and product application rate. [b] *N*: number of samples. [c] ND: not detected (detection limit in parentheses). [d] NT: not tested; similar article group used as surrogate in assessment. [e] NA: not applicable.

As shown in Table 1, PFO concentrations in fluorotelomer-based products applied to upholstery, technical textiles, nonwoven medical garments, and stone, tile, and wood sealants were below detection limits. Total concentrations of PFO were not required in the exposure assessment for fluoropolymer-containing articles, which were evaluated using the extraction test results discussed next.

The PFO data from extraction tests performed on new (i.e., unused) consumer articles manufactured with fluorotelomer-based products or fluoropolymers are summarized in Table 1. The extraction test results are intended to provide an upper bound on the amount of PFO that may be extracted from the surface of the consumer articles under conditions that simulate human exposure (e.g., dermal contact). Accordingly, these tests were performed with a range of extractants—including water, simulated saliva, and simulated perspiration—that are relevant to assessing exposures to consumers.

As shown in Table 1, PFO was not detected in over 40 extraction tests on nonstick cookware, under test conditions simulating cooking and prolonged food or consumer contact. The manufacture of nonstick cookware includes a high-temperature step (i.e., sintering) (*23*−*25*) that would degrade residual PFO prior to article use by consumers (*26*). In addition, PFO was not detected in any samples of treated nonwoven medical garments nor in some samples of mill-treated carpeting and treated apparel. Thus, PFO may not be present in these articles or is present only at very low levels that are not readily detectable. In contrast, PFO was detected in extraction tests on treated upholstery even though it was not detected in the fluorotelomer-based product applied to the upholstery. This may result from unrelated background sources of PFO on upholstery.

The use of the test results for new articles, as opposed to aged articles, in the exposure calculations does not account for potential changes in source strength over time. This approach most likely leads to an overestimation of exposure; however, this is an area of ongoing investigation. Additional details on the calculation of total PFO concentrations in consumer articles and on the extraction tests are provided in the Supporting Information.

Dermal Permeability Tests. Absorption of PFO across the skin is a key parameter in the exposure assessment. In vitro studies of the permeability of APFO were conducted on nine samples of human epidermal membrane to estimate the dermal permeability coefficient (K_p) and the cumulative percent of PFO absorbed at 48 h (*27*). The K_p was reported as the mean (9.5×10^{-7} cm/h) and as the mean plus two standard deviations (1.5×10^{-6} cm/h). A dermal absorption coefficient (K_t) of 1.0×10^{-5} per h was calculated based on the cumulative percent absorbed at 48 h divided by the study period (48 h).

In this same study, the dermal permeability of APFO was tested using rat epidermal membranes. The in vitro dermal K_p was then used to predict the amount of APFO absorbed systemically in male rats in a 1985 dermal toxicity study (*28*). The low-effect level (for liver toxicity) derived based on the estimated absorbed dose was shown to be comparable to dietary and inhalation low-effect levels from in vivo studies (*29*−*31*), indicating that the in vitro dermal permeability coefficient for rat skin is predictive of in vivo penetration. These results suggest that the values of the similarly derived K_p for human skin would also be predictive of in vivo dermal penetration in humans.

Exposure Assessment

The objective of this study was to assess exposure to PFO through consumer use of certain articles manufactured with fluoropolymers or fluorotelomer-based products. Thus, the exposure assessment considered residents who use the articles as well as professionals who may be involved in the installation, application, or maintenance of the articles (e.g., carpet installers, tailors). Potential worker exposures associated with the manufacture of the product formulations or articles were not evaluated. Potential consumers were broken down by age groups (infants, children, adolescents, and adults) to reflect different behaviors and physiological parameters. Professionals were considered to be adults.

For each of these populations, exposures were quantified for mill-treated carpeting, solution-treated carpeting (including home application of carpet-care solution), apparel (treated with fluorotelomer-based product and sometimes containing a fluoropolymer membrane), treated nonwoven medical garments, nonstick cookware, and thread seal tape. Measurements of PFO levels in the consumer environment (e.g., indoor air, household dust, residential surfaces) are generally lacking and, even if available, would not be specific to the articles evaluated in this study. Instead, the analytical test results presented in Table 1 were used with exposure

TABLE 2. Consumer Articles and Exposure Pathways

article group	dermal contact with article	ingestion via hand-to-mouth contact	mouthing of article by infants	incidental ingestion of dust	inhalation of particulates	inhalation of vapor from article	ingestion of food in contact with article	inhalation of droplets
mill-treated carpeting	X[a]	X	U[b]	X	X	U	U	NE[c]
carpet-care solution and solution-treated carpeting	X[d]	X	U	X	X	U	U	X[e]
treated apparel	X	X	X	X	X	U	U	NE
treated nonwoven medical garments	X[f]	X[f]	X[f]	NE	NE	NE	NE	NE
nonstick cookware	X[f]	X[f]	NE	NE	NE	X[f]	X[f]	NE
thread seal tape	X	X	NE	NE	NE	NE	NE	NE

[a] X: exposures quantified. [b] U: evaluated in an uncertainties assessment. [c] NE: exposures not quantified. [d] Dermal contact is evaluated for both solution-treated carpeting and liquid carpet-care solution. [e] Inhalation of droplets evaluated for liquid carpet-care solution during spray application. [f] PFO was not detected in extraction tests conducted on treated nonwoven medical garments or nonstick cookware. To provide estimates for these articles, calculations were performed assuming PFO present at one-half the detection limit in the extraction medium.

pathway models developed for the selected consumer articles. Table 2 summarizes the exposure pathways quantified for each article group.

For each combination of receptor and exposure pathway, the exposure assessment framework was selected to (a) provide high-end estimates of potential intakes (referred to as reasonable maximum exposure [RME] estimates), (b) be consistent with or build upon regulatory guidance, and (c) correspond to the types of available analytical test data. The RME estimates were based on a combination of assumptions expected to substantially overstate typical exposure levels in the general consumer population and on the high end of the range of estimated total PFO concentrations and extraction test results. More typical exposure (MTE) estimates were also characterized using assumptions that represent more typical consumer conditions and central values (e.g., the mean or median) for estimated total PFO concentrations and extraction test results.

The models and input parameters are consistent with guidance and risk assessments issued by regulatory agencies under a variety of programs including the U.S. EPA (e.g., refs *32*−*34*), the Contaminants of Potential Concern (COPC) Committee of the World Trade Center (WTC) Indoor Air Task Force Working Group (*35*), and the U.S. Consumer Product Safety Commission (CPSC) (*36*). The overall approaches for assessing dermal, ingestion, and inhalation exposures are summarized next, with spreadsheets detailing all equations and input parameters provided in the Supporting Information.

Dermal Exposure Pathways

Dermal Exposure to Solid Articles. The transfer of PFO from a solid article across the skin and into the blood was characterized as a two-step process: (a) transfer of PFO from the surface of the article to perspiration on the surface of the skin and (b) absorption of PFO through the skin and into the blood. This two-step process is consistent with the approach used by the CPSC in its exposure and risk assessment of flame retardants in upholstered furniture (*36*) and by the U.S. EPA Office of Pesticide Programs to evaluate the transfer of residual pesticides on treated carpeting and other surfaces to the skin (*33*, *34*).

The consumer article extraction test results summarized in Table 1 were used to estimate the transfer of PFO from solid articles to perspiration on the skin (*20*, *22*). The K_t derived from the dermal permeability study results was used to characterize PFO absorption through the skin and into the blood. An expanded discussion of the dermal contact pathway is provided in the Supporting Information.

Dermal Exposure to Liquids. Transfer of PFO from liquid consumer articles (e.g., carpet-care solution) across the skin and into the blood was characterized as a one-step process. The amount of PFO transferred is based on the estimated PFO concentration in the liquid article, the skin surface area in contact with the liquid, the length of contact, and the K_p derived from the dermal permeability tests for PFO.

Ingestion Pathways

Ingestion of Chemical via Hand-to-Mouth Transfer. This pathway involves the transfer of PFO from an article to hands and subsequent ingestion as a result of hand-to-mouth contact. Critical exposure parameters include the frequency of hand-to-mouth events (in events per hour), the surface area of the portion of the hand in contact with the mouth, and the transfer efficiency of the chemical from article to hand and from hand to saliva. The hands are assumed to replenish with PFO through contact with the article prior to each hand-to-mouth event. The approach used to quantify exposures is based on U.S. EPA guidance (*33*, *34*).

A detailed discussion of the individual factors used to characterize hand-to-mouth transfer is presented in the Supporting Information since this pathway results in the highest calculated exposures for most consumer articles.

Ingestion of Indoor Dusts. This pathway involves the ingestion of dust that originates from the carpeting or apparel due to abrasion or other processes. The amount of PFO ingested was estimated based on indoor dust ingestion rates, the fraction of indoor dust attributable to the subject article, and the concentration of PFO in the abraded particles. Indoor dust ingestion rates and the fraction of dust from the subject article were based on information compiled by the U.S. EPA (*37*, *38*). The concentration of PFO in dust from the articles was assumed to be equal to the calculated total concentration in carpet or apparel fibers.

The PFO concentration in dust calculated in this study is within, but toward the lower end of, the range of PFO concentrations reported in household dust in Japan (*39*). Such household dust may be affected by sources other than treated carpeting and apparel.

For dust particles, oral absorption is modeled as a two-step process: extraction of PFO from the particle by body fluids (i.e., saliva and gastrointestinal fluids) and subsequent absorption from the gastrointestinal fluid into the blood.

Ingestion of Foods. This pathway was evaluated for treated cookware, assuming that PFO could be transferred from cookware into foods and subsequently ingested. PFO was not detected in extraction tests conducted on treated cookware under conditions simulating cooking or food contact. Thus, to quantify exposures, one-half the detection limit achieved in the extraction tests was assumed. As an uncertainty analysis, this pathway was also evaluated for treated carpeting and apparel, even though food is likely to

be in contact with these articles for only very short periods of time (on the order of minutes) and/or on a very infrequent basis.

Mouthing of Articles (by Infants). This pathway models the transfer of PFO from the article to saliva and subsequent swallowing of saliva, based on the approach described by CPSC (*36*). The surface area of article mouthed per day was assumed to be the area of an article that fits in a child's mouth (*36*, *40*). The amount of PFO ingested during the mouthing of an article was assumed to equal the mass extracted in the extraction tests.

Inhalation Pathways

Inhalation of airborne particles released from the article due to normal aging, abrasion, cutting, or other particle-generating processes was quantified for treated carpeting and apparel. Because of the lack of indoor airborne dust measurements for PFO, levels of respirable particulate matter (PM_{10}) in indoor air and the estimated concentration of PFO on the inhaled particles were derived from information in the U.S. EPA's Particle Team study (*38*). The concentration of PFO in dust from the articles was assumed to be equal to the total concentration in the article. Inhalation of liquid droplets was quantified for the carpet-care solution, which is typically applied to carpeting through a spray.

The volatility of PFO, an anion, was evaluated as a salt rather than as PFOA since PFOA is not expected to be present in finished articles for consumer distribution, and significant transformation from the salt form to PFOA is not expected under normal conditions of use. Although some volatile fluorinated organics have been reported in air (*41*, *42*), APFO and other common PFO salts are relatively nonvolatile; thus, negligible volatilization is anticipated except perhaps at elevated temperatures. For example, DuPont reports the vapor pressure for APFO to be only 0.00006 mm of Hg at 20 °C (see Supporting Information). Despite the limited volatility of PFO salts, screening-level calculations were conducted for articles where high temperatures are expected (i.e., ironing of apparel and heating of nonstick cookware) and for carpeting due to its potentially large surface area within the home and office.

Exposure Evaluation for Additional Article Groups

Several additional articles were evaluated using a surrogate approach based on the analytical data presented in Table 1 and estimated contact frequency relative to the article groups in Table 2. The additional articles were divided into two groups based on their physical characteristics and similarities in potential pathways for exposure. Treated apparel was selected as the surrogate for upholstery, home textiles, and technical textiles. The carpet-care solution was selected as the surrogate for liquid articles (i.e., stone, tile, and wood sealants; industrial floor waxes and removers; latex paint; and home and office cleaners). Details of the surrogate evaluation are presented in the Supporting Information.

Hazard Assessment and Risk Characterization

The risk characterization was conducted by comparing the intake estimates of PFO to Health Benchmarks, both expressed in milligrams per kilogram per day (mg/kg/day), to develop a margin of exposure (MOE) for each combination of consumer article, human receptor, and Health Benchmark. According to the U.S. EPA (*10*), the MOE calculated as the ratio of the administered dose from the animal toxicology study to the estimated human exposure level is a standard approach to risk characterization and is currently the standard approach to risk assessment for the U.S. EPA Office of Pesticide Programs (*43*). Although the U.S. EPA has concluded that a more accurate estimate of the MOE can be derived if measures of internal dose are available for humans and the animal model (*10*), there are significant limitations to reliably estimating the internal PFO dose in humans from exposure to specific consumer articles.

The Health Benchmarks used in this study are chronic exposure levels of PFO below which adverse effects are not expected to occur in the population considered in the toxicity studies. In the absence of the U.S. EPA-derived Health Benchmarks for PFO, a toxicity assessment for PFO was conducted, as summarized in the Supporting Information. This evaluation identified a noncancer systemic toxicity (liver effects) Health Benchmark of 3.9 mg/kg/day (corresponding human exposure is the annual average daily intake during each life stage), a developmental effects Health Benchmark of 22 mg/kg/day (corresponding human exposure is the annual average daily intake during the infant life stage), and a carcinogenic effects Health Benchmark of 5.1 mg/kg/day (corresponding human exposure is lifetime average daily intake). These Health Benchmarks are consistent with the results of previous investigations (*44*−*48*).

It is appropriate to consider potential interspecies differences in the pharmacodynamics, pharmacokinetics, and other factors when interpreting MOEs based on a comparison to Health Benchmarks derived from animal experiments. In particular, the clearance of PFO in the human appears to be significantly slower than in smaller animals. In evaluating MOEs across species, it is necessary to consider the effect of this difference in the clearance on the internal exposure (e.g., steady-state blood concentration) associated with a given external exposure. Furthermore, health effects observed in animals exposed to PFO are consistent with a mode of action involving the activation of peroxisome proliferators activated receptor alpha (PPARα), a mode of action to which rodents have been shown to be particularly sensitive. The likely role of PPARα-mediated processes in the observed effects argues against the default assumption of a greater sensitivity of the human as compared to the rodent. Overall, despite the large difference in pharmacokinetics between the studied animals and humans, MOE values exceeding a range of 100−1000 correspond to intakes that would not be expected to cause adverse human health effects, even in sensitive individuals within the general population, based on a consideration of PFO pharmacodynamics, pharmacokinetics, and other factors (see Supporting Information). This range is consistent with the U.S. EPA's typical application of an overall uncertainty factor between 100 and 3000 in deriving reference dose (RfD) values for humans from laboratory animal experiments (*49*). Given the potential severity of cancer and developmental effects, an additional factor of 10 may also be included, resulting in a range of 1000−10 000 when evaluating cancer and developmental endpoints for PFO.

Results and Discussion

Reasonable Maximum Exposure (RME) Scenarios. The input parameters and assumptions selected for the RME scenario included conservative estimates for the source concentrations and intermedia transfer factors and a combination of representative and high-end values for the contact frequency and physiological parameters. The RME estimates also incorporate screening-level article use patterns (e.g., all apparel and carpeting is assumed to be treated), such that the RME estimates represent intakes that are likely to be higher than the range of intakes that would be anticipated. The U.S. EPA and other agencies frequently rely on such RME estimates in evaluating individual exposures to avoid underestimating potential health risks.

Table 3 summarizes hypothetical aggregate intakes for each of the article groups and the corresponding MOE values under the RME case. (Results for the pathways evaluated in the uncertainty evaluation, as identified in Table 2, are

TABLE 3. Hypothetical Aggregate RME and MTE Intakes and Corresponding MOE Values

human receptor	hypothetical annual average intake (mg/kg/day)	hypothetical lifetime average intake (mg/kg/day)	MOE for developmental effects	MOE for noncancer effects	MOE for cancer effects
		Mill-Treated Carpeting			
infant	RME 6×10^{-5}	*[a]	RME 4×10^{5}	RME 7×10^{4}	*
	MTE 8×10^{-7}		MTE 3×10^{7}	MTE 5×10^{6}	
child	RME 5×10^{-5}	*	NA[b]	RME 8×10^{4}	*
	MTE 6×10^{-7}			MTE 6×10^{6}	
adolescent	RME 2×10^{-6}	*	NA	RME 2×10^{6}	*
	MTE 3×10^{-8}			MTE 1×10^{8}	
adult resident	RME 9×10^{-7}	RME 9×10^{-6}	NA	RME 5×10^{6}	RME 6×10^{5}
	MTE 2×10^{-8}	MTE 1×10^{-7}		MTE 3×10^{8}	MTE 4×10^{7}
professional	RME 7×10^{-7}	RME 3×10^{-7}	NA	RME 5×10^{6}	RME 2×10^{7}
	MTE 2×10^{-8}	MTE 8×10^{-9}		MTE 2×10^{8}	MTE 6×10^{8}
		Solution-Treated Carpeting			
infant	RME 1×10^{-4}	*	RME 2×10^{5}	RME 3×10^{4}	*
	MTE 4×10^{-6}		MTE 5×10^{6}	MTE 1×10^{6}	
child	RME 1×10^{-4}	*	NA	RME 4×10^{4}	*
	MTE 3×10^{-6}			MTE 1×10^{6}	
adolescent	RME 4×10^{-6}	*	NA	RME 9×10^{5}	*
	MTE 1×10^{-7}			MTE 3×10^{7}	
adult resident	RME 2×10^{-6}	RME 2×10^{-5}	NA	RME 2×10^{6}	RME 3×10^{5}
	MTE 6×10^{-8}	MTE 6×10^{-7}		MTE 7×10^{7}	MTE 8×10^{6}
professional	RME 2×10^{-6}	RME 6×10^{-7}	NA	RME 2×10^{6}	RME 8×10^{6}
	MTE 1×10^{-7}	MTE 4×10^{-8}		MTE 3×10^{7}	MTE 1×10^{8}
		Treated Apparel			
infant	RME 8×10^{-6}	*	RME 3×10^{6}	RME 5×10^{5}	*
	MTE 4×10^{-7}		MTE 6×10^{7}	MTE 1×10^{7}	
child	RME 5×10^{-6}	*	NA	RME 7×10^{5}	*
	MTE 8×10^{-8}			MTE 5×10^{7}	
adolescent	RME 5×10^{-7}	*	NA	RME 8×10^{6}	*
	MTE 1×10^{-8}			MTE 3×10^{8}	
adult resident	RME 2×10^{-7}	RME 1×10^{-6}	NA	RME 2×10^{7}	RME 4×10^{6}
	MTE 7×10^{-9}	MTE 3×10^{-8}		MTE 6×10^{8}	MTE 2×10^{8}
professional	RME 2×10^{-7}	RME 8×10^{-8}	NA	RME 2×10^{7}	RME 7×10^{7}
	MTE 2×10^{-8}	MTE 5×10^{-9}		MTE 3×10^{8}	MTE 1×10^{9}
		Treated Nonwoven Medical Garments			
all populations	ND	ND	ND	ND	ND
		Nonstick Cookware			
all populations	ND[c]	ND	ND	ND	ND
		Thread Seal Tape			
adult resident	RME 8×10^{-10}	RME 6×10^{-10}	NA	RME 5×10^{9}	RME 9×10^{9}
	MTE 2×10^{-11}	MTE 2×10^{-11}		MTE 2×10^{11}	MTE 3×10^{11}
professional	RME 1×10^{-7}	RME 5×10^{-8}	NA	RME 3×10^{7}	RME 1×10^{8}
	MTE 5×10^{-9}	MTE 2×10^{-9}		MTE 7×10^{8}	MTE 3×10^{9}

[a] *Lifetime average daily intake for adult resident and corresponding MOE for cancer effects includes intakes for the infant, child, and adolescent. [b] NA: not Applicable. MOEs corresponding to developmental effects calculated for the infant only. [c] ND: not detected. PFO was not detected in any extraction test. Evaluation of exposure using one-half the detection limit is included in the Supporting Information.

presented in the Supporting Information.) All estimated MOE values exceed, by at least a factor of 30, the range of 100−1000 that may be applied to account for uncertainties in the development of the noncancer systemic toxicity Health Benchmark for PFO. For the cancer and developmental effect endpoints, all estimated MOE values also greatly exceed the range of 1000−10 000 that incorporates an additional uncertainty factor of 10 to account for possible concerns regarding the severity of the effect. Thus, based on available toxicity and analytical data, hypothetical exposures to PFO during consumer use of the articles evaluated in this study would not be anticipated to cause adverse health effects, even in sensitive individuals within the general population.

As noted in Table 3, analytical tests did not detect PFO in any samples of treated nonwoven medical garments or nonstick cookware. Screening calculations for nonstick cookware and treated nonwoven medical garments were performed assuming that PFO is present at one-half the detection limit in the extraction medium. As shown in the Supporting Information, the theoretical intakes and MOE values estimated in the screening calculations for treated nonwoven medical garments and for nonstick cookware are no higher than the range estimated for the other articles considered in the exposure assessment. Thus, detection limits achieved in the analytical tests were sufficiently low to assess and draw conclusions regarding potential health risks from exposure to PFO in the consumer articles.

More Typical Exposure (MTE) Scenarios. For the MTE scenarios, the combination of input parameters and assumptions were selected to represent more typical consumer conditions and behavior in the general population.

Table 3 summarizes hypothetical aggregate intakes for each of the article groups, and corresponding MOE values, under the MTE case. The MTE intake estimates are generally 1−2 orders of magnitude lower than the corresponding RME intakes, and the MOEs are correspondingly higher.

Compartmental Modeling of Serum Concentrations in Adolescents, Adults, and Professionals. A considerable amount of the interest in PFO is associated with its detection in serum from the general population. At this time, it is not

possible to develop an accurate prediction of the levels of PFO that would occur in the serum of the human population as a result of exposures to the consumer articles evaluated because of substantial limitations in the understanding of the pharmacokinetics of PFO in humans (*50*). Nevertheless, to help in understanding the significance of the potential exposures described in this assessment, an approach was developed to provide a point of departure for interpreting estimated intakes in the context of reported PFO concentrations in human serum in the general population. This approach is based on the measured half-life of 1600 days for PFO in humans (*51*) and a volume of distribution ranging from 1.25 to 6.0 derived from subchronic monkey toxicity studies (*29*, *52*). This volume of distribution range is more appropriate for modeling chronic human exposure than the value of 0.2 from a single-dose monkey study (*44*) or chronic rat studies, as discussed in the Supporting Information. In the comparison to reported mean PFO concentrations in the human population, MTE rather than RME estimates were used in the compartmental model since MTE estimates reflect exposures more likely encountered in the general population.

Using the simple compartmental model, these hypothetical aggregate exposures to the consumer articles evaluated in this study correspond to serum concentrations ranging from approximately 0.05 to 0.25 ppb for the residential adolescent and adult and from about 0.05 to 0.25 ppb for the professional. The range of concentrations is less than the current quantitation limit for PFO in serum (i.e., approximately 0.5 ppb) and is in all cases well below the geometric mean of approximately 5 ppb typically reported in adults in the general U.S. population (*1*−*4*, *6*). Thus, theoretical aggregate exposure to PFO from the use of the consumer articles evaluated in this assessment would not be expected to result in quantifiable levels of PFO in human serum.

These estimated serum concentrations can be used to calculate internal MOEs for adolescents and adults, based on comparisons to internal benchmark concentrations. Such internal benchmark concentrations have been determined by Butenhoff et al. (*44*) as the lower 95% confidence limit of a modeled 10% response or incidence level ($LBMIC_{10}$). Using the internal benchmark concentrations from Butenhoff et al. (*44*) and the previous range of serum levels based on the MTE scenario, the internal MOEs exceed 90 000. Even under the RME scenario, the corresponding internal MOEs exceed 2000. Internal MOEs of this magnitude represent substantial protection of potentially exposed populations (*44*).

In summary, conservative exposure estimates, when combined with Health Benchmarks derived from robust toxicity studies, result in MOEs that indicate that exposure to PFO from consumer use of the articles examined in this study would not have the potential to cause adverse health effects in infants, children, adolescents, adult residents, or professionals, even in sensitive individuals within the general population.

Acknowledgments

The authors thank the reviewers of an early version of this study—Dr. Thomas Burke (Johns Hopkins University), Dr. F. Jay Murray (Murray and Associates), and Dr. Paul Price (The LifeLine Group)—and moderator Dr. George Gray (Harvard University) for their valued perspectives.

Supporting Information Available

Chemical and physical properties of perflurooctanoate (PFO), determining total PFO concentration in consumer articles, extraction tests, exposure to PFO via hand-to-mouth transfer, example intake equations and exposure parameters: dermal contact with treated apparel, spreadsheets detailing intake equations and exposure parameters, surrogate assessments, selection of health benchmarks, comparison of Health Benchmarks to human exposures, and compartmental modeling of serum concentrations. This material is available free of charge via the Internet at http://pubs.acs.org.

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Received for review October 21, 2004. Revised manuscript received February 16, 2005. Accepted March 16, 2005.

ES048353B