Environ. Sci. Technol. **2010,** *44,* 7852–7857

Long-Term Simulation of Human Exposure to Atmospheric Perfluorooctanoic Acid (PFOA) and Perfluorooctanoate (PFO) in the Osaka Urban Area, Japan

TAMON NIISOE,[†] KOUJI H. HARADA,[†] HIROHIKO ISHIKAWA,[‡] AND AKIO KOIZUMI*[,†]

Department of Health and Environmental Sciences, Graduate School of Medicine, Kyoto University, Kyoto 606-8501, Japan, and Research Division of Atmospheric and Hydrospheric Disasters, Disaster Prevention Research Institute, Kyoto University, Uji 611-0011, Japan

Received January 25, 2010. Revised manuscript received August 26, 2010. Accepted September 9, 2010.

A publicly available atmospheric transport model, the Weather Research and Forecasting Chemistry Model (http://ruc.noaa.gov/wrf/WG11/), was used to simulate atmospheric perfluorooctanoic acid (PFOA) and perfluorooctanoate (PFO) emitted from a point source in the Osaka urban area (also known as Keihanshin), Japan. The time period of the simulation was from 1983 to 2008. The modeled air concentrations were highly correlated ($r = 0.91$) with the observed air concentrations. Intake levels by inhalation of simulated air concentrations and through the gastrointestinal tract as estimated by the food duplicate method were input to a pharmacokinetic model of the human body to simulate serum concentrations of PFOA and PFO (PFO(A)). For validation of the atmospheric model, simulated values were compared with those observed in serum samples. The simulated values generally agreed with those observed in serum samples from residents of the Keihanshin area ($r = 0.93$). It was confirmed that the atmospheric model was generally capable of projecting features of atmospheric PFO(A) as well as serum concentrations of PFO(A) in this case. The results indicated a dominant contribution of the atmospheric component to serum PFO(A) in humans near the point source in the Keihanshin area. In 2008, that contribution was about 70%.

Introduction

Perfluorooctanoic acid (PFOA) and its conjugate base, perfluorooctanoate (PFO), are artificial carboxylic acid and carboxylate used for industrial and commercial purposes such as lubricants, paints, surfactants, and additives for fluoropolymer (FP) production. PFOA and PFO are collectively referred to as PFO(A). PFO(A) has been produced and widely used since the 1940s and has accumulated in the environment because of its persistent character. In recent years, PFO(A) has become recognized as a hazardous substance owing to its toxicity and carcinogenic potential in animals (*1*).

The sources of human exposure to PFO(A) are still unknown. PFO(A) concentrations in human serum collected in the Keihanshin area of Japan have been reported to be much higher than those collected in other regions (*2, 3*). Contamination levels in wastewater and ecological samples strongly suggest that the Daikin Industries plant in Settsu city in Osaka prefecture is an emission source of PFO(A) (*4, 5*). Assessment of the gastrointestinal tract (GIT) intake of PFO(A) by females residing within 4.5 km of the Settsu plant and females living in Karakuwa, a small town in northern Japan (Figure 1A), in 2004 strongly suggests a large contribution of inhaled PFO(A) to the total body burden of PFO(A) (*3*). Although there have been several air monitoring campaigns in the Keihanshin area (*6*−*8*), understanding of the contribution of exposure through inhalation is incomplete. To obtain a more comprehensive understanding, we propose a novel approach that combines atmospheric modeling and pharmacokinetic (PK) modeling.

In this work, we applied an atmospheric transport model to simulate long-term inhalation exposure to PFO(A) in the Keihanshin area from 1983 to 2008. The modeled surface air concentrations of PFO(A) served as inputs to a PK model to calculate PFO(A) concentrations in human serum. The current study demonstrated that a unified model could simulate effects of exposure by inhalation under the scenario in which a point emission source and its industrial activity are reasonably well-characterized.

Materials and Methods

Atmospheric Transport Model. We applied version 3.0 of the fully coupled Weather Research and Forecasting/Chemistry (WRF-Chem) model (*9*) (http://ruc.noaa.gov/wrf/WG11/). WRF is a nonhydrostatic mesoscale meteorological forecasting model developed by the collaboration of several atmospheric research institutes (*10*). Various chemical modules have been implemented in the WRF framework, creating WRF-Chem. Meteorological fields such as wind and precipitation are predicted simultaneously by the same model. In WRF-Chem, air constituents are transported by the predicted meteorological fields using the same grid, the same time step, and the same physical schemes without interpolation. The target domain was square (450 km wide) and centered on Settsu (Figure 1A). The horizontal resolution was 9 km. The vertical structure consisted of 18 layers from the surface to 300 hPa. Typically, the depth of the lowest layer was about 50 m. The boundary and initial conditions for meteorological prediction were derived from 6-h meteorological fields determined from JRA-25 reanalysis data sets provided by the Japan Meteorological Agency and the Central Research Institute of Electric Power Industry (*11*). Model options are described further in the Supporting Information (section S1).

In WRF-Chem, PFO(A) is transported by grid-resolved wind fields and subgrid scale mixing both as soluble gas and as particulate matter without any chemical production or degradation. The residence time of the chemical related to advection (out of model domain) probably dominates at the spatial scale of the model. The removal processes are wet deposition and dry deposition. Model formulations for wet deposition, including in-cloud and subcloud scavenging, were modified as described in the Supporting Information (section S2). Gravitational settling was considered in the transport and dry deposition of particles.

Few observational data have been collected on the state of atmospheric PFO(A). In 2005, we observed a bimodal size distribution of atmospheric PFO(A) with peaks around

* Corresponding author phone: 81-75-753-4456; fax: 81-75-753-4458; e-mail: Akio.Koizumi@z06.mbox.media.kyoto-u.ac.jp.
[†] Graduate School of Medicine.
[‡] Disaster Prevention Research Institute.

10.1021/es101948b

Published on Web 09/22/2010

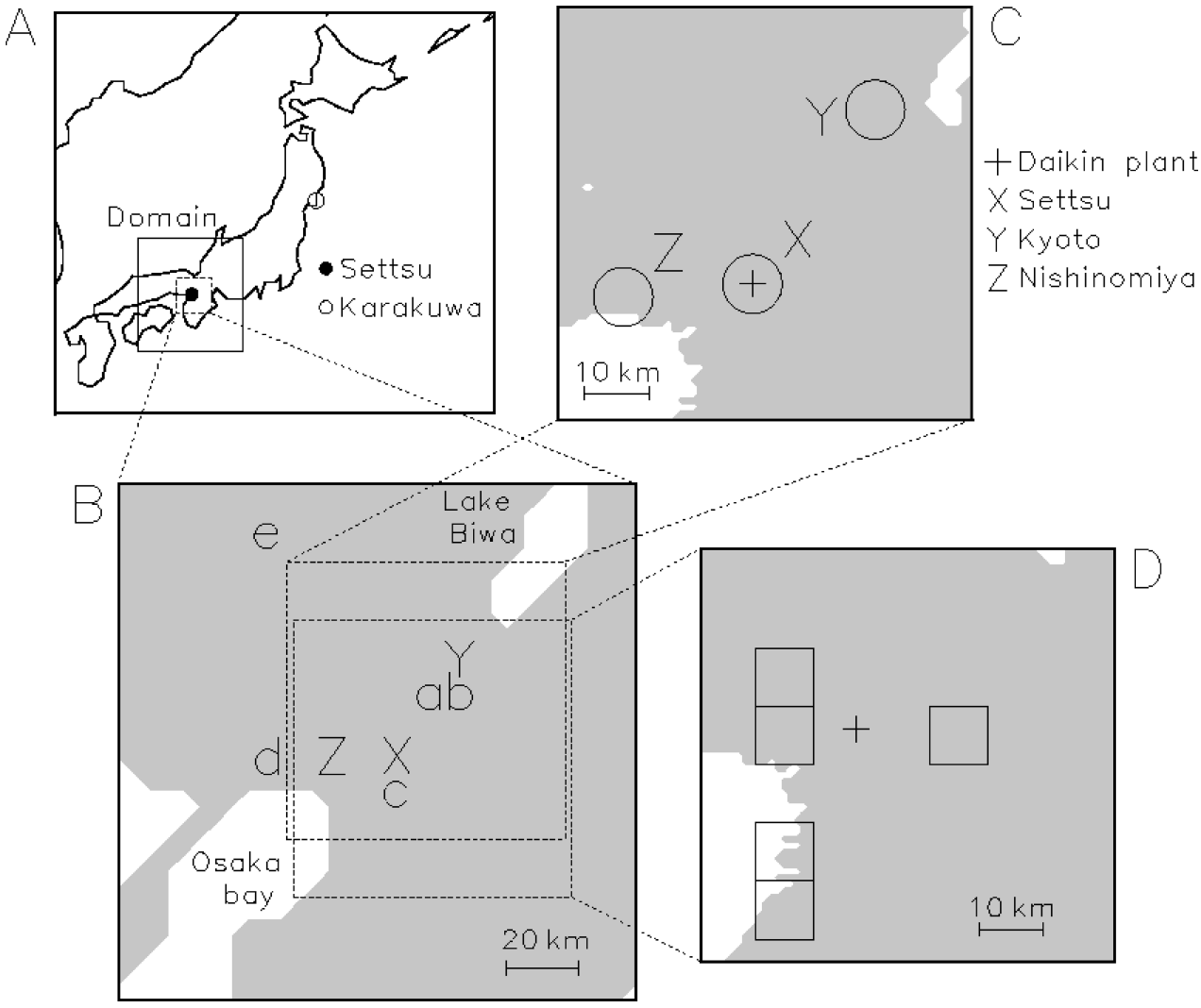

FIGURE 1. (A) Geographical locations of Settsu, Karakuwa, and the target domain. (B) An enlargement of the central region of the target domain. The characters represent the model grids corresponding to the observation sites (a-e for air and X-Z for serum) listed in Tables S3 and S4 (*2, 3, 6–8, 23, 24*). (C) Location of the Daikin plant and the three target population areas in the serum PFO(A) simulation of the Osaka urban area. Target areas have radii of 4.5 km and are centered at 34.761°N, 135.560°E (the Daikin plant location) for Settsu, 35.011°N, 135.768°E for Kyoto, and 34.738°N, 135.342°E for Nishinomiya. (D) Locations of the five grid elements of the atmospheric model used in the serum PFO(A) simulation for Osaka residents. The five grid elements are centered at 34.560°N, 135.470°E; 34.728°N, 135.470°E; 34.806°N, 135.470°E; 34.728°N, 135.770°E; and 34.482°N, 135.470°E. The position of the Daikin plant (+) is shown.

diameters of 0.7 and 3.3 μm in the town of Oyamazaki, which is about 20 km northeast of the Daikin plant (*6*), as shown in Figure S1. Although we did not measure gaseous PFOA directly, we trapped both gaseous PFOA and PFO(A) on particulate matter using quartz fiber filters (QFFs), on which gaseous PFOA has been reported to be absorbed irreversibly (*12*). Therefore, gaseous PFOA was included in the observed concentrations of atmospheric PFO(A). The air was collected with an Andersen cascade impactor sampler (AN-200, Tokyo Dylec Co., Tokyo, Japan). This sampler could divide atmospheric substances into nine size bins according to their aerodynamic size. Molecules of gaseous constituents were grouped as the smallest particles in the atmosphere. Accordingly, we recognized that gaseous PFOA belonged in the smallest size bin, which contained less than 10% of the total mass. In the present study, we assumed that 10% of PFO(A) is gaseous PFOA and the rest is particulate PFO(A), for which a fixed diameter of 5.0 μm was used. The effects of the fraction of gas and particle diameter on atmospheric concentrations were explored using sensitivity tests as described in the Supporting Information (section S6). The simulation period was from 1983 to 2008. An initial atmospheric concentration of zero was assumed.

PFO(A) Emission from the Daikin Plant in Settsu. The Daikin plant (34.761°N, 135.560°E) is the only major chemical plant manufacturing FP in Settsu. We estimated the annual flux of PFO(A) in discharged water at 6.6 t yr^{-1} in 2003 on the basis of an investigation of wastewater at the Aikawa Ryuiki disposal site (*4*). We derived the PFO(A) emission flux to the air as 2.3 t yr^{-1} in 2003 using an estimated ratio of the discharged portion in water to air of 65%:23% (*13*). The remaining 12% was discharged into the soil. The volatilization of gas from the surface water and soil was assumed to be negligible relative to the direct emission from the plant. The magnitude of the estimated emission flux was evaluated in relation to the national FP production, as described in the Supporting Information (section S3).

Annual emission rates were estimated from those in 2003 using the scale factors listed in Table S1. The scale factors were equal to the ratio of yearly national FP production to that for 2003 (*14*) before 2004; thereafter, they decreased following the values given in a press release from Daikin

(*15*). Estimated emission rates from the Daikin plant in Settsu peaked in 2000 and decreased after 2005 (Figure S2). Emission was assumed to occur exclusively in the lowest layer at the point corresponding to Settsu.

PFO(A) may originate from the degradation of fluorotelomer-based precursors. However, these indirect sources were considered to be negligible near such a strong point source in the Keihanshin area because they contribute very little even at the global scale (*13*). Wallington et al. used a three-dimensional global model to simulate PFO(A) production in the atmosphere from the oxidation of 8:2 fluorotelomer alcohols (*16*). The highest simulated PFO(A) concentration at 50 m was approximately 3×10^3 molecules cm^{-3}, which corresponds to 2×10^{-2} pg m^{-3} and is thus negligible in the context of the present study.

Air Monitoring Data Sets. We conducted air sampling to observe atmospheric PFO(A) concentrations in the town of Oyamazaki in 2001 and 2005, and in Fukuchiyama city (northern Kyoto prefecture) in 2005 (Figure 1B) (*6, 7*). We also used atmospheric concentrations observed in the Keihanshin area during an environmental survey sponsored by the Ministry of Environment of Japan in 2004 (*8*) (Table S3). Since those air samples were collected on QFFs, the data represent the sum of gaseous PFOA and particulate PFO(A). The total amounts of gaseous PFOA and particulate PFO(A) simulated by the current model were compared to those data.

Target Population and the PK Model. We simulated serum levels of PFO(A) in residents of three urban areas having radii of 4.5 km in the Keihanshin area. The three urban areas were Settsu, Kyoto, and Nishinomiya as shown in Figure 1C. The urban areas were centered at 34.761°N, 135.560°E (the location of the Daikin plant) for Settsu, 35.011°N, 135.768°E for Kyoto, and 34.738°N, 135.342°E for Nishinomiya. In addition, we simulated inhaled amounts of PFO(A) for Osaka residents, for which the geometric mean (GM) serum concentration of PFO(A) in 2003 was known (*2*). Inhaled amounts for Osaka residents were derived from surface air concentrations averaged over five grid elements determined from their geographical addresses (Figure 1D).

The serum level of PFO(A) was predicted using a one-compartment PK model (*17*)

$$V\frac{dC(t)}{dt} = \frac{E}{W} - (k_t + k_m) \cdot C(t) \quad (1)$$

$$k_t = \frac{\ln(2)}{T(1/2)}V,\ k_m = \frac{V_m}{W \cdot N_d} \quad (2)$$

where V is the volume distribution (300 mL kg^{-1} (*17*)), and C is the serum concentration (ng mL^{-1}) of PFO(A). E is the PFO(A) intake (ng day^{-1}), and W is the body weight (50 kg (*17*)). k_t and k_m represent the total clearance of males and menstrual serum loss (mL kg^{-1} day^{-1}), respectively. $T(1/2)$ is the biological half-life (1273 day (*18*)) of PFO(A). V_m is the menstrual serum loss volume (42.0 mL (*19*)), and N_d is the total number of days in the month.

In some previous studies, much greater values of V were applied (*20*). The rationale for selecting the current value (300 mL kg^{-1}) for the volume distribution was based on the total mass balance observed in our previous study (*21*) (see discussion in the Supporting Information; section S7). The Euler forward time step was set to 1 day. The initial concentrations were set at 2.6 ng mL^{-1} based on a linear regression of serum sample observations (*2*). In preliminary tests, we confirmed that the effects of initial concentrations persisted for only a few years.

The current PK model has two routes of exposure to PFO(A): inhalation and GIT intake. The exposure concentration of PFO(A) in inhaled air was derived from the surface air concentration calculated by the atmospheric model. The inhaled volume was assumed to be 20 m^3 day^{-1} (*22*). PFO(A) in the lungs was assumed to be absorbed completely by the respiratory tract. The absorption rates through respiration did not have significant effects as discussed in the Supporting Information (section S6). Intake, which represents GIT intake including PFO(A) intake from both diet and drinking water (*3*), was considered to be a function of time and proportional to the emission rate of PFO(A) from the plant until 2004. We assumed the lower and upper limits of intake for 2004 to be the 25th (43.4 ng day^{-1}) and the 75th (98.0 ng day^{-1}) percentiles of the GIT PFO(A) intake observations in food duplicate samples collected in Settsu in 2004 (*3*). Intake was assumed to be constant after 2004.

Diet, Drinking Water, and Serum Samples. To estimate intake of PFO(A) by the GIT, we used concentrations in food and drinking water consumed during 24-h periods by participants in the Settsu area by the food duplicate method (*23*). Those participants also donated serum samples. Daily intake of PFO(A) estimated from those samples was 61.4 ng day^{-1} [GM] with a standard deviation of 1.62 [geometric standard deviation (GSD)] (*3*). Serum samples for adult females living in the Settsu area, Kyoto area, Nishinomiya area, and Osaka areas (*2, 3, 24, 25*) (Table S4) were used for comparison with serum levels simulated by the PK model. The samples were donated by the Kyoto University Human Specimen Bank (*23*).

Evaluation of Model Fit. The fit of the simulated values to the observed values was evaluated by the fractional difference f (*26*) averaged over all samples

$$f = \frac{V_{mdl} - V_{obs}}{V_{mdl} + V_{obs}} \quad (3)$$

where V_{mdl} and V_{obs} are the modeled value and observed value, respectively. $|f| < 0.33$ indicates an error factor of less than 2.

Results and Discussion

Surface Air Concentration. Since PFO(A) has one strong point source and it is not produced in the atmosphere in these simulations, modeled air concentrations were quite variable and dependent on the wind field. The predicted winds agreed well with observed data in all seasons as described in the Supporting Information (section S4). The monthly average concentrations of PFO(A) modeled reflected wind directions, which were mainly northerly in January and southerly in July as shown in Figure S3, demonstrating the seasonality of modeled surface air concentrations in 2001. The monthly average concentration modeled in the town of Oyamazaki, which is grid point "a" in Figure S3, was 168 pg m^{-3} in January and 677 pg m^{-3} in July, whereas the instantaneous modeled concentrations in the 2-h interval changed markedly from greater than 2 ng m^{-3} to less than 10 pg m^{-3} depending on whether the location was downwind or upwind of the point source. The annual average distribution simulated showed no particular horizontal tendency. The modeled concentrations were greatest (>1 ng m^{-3}) near the source and were more than 100 pg m^{-3} throughout the Keihanshin area (Figure S3). Almost half (48%) of the PFO(A) emitted to the atmosphere was transported out of the domain area by air flow. The percentage of PFO(A) removed within the domain by dry and wet deposition were 46% and 6%, respectively (Supporting Information; section S5).

Modeled surface air concentrations of PFO(A) were compared with observations in the target domain listed in Table S3 (*6*–*8*). Predicted concentrations were averaged over the same periods as the observations. Observed PFO(A) concentrations ranged widely from 15.2 pg m^{-3} in Fukuchiyama city to 1261 pg m^{-3} in Osaka city (Table S3). The

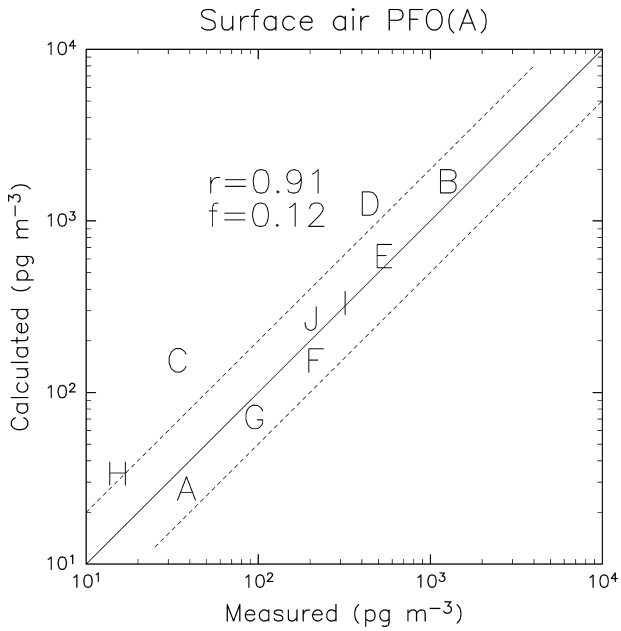

FIGURE 2. Comparison of observed and modeled surface air concentrations in the 2000s (pg m^{-3}) at various sampling sites. Agreement is indicated by a correlation coefficient *r* of 0.91 ($p = 2.6 \times 10^{-4}$) and an averaged fractional difference *f* of 0.12. Observations at sampling sites (*6*–*8*) are denoted A, B, and so on. Geographical locations are given in Table S3. Symbols on the solid line indicate a perfect fit between observation and calculation, and those lying between the two dashed lines indicate error factors of less than 2.

model simulations generally matched observed concentrations in the 2000s as indicated by a high correlation coefficient of 0.91 ($p = 2.6 \times 10^{-4}$) as shown in Figure 2. General agreement was also indicated by an *f* value of 0.12. Seven out of ten samples were reproduced with an error factor lower than 2. The error factors of the three other samples (C, D, and H) were lower than 5. The presence of error factors higher than 2 may have been due to an inaccuracy of the predicted wind fields or of the topography around the sampling sites. Additional observations are necessary to further evaluate the atmospheric model.

Estimated PFO(A) Intake. Reflecting surface air concentrations, estimated inhaled intake in Settsu was 1 order of magnitude greater than that in Kyoto and Nishinomiya, which was comparable to our previous estimate of 3.9 ng day^{-1} (*6*) (Figure S4). Likewise, the inhaled intake in Osaka was negligible, although it was consistently greater than in Kyoto and Nishinomiya. The inhaled intake in Settsu exceeded 50 ng day^{-1} for most of the period, and it was much greater than the estimated GIT intake until 2005. Spikes in inhaled intake levels resulted from variability in air concentrations.

Serum Levels of PFO(A) in Residents of the Keihanshin Area. Figure 3 shows temporal trends of serum PFO(A) levels on a logarithmic scale for residents of the Settsu area, Kyoto area, Nishinomiya area, and Osaka areas. Inhaled intakes were assumed to be homogeneous for each target population, whereas GIT intakes were variable among individuals in general population. The model results represented variable in GIT intakes by the lower and upper bounds. Figure 3 also compares calculated serum levels with observed levels in the samples collected in these areas (*2*, *3*, *24*, *25*). The model reproduces temporal trends found in the samples in Settsu and Kyoto, where levels increased until 2005 and then decreased. Calculated serum levels generally agreed with observations as indicated by a high correlation coefficient *r* of 0.93 ($p = 9.5 \times 10^{-5}$) and a small

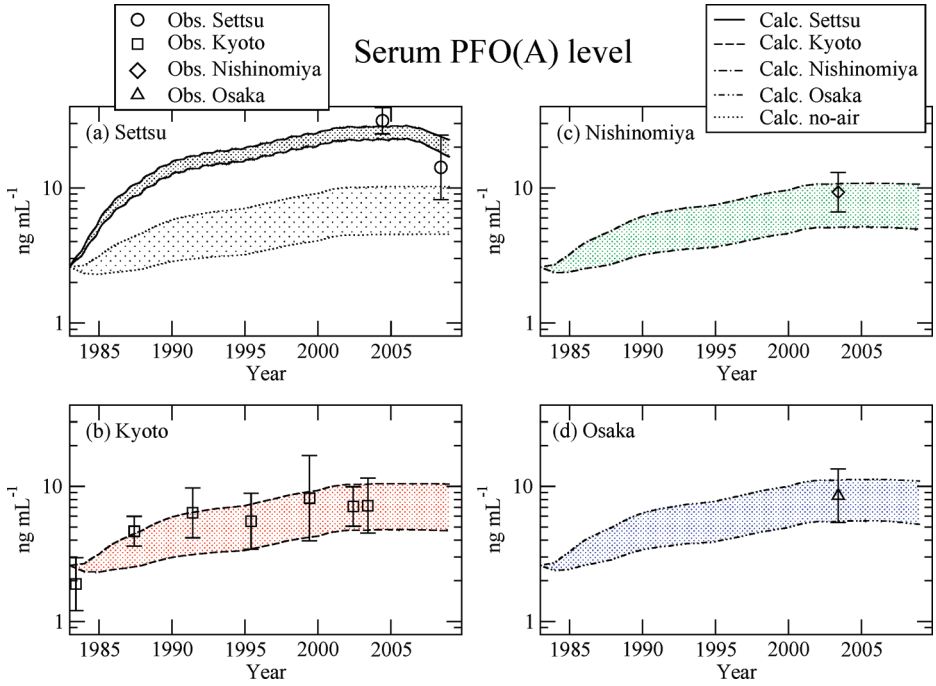

FIGURE 3. Serum PFO(A) levels on a logarithmic scale (lines, in ng mL^{-1}) calculated using simulated surface air concentrations and observed in samples from residents. The model reproduced the temporal trend of serum concentrations of PFO(A) in residents living in the Settsu area (a) and the Kyoto area (b). The modeled levels also agreed with observations in 2003 from the Nishinomiya area (c) and from Osaka residents (d). The case without respiratory exposure (no-air) is also shown (a). The results of the no-air run almost overlapped with those of the control run for Kyoto, Nishinomiya, and Osaka. Symbols represent GM of observed serum PFO(A) levels (*2, 3, 24, 25*) for Settsu (circle), Kyoto (square), Nishinomiya (diamond), and Osaka (triangle). Error bars represent one GSD. Lower and upper bounds of calculated serum values are shown by belts. The values correspond to serum levels for GIT intake at the 25th and 75th percentiles of values extrapolated from observed values in 2004 (*3*).

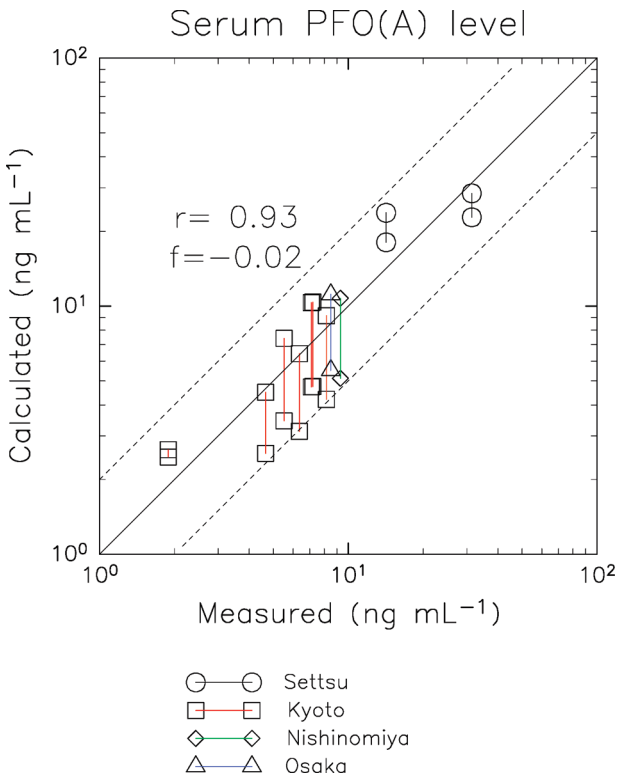

FIGURE 4. Comparison of serum PFO(A) levels (ng mL^{-1}) between model results and observations listed in Table S4 (*2, 3, 24, 25*). Agreement is indicated by a correlation coefficient *r* of 0.93 ($p = 9.6 \times 10^{-5}$) and an averaged fractional difference *f* of −0.02. The calculated concentrations are represented by line segments using the lower and the upper limits of GIT intake (black for Settsu, red for Kyoto, green for Nishinomiya, and blue for Osaka). The observed concentrations are GM from each set of samples. The two dashed lines indicate an error factor of 2; *r* and *f* were calculated using the average of the lower and upper limits of modeled concentrations.

fractional difference *f* of −0.02 (Figure 4). All eleven samples were reproduced by error factors less than 2.

Serum levels for the case without inhaled intake (no-air run) are also shown in Figure 3. Differences between the control run and the no-air run represent the atmospheric PFO(A) contribution to total serum levels. The atmospheric contributions are dominant in Settsu (from 67.4% in the upper oral intake case to 79.8% in the lower oral intake case in 2008) but negligible in Kyoto and Nishinomiya. Modeled PFO(A) levels for Osaka residents are similar to those of the Kyoto area and Nishinomiya area. The model results reveal that the high PFO(A) level of 31.4 ng mL^{-1} observed in Settsu in 2004 is attributed mainly to the atmospheric component. It should be noted that serum concentration levels of PFO(A) in the Keihanshin area are greater than those in other areas (*2, 3*). Excess PFO(A) intake by residents of the Keihanshin area may be attributed to their consumption of drinking water (*4*). However, specifying contributions of various sources of intake requires further study.

The serum levels of Settsu residents decreased after 2005 as a result of emission control by the manufacturer. However, PFO(A) levels in Keihanshin residents remained higher than levels in other areas, which were less than 5 ng mL^{-1} in the 2000s (*2, 3*). The persistence of PFO(A) is attributed to its long half-life.

Recent epidemiological studies have suggested that PFO(A) may have adverse health effects on fetal growth at much lower serum concentrations in mothers (*27, 28*) than those observed in females of Settsu in 2008. For this reason, adverse health effects on fetal and neonatal growth should be evaluated epidemiologically in the population within a 4.5 km radius of the Daikin plant.

In this study, we combined an atmospheric model and a PK model to evaluate long-term inhalation exposure to PFO(A) in the Osaka urban area. The model results for PFO(A) concentrations both in surface air and in human serum generally agree with observations. Sensitivity analysis demonstrated that changes in model parameters did not have profound effects on the simulation results [Supporting Information (section S6)]. However, it is necessary to characterize chemical and physical properties in the atmosphere as well as the pharmacokinetic behavior of PFO(A) in greater detail. For example, particle size and absorption by the respiratory tract are not fully understood.

It should be noted that the target domain in this study is small and near a strong point source. Other sources are assumed to be negligible. For large-scale modeling, other sources should be included such as gaseous PFOA emission by volatilization from the surface of the earth (*29*) and by release from marine aerosols enriched with surfactant PFO (*30*). It should be also noted that there is an argument regarding the irreversibility of gaseous PFOA sorption by QFFs (*31, 32*). To observe the atmospheric PFO(A) more accurately, it might be necessary that PFO(A) on particulate matter and gaseous PFOA are collected separately and simultaneously by appropriate devices, such as surface-deactivated QFFs and downstream sorbents (*12*).

The combination of atmospheric transport modeling and PK modeling has great potential. When modeling results are validated by comparisons with monitoring samples from human specimen banks, they can aid in reconstruction of human exposure intensity over previous decades. This approach can be applied to other chemicals and to other regions where both human blood and food duplicate samples are available. In an earlier study, we developed a global atmospheric transport model for long-term simulation of atmospheric lead (*33*). Using the approach described herein, we are now expanding that work to the study of human exposure to atmospheric lead from 1979 to 2009 in four East Asian countries: Japan, Korea, China, and Vietnam.

Here, we have demonstrated an approach to reconstruction of historical human exposure using existing estimates of emissions. Atmospheric modeling in combination with PK modeling can also serve to assess unknown emissions or to predict human exposure trends in the future using various emission scenarios. Therefore, this approach will be useful not only in emission control but also in environmental decision making.

Acknowledgments

This project was supported primarily by the Japan Science and Technology Agency (1300001, 2008−2010). The meteorological data used in this study were from the JRA-25 long-term reanalysis data set developed in a cooperative research project of the Japan Meteorological Agency and the Central Research Institute of Electric Power Industry.

Supporting Information Available

Information regarding model options and modifications as well as additional results and discussion. This material is available free of charge via the Internet at http://pubs.acs.org.

Literature Cited

(1) *The Science Advisory Board (SAB) review of EPA's draft risk assessment of potential human health effects associated with PFOA and its salts*; EPA-SAB-06-006; U.S. Environmental Protection Agency: Washington, DC, 2006. www.epa.gov/sab/pdf/sab_06_006.pdf (accessed January 10, 2010).

(2) Harada, K.; Koizumi, A.; Saito, N.; Inoue, K.; Yoshinaga, T.; Date, C.; Fujii, S.; Hachiya, N.; Hirosawa, I.; Koda, S.; Kusaka, Y.; Murata, K.; Omae, K.; Shimbo, S.; Takenaka, K.; Takeshita,

T.; Todoriki, H.; Wata, Y.; Watanabe, T.; Ikeda, M. Historical and geographical aspects of the increasing perfluorooctanoate and perfluorooctane sulfonate contamination in human serum in Japan. *Chemosphere* **2007**, *66*, 293–301, DOI 10.1016/j.chemosphere.2006.05.010.

(3) Kärrman, A.; Harada, K.; Inoue, K.; Takasuga, T.; Ohi, E.; Koizumi, A. Relationship between dietary exposure and serum perfluorochemical (PFC) levels—A case study. *Environ. Int.* **2009**, *35*, 712–717, DOI 10.1016/j.envint.2009.01.010.

(4) Saito, N.; Harada, K.; Inoue, K.; Sasaki, K.; Yoshinaga, T.; Koizumi, A. Perfluorooctanoate and perfluorooctane sulfonate concentrations in surface water in Japan. *J. Occup. Health* **2004**, *46*, 49–59.

(5) Morikawa, A.; Kamei, N.; Harada, K.; Inoue, K.; Yoshinaga, T.; Saito, N.; Koizumi, A. The bioconcentration factor of perfluorooctane sulfonate is significantly larger than that of perfluorooctanoate in wild turtles (*Trachemys scripta elegans* and *Chinemys reevesii*): An Ai river ecological study in Japan. *Ecotoxicol. Environ. Saf.* **2006**, *65*, 14–21, DOI 10.1016/j.ecoenv.2005.03.007.

(6) Harada, K.; Nakanishi, S.; Sasaki, K.; Furuyama, K.; Nakayama, S.; Saito, N.; Yamakawa, K.; Koizumi, A. Particle size distribution and respiratory deposition estimates of airborne perfluorooctanoate and perfluorooctanosulfonate in Kyoto area, Japan. *Bull. Environ. Contam. Toxicol.* **2006**, *76*, 306–310, DOI 10.1007/s00128-006-0922-1.

(7) Harada, K.; Nakanishi, S.; Saito, N.; Tsutsui, T.; Koizumi, A. Airborne perfluorooctanoate may be a substantial source contamination in Kyoto area, Japan. *Bull. Environ. Contam. Toxicol.* **2005**, *74*, 64–69.

(8) *Chemicals in the environment: Report on environmental survey and monitoring of chemicals in FY2005*; Environmental Health Department, Ministry of the Environment, Ministry of Japan: Tokyo, 2005 www.env.go.jp/chemi/kurohon/en/http2005e/03-cie/cie2005.pdf (accessed January 10, 2010).

(9) Grell, G. A.; Peckham, S. E.; Schmitz, R.; McKeen, S. A.; Frost, G.; Skamarock, W. C.; Eder, B. Fully coupled "online" chemistry within the WRF model. *Atmos. Environ.* **2005**, *39*, 6957–6975, DOI 10.1016/j.atmosenv.2005.04.027.

(10) Skamarock, W. C.; Klemp, J. B.; Klemp, J. B.; Dudhia, J.; Gill, D. O.; Barker, D. M.; Duda, M. G.; Huang, X.-Y.; Wang, W.; Powers, J. G. A description of the Advanced Research WRF Version 3. *NCAR Tech. Note* 2008NCAR/TN-475+STR.

(11) Onogi, K.; Tsutsui, J.; Koide, H.; Sakamoto, M.; Kobayashi, S.; Hatsushika, H.; Matsumoto, T.; Yamazaki, N.; Kamahori, H.; Takahashi, K.; Kadokura, S.; Wada, K.; Kato, K.; Oyama, R.; Ose, T.; Mannoji, N.; Taira, R. The JRA-25 reanalysis. *J. Meteorol. Soc. Jpn.* **2007**, *85*, 369–432.

(12) Arp, H. P. H.; Goss, K.-U. Irreversible sorption of trace concentrations of perfluorocarboxylic acids to fiber filters used for air sampling. *Atmos. Environ.* **2008**, *42*, 6869–6872, DOI 10.1016/j.atmosenv.2008.05.012.

(13) Prevedouros, K.; Cousins, I. T.; Buck, R. C.; Korzeniowski, S. H. Source, fate and transport of perfluorocarboxylates. *Environ. Sci. Technol.* **2006**, *40*, 32–44, DOI 10.1021/es0512475.

(14) *The supply and demand trend of material fluoropolymer* (in Japanese). www.jfia.gr.jp/jfiadata/jyukyu.htm (accessed January 10, 2010).

(15) *PFOA abolition in fluorochemicals* (in Japanese). www.daikin.co.jp/press/2007/071221/press_20071221.pdf (accessed January 10, 2010).

(16) Wallington, T. J.; Hurley, M. D.; Xia, J.; Wuebbles, D. J.; Sillman, S.; Ito, A.; Penner, J. E.; Ellis, D. A.; Martin, J.; Mabury, S. A.; Nielsen, O. J.; Sulbaek Andersen, M. P. Formation of $C_7F_{15}COOH$ (PFOA) and other perfluorocarboxylic acids during the atmospheric oxidation of 8:2 fluorotelomer alcohol. *Environ. Sci. Technol.* **2006**, *40*, 924–930.

(17) Harada, K.; Inoue, K.; Morikawa, A.; Yoshinaga, T.; Saito, N.; Koizumi, A. Renal clearance of perfluorooctane sulfonate and perfluorooctanoate in humans and their species-specific excretion. *Environ. Res.* **2005**, *99*, 253–261, DOI 10.1016/j.envres.2004.12.003.

(18) Olsen, G. W.; Burris, J. M.; Ehresman, D. J.; Froehlich, J. W.; Seacat, A. M.; Butenhoff, J. L.; Zobel, L. R. Half-life of serum elimination of perfluorooctanesulfonate, perfluorohexanesulfonate, and perfluorooctanoate in retired fluorochemical production workers. *Environ. Health Perspect.* **2007**, *115*, 1298–1305.

(19) Hallberg, L.; Hoddahl, A. M.; Nilsson, L.; Rybo, G. Menstrual blood loss—a population study: variation at different ages and attempts to define normality. *Acta Obstet. Gynecol. Scand.* **1966**, *45*, 320–351.

(20) Vestergren, R.; Cousins, I. T. Tracking the pathways of human exposure to perfluorocarboxylates. *Environ. Sci. Technol.* **2009**, *43*, 5565–5575, DOI 10.1021/es900228k.

(21) Harada, K. H.; Hashida, S.; Kaneko, T.; Takenaka, K.; Minata, M.; Inoue, K.; Saito, N.; Koizumi, A. Biliary excretion and cerebrospinal fluid partition of perfluorooctanoate and perfluorooctane sulfonate in humans. *Environ. Toxicol. Pharmacol.* **2007**, *24*, 134–139, DOI 10.1016/j.etap.2007.04.003.

(22) *Report of the Task Group on Reference Man: a report/prepared by a task group of Committee 2 of the International Commission on Radiological Protection*; ICRP publication No. 23; Pergamon Press: Oxford, New York, 1975.

(23) Koizumi, A.; Harada, K.; Inoue, K.; Hitomi, T.; Yang, H.-R.; Moon, C.-S.; Wang, P.; Hung, N. N.; Watanabe, T.; Shimbo, S.; Ikeda, M. Past, present, and future of environmental specimen banks. *Environ. Health Prev. Med.* **2009**, *14*, 307–318, DOI 10.1007/s12199-009-0101-1.

(24) Harada, K.; Saito, N.; Inoue, K.; Yoshinaga, T.; Watanabe, T.; Sasaki, S.; Kamiyama, S.; Koizumi, A. The influence of time, sex and geographic factors on levels of perfluorooctane sulfonate and perfluorooctanoate in human serum over the last 25 years. *J. Occup. Health* **2004**, *46*, 141–147.

(25) Harada, K. H.; Yang, H.-R.; Moon, C.-S.; Hung, N. N.; Hitomi, T.; Inoue, K.; Niisoe, T.; Watanabe, T.; Kamiyama, S.; Takenaka, K.; Kim, M.-Y.; Watanabe, K.; Takasuga, T.; Koizumi, A. Levels of perfluorooctane sulfonate and perfluorooctanoic acid in female serum samples from Japan in 2008, Korea in 1994−2008 and Vietnam in 2007−2008. *Chemosphere* **2010**, *79*, 314–319, DOI 10.1016/j.chemosphere.2010.01.027.

(26) Kasibhatla, P.; Chameides, W. L.; St. John, J. A three-dimensional global model investigation of seasonal variations in the atmospheric burden of anthropogenic sulfate aerosols. *J. Geophys. Res.* **1997**, *102*, 3737–3760.

(27) Fei, C.; McLaughlin, J. K.; Lipworth, L.; Olsen, J. Maternal levels of perfluorinated chemicals and subfecundity. *Hum. Reprod.* **2009**, *24*, 1200–1205, DOI 10.1093/humrep/den490.

(28) Washino, N.; Saijo, Y.; Sasaki, S.; Kato, S.; Ban, S.; Konishi, K.; Ito, R.; Nakata, A.; Iwasaki, Y.; Saito, K.; Nakazawa, H.; Kishi, R. Correlations between prenatal exposure to perfluorinated chemicals and reduced fetal growth. *Environ. Health Perspect.* **2009**, *117*, 660–667.

(29) Kim, S.-K.; Kannan, K. Perfluorinated acids in air, rain, snow, surface runoff, and lakes: Relative importance of pathways to contamination of urban lakes. *Environ. Sci. Technol.* **2007**, *41*, 8328–8334, DOI 10.1021/es072107t.

(30) Mcmurdo, C. J.; Ellis, D. A.; Webster, E.; Butler, J.; Christensen, R. D.; Reid, L. K. Aerosol enrichment of the surfactant PFO and mediation of the water−air transport of gaseous PFOA. *Environ. Sci. Technol.* **2008**, *42*, 3969–3974.

(31) Barton, C. A.; Kaiser, M. A.; Butler, L. E.; Botelho, M. A. Comment on "Irreversible sorption of trace concentrations of perfluorocarboxylic acids to fiber filters used for air sampling" by Arp and Goss (Atmospheric Environment 42, 6869−6872, 2008). *Atmos. Environ.* **2009**, *43*, 3652–3653.

(32) Arp, H. P. H.; Goss, K.-U. Response to Comment on "Irreversible sorption of trace concentrations of perfluorocarboxylic acid to fiber filters used for air sampling" by Arp and Goss (Atmospheric Environment 42, 6869−6872, 2008). *Atmos. Environ.* **2009**, *43*, 3654–3655.

(33) Niisoe, T.; Nakamura, E.; Harada, K.; Ishikawa, H.; Hitomi, T.; Watanabe, T.; Wang, Z.; Koizumi, A. A global transport model of lead in the atmosphere. *Atmos. Environ.* **2010**, *44*, 1806–1814, DOI 10.1016/j.atmosenv.2010.01.001.

ES101948B