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Sprague-Dawley rats were given (oral gavage) 3 or 5 mg/kg PFOS/K+ for 21 days, while controls received 0.5% Tween-20 vehicle. Serum thyroxine (T4) and triiodothyronine (T3), and liver uridine diphosphate-glucuronosyl transferase (UDP-GT), a microsomal enzyme that metabolizes (T4), were determined at days 3, 7, 14 and 21 after initiation of treatment. Significant reductions in serum total T4 (58%), free T4 (70%), and total T3 (23%) were noted in the PFOS-treated rats in as little as three days in both dose groups. Hormonal deficits were sustained throughout the study. However, no significant alterations in T4-UDP-GT activities were detected; at day 21, mean T4-UDP-GT activities were 0.614, 0.571, and 0.654 pmol/mg protein/min for control, 3, and 5 mg/kg PFOS groups, respectively. Previously, we have shown that prenatal exposure to PFOS led to hypothyroxinemia in rat pups during postnatal development, while serum T3 levels were not affected. The current study extended the chemical exposure to the postnatal period. PFOS (10 mg/kg, p.o.) was given to rat pups daily from PD1 to PD48. All pups survived the chemical treatment, but serum tT4, fT4 and tT3 were significantly reduced by 64%, 68% and 29% of controls, respectively. The hormonal deficits persisted into young adulthood. These results suggest that PFOS reduces circulating thyroid hormones effectively in both mature and developing rats, but enhancement of hepatic metabolism of the hormones is not likely involved in altering the hormone economy. (Funded by EPA/NCCU Toxicology research program, training agreement CT 829460 with the Department of Biology, NCCU. This is an abstract of a proposed presentation and does not necessarily reflect EPA policy.)

1918 PERFLUOROOCTANOIC ACID: RELATIONSHIP BETWEEN REPEATED INHALATION EXPOSURES AND PLASMA PFOA CONCENTRATION IN THE RAT.

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A large pharmacokinetic database exists describing the behavior of perfluorooctanoic acid (PFOA) following oral exposure. The objective of this study was to quantify plasma PFOA concentrations in male and female rats, following single and repeated inhalation exposures, for the purpose of bridging the oral and inhalation exposure data sets. The study was comprised of two separate experiments: single (6 hour) and repeated nose only exposures (6 hours per day, 5 days per week for three weeks) to an aqueous aerosol of 0, 1, 10, or 25 mg/m³ PFOA. Levels were selected to produce plasma concentrations similar to those observed in previous oral gavage studies. For the single exposure, blood was drawn pre-exposure, during exposure and post-exposure. For the repeated exposure, blood was collected immediately before and after the daily inhalation exposure period three days per week. Plasma derived from the whole blood samples was analyzed by liquid chromatography-mass spectrometry (LC-MS). PFOA appeared rapidly in the blood of both male and female rats exposed *via* the inhalation route. PFOA elimination was sex-dependent, with female rats eliminating PFOA from the plasma much more efficiently than male rats. PFOA plasma concentrations were proportional to atmospheric exposure concentrations from 1 to 25 mg/m³. Repeated daily inhalation exposures produced little plasma carryover in female rats, but significant carryover in male rats. Male rats reached a steady state plasma concentration by three weeks with plasma concentrations of 8, 21, and 36 µg/mL respectively when exposed to 1, 10, and 25 mg/m³ PFOA. Female rats reached post exposure plasma concentrations of 1, 2, and 4 µg/mL respectively but returned to baseline levels for the pre-exposure time points. This study provides the data necessary to relate external atmospheric concentrations of PFOA to PFOA levels in male and female rat plasma. This research was sponsored by the Association of Plastics Manufacturers in Europe (APME) Fluoropolymers Committee.

1919 CONSIDERATIONS RELEVANT TO CONSTRUCTING A HUMAN PBPK MODEL FOR PERFLUOROOCTANOIC ACID (PFOA).

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Perfluorooctanoic acid (PFOA) is a surfactant, which has received significant interest in recent years due to its reported prevalence in blood samples from many US citizens. Consequently, there has been some activity associated with constructing a human PBPK model to relate inhalation and oral exposures to PFOA levels in plasma. While there have been many kinetic studies conducted on rodents, the rodent kinetic data have not been useful in extrapolation to PFOA kinetics in humans. There are several considerations relevant to the construction of a human PBPK model that will determine how, or even if, such a model is appropriate for PFOA. First, PFOA is a surface-active chemical, which will affect its behavior in biological systems and has thus far complicated any efforts to determine tissue to blood partition coefficients. Second, PFOA is reported to be unmetabolized in mammalian systems, thereby eliminating the need for explicit description of me-

tabolizing organs or tissues. Third, the elimination rate is dramatically different between humans and rodents. The reported half-life in humans is approximately 4 years as compared to 2 hours in the female rat. Further, rats have sex dependent elimination rates, which do not appear to be relevant to humans. Fourth, controlled human exposures to PFOA are lacking; therefore, any attempts to validate a PBPK model would be severely limited. This is further complicated by the fact that elimination mechanisms have not been completely elucidated in rats and humans. These considerations and gaps in the understanding of species-specific elimination of PFOA make it impractical to construct and apply a human PBPK or generic kinetic model to predict PFOA concentrations in plasma following ingestion or inhalation of PFOA. The basis for constructing and validating a human PBPK model for PFOA was described and evaluated.

1920 A LONG-TERM TREND OF SERUM LEVELS OF PERFLUOROOCTANE SULFONATE (PFOS) AND PERFLUOROOCTANOATE (PFOA) IN JAPANESE.

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PFOS and PFOA are chemicals of a new class of Pops. They have been used from 1950s as various purposes. The aim of this study is to assess a long-term trend of PFOS and PFOA exposures using serum samples collected from late 1970s to 2003 in Japan. Methods: Human serum. We used samples in the sample bank. We collected serum samples in Miyagi (Miyagi samples), Akita (Akita samples) and Kyoto (Kyoto samples). In Miyagi, Akita, Kyoto, we collected samples in 1970s and 2003, in the early 1990s and 2003, in 2002 and 2003 respectively. Analysis: The 0.5 ml of serum were used for determination of PFOA and PFOS by LC/MS (Saito et al., 2003). Results. The PFOS and PFOA levels in serums [GM(GSD)](PFOS and PFOA in order :microgram/L) were; in Miyagi samples in 1970s 1.1(1.8) and 0.2(2.0) for females (n=40); in 2003 5.7(1.8) and 3.3(2.0) for males (n=32) and 3.5(2.9) and 2.8(1.5) for females (n=23). In Akita samples they were; in 1991, 10.2(1.5) and 2.2(1.4) for males (n=16) and 8.0(1.4) and 1.7(1.5) for females (n=40) and in 2003 12.9(1.5) and 3.4(1.5) for males (n=66) and 5.0(3.2) and 2.4(1.7) for females (n=54). In Kyoto, they were in 2003; 21.8(1.7) and 9.4(1.5) for males (n=28) and 12.7(1.5) and 6.1(1.5) for females (n=26). In Miyagi PFOS and PFOA concentrations have increased 3 times and 14 times, respectively. In Akita, there are no increase between 1990s and 2003 for PFOS but the level of PFOA was increasing. There are large gender differences in the concentrations of PFOS and PFOA at three locations. Furthermore, there are predominant regional differences for both PFOS and PFOA concentrations. Systematic collection of samples at different time periods, genders, and locality enabled us to analyze the exposure trends. Reference: Saito et al.; (2003) Arch. Environment Contam. Toxicol. 45: 149-58

1921 PERFLUOROOCTANOATE AND PERFLUOROOCTANE SULFONATE CONCENTRATIONS IN SURFACE WATERS IN JAPAN.

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Perfluorooctanoate (PFOA) and perfluorooctane sulfonate (PFOS) are Pops widely used in Japan. We analyzed their concentrations in surface water samples collected from all over Japan. Methods: Water samples were collected from rivers, coastal sea waters and tap waters. For all sampling, a two-L sample was collected. Samples were passed through the Presep-C Agri column at a flow rate of 10 mL /min using a Waters Concentrator System (Concentrator Plus, Waters, Tokyo, Japan). Presep-C cartridges were then eluted with 1.5 mL of methanol and concentrated at room temperature. The methanol extracts were chromatographed using HPLC and Mass spectra were taken on an LC/MS. The fragment ions for PFOA m/z 413 (C7F15CO₂⁻) and for PFOS m/z 499 (C8F17SO₃⁻) were monitored for quantification. Results and discussion: The lowest limits of detection (LOD) (ng/L) were 0.06 for PFOA and 0.04 for PFOS. The lowest limits of quantification (LOQ) (ng/L) were 0.1 for both analytes. The levels [geometric mean (GM); geometric standard deviation (GS)] (ng/L) of PFOA and PFOS in the surface waters were GM (GS): 0.97 (3.06) and 1.19 (2.44) for Hokkaido-Tohoku (n=16); 2.84(3.56) and 3.69 (3.93) for Kanto (n=14); 2.50 (2.23) and 1.07 (2.36) for Chubu (n=17); 21.5 (2.28) and 5.73 (3.61) for Kinki (n=8); 1.51 (2.28) and 1.00 (3.42) for Chugoku (n=9); 1.93 (2.40) and 0.89 (3.09) for Kyushu-Shikoku (n=15). The GM of PFOA in Kinki was significantly higher than in other areas (ANOVA p<0.01). Systematic searches of Yodo and Kanazaki Rivers revealed two potential sources, a public-water-disposal site for PFOA and an airport for PFOS. The former was estimated to release 18 kg of PFOA/day. PFOA in drinking water in Osaka city [40