# Consumption of PFOA and PFOS Contaminated Beef: Rapid Risk Evaluation

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**At a site in the Southeastern United States, biosludge containing perfluorinated compounds (PFCs) was applied to agricultural lands. These lands included cattle grazing areas, thus exposing cattle to PFCs which could have led to impacts to the cattle and subsequent human exposure. A model was developed to provide a rapid risk evaluation of potential beef concentration of PFCs, specifically concentrations of perfluorooctane sulfonate (PFOS) and perfluorooctanoic acid (PFOA), that may result from this environmental situation. Samples of beef were subsequently obtained and measured for PFOS and PFOA, and the measurements of PFOS and PFOA in the range of 6 ng/g and 1 ng/g, respectively, were consistent with modeled values. Consumption of beef at these modeled concentrations was shown to be lower than acute and subchronic levels of concern for PFOA and acute levels of concern for PFOS. Likely PFOS subchronic and chronic exposure scenarios would also result in exposures less than subchronic levels of concern; however, potential concern for subchronic and chronic exposures to meat from a single highly contaminated animal was identified, though unlikely. These analyses suggest that there is an unlikely public health threat for meat consumers posed by use of biosolids on the agricultural lands in this setting.**

KEYWORDS: beef, perfluorooctane sulfonate (PFOS), perfluorooctanoic acid (PFOA), risk assessment

Perfluorinated compounds (PFCs), such as perfluorooctane sulfonate (PFOS) and perfluorooctanoic acid (PFOA), are used in the manufacturing of plastics, electronics, non-stick coatings, and stain repellents. PFOS and PFOA are environmentally stable and have been detected in wildlife and livestock (Lau *et al.*, 2007) Animal exposure to PFOS may result in decreased bodyweight, liver toxicity and abnormal cholesterol and sex hormones. Animal studies also indicate that PFOS associated developmental effects include reduced bodyweight, cleft palate, edema, delayed ossification of bones and cardiac abnormalities. Animal studies also indicate that PFOA exposure may result in reduced bodyweight, reduced serum cholesterol concentrations, liver hypertrophy, spleen and thyroid atrophy, abnormal thyroid and sex steroid hormone levels, lipoprotein abnormalities, increased tumor formation and increased mortality. PFOA associated developmental effects include decreased birth weight and increased neonatal mortality (Lau *et al*., 2004; Minnesota Department of Health, 2008; U.S. Environmental Protection Agency, 2002) Human exposure to PFOA in occupational settings has been associated with cholesterol and sex hormone abnormalities, diabetes and prostate, bladder and kidney cancers. Human exposure to PFOS has been associated with increased rate of bladder cancer (Lau *et al.*, 2007). The major human exposure pathways for PFOS in North America and Europe are food and water ingestion, dust ingestion, followed by hand-to-mouth transfer from mill-treated carpets. For PFOA, major exposure pathways are oral exposure resulting from migration from paper packaging and wrapping into food, general food and water ingestion. PFOS and PFOA exposure pathways are similar for children except that exposure from hand-to-mouth transfer from treated carpets is greater (Fromme et al., 2010).

At an area in Southeastern United States, biosludge contaminated with PFCs including PFOS and PFOA was applied to agricultural fields (Washington *et al*., 2010). Mean and maximum United States Environmental Protection Agency (EPA) reported PFOS and PFOA soil concentrations were 135, 408 and 159, 317 ng/g, respectively(Washington *et al*., 2009). Mean and maximum PFOS and PFOA water concentrations were 11.5, 151 and 600, 11,000 ng/L, respectively (Lindstrom *et al*., 2009). Cattle

consumed vegetation and soil from the treated fields and likely drank PFOS and PFOA contaminated water which could result in PFOS and PFOA accumulation in the tissues of cattle intended for subsequent human consumption. The U.S. Department of Agriculture's Food Safety and Inspection Service (USDA's FSIS) examined the potential adverse public health effects from beef consumption associated PFOS and PFOA exposure to cattle.

FSIS developed a rapid technique to assess the magnitude of public health concern associated with this scenario. Using the initially available data (site-specific soil and water PFOS and PFOA concentrations), FSIS developed a quantitative model based on the environmental fate of these contaminants, the absorption, distribution and excretion of these chemical hazards in food animal tissues, and dietary patterns of U.S. consumers. This model provided estimates of cattle exposure to PFOA and PFOS, subsequent human exposure and associated public health impact to beef consumers. (Scheme 1). This rapid estimation was needed to determine if immediate actions were required to reduce human exposure to this beef. To validate the model's estimates, differences between the model estimates and subsequent measured concentrations were assessed.

## MATERIALS AND METHODS

*Model Development*

***Estimation of Cattle PFOS and PFOA Exposure.*** Site specific water and soil PFOS and PFOA concentrations were obtained from the U.S. Environmental Protection Agency (EPA) (Lindstrom *et al*., 2009; Washington *et al*., 2009; Washington *et al*., 2010). Mean and upper 95th percentile soil and water PFOS and PFOA concentrations were estimated from these data (*Supporting Information Tables S1, S2*). Forage PFOS (PFOX, X=S) and PFOA (PFOX, X=A) concentrations ($C_{forage}$) were estimated as the product of PFOX soil concentration ($C_{soil}$) and the soil to plant accumulation factors ($AF_{plant/soil}$) for each compound reported by Kordel and Herchen (2008) (*Supporting Information Table S3*) (Eqn. 1)

$$C_{forage}(PFOX) = C_{soil}(PFOX) * AF_{plant/soil}(PFOX) \quad (1)$$

A report by the Department of Agriculture, Alberta, Canada (2008) provided mean and high cattle forage estimates. Water consumption estimates were obtained from Ward and McKague (2007). Mean and high cattle soil consumption estimates were obtained from Thornton and Abrahams(1983) (*Supporting Information Table S4*).

Using these data, PFOS and PFOA concentration estimates were calculated for forage plants, water, soil, cattle and beef tissue (Scheme 1). Mean and high cattle PFOA and PFOS exposures for each matrix (forage, water, soil) were estimated as the product of the mean or 95$^{th}$ percentile concentrations of PFOS or PFOA ($C_{matix}$) and the mean or high cattle consumption rates ($E_{matrix}$), respectively. Mean and high total cattle PFOS and PFOA exposures were estimated as the sum of the mean or high exposures from forage, water and soil, respectively (Eqn 2).

$$\frac{mass\ PFOX}{Kg_{bw}\ day} = \left(C_{forage}(PFOX) * E_{forage}\right) + \left(C_{water}(PFOX) * E_{water}\right) + \left(C_{soil}(PFOX) * E_{soil}\right) \quad (2)$$

***Estimation of Beef PFOS and PFOA Concentrations***. Beef PFOS and PFOA concentrations were estimated by determining the whole-body steady state concentrations based on mean and high exposures. While a wide range of interspecies differences for PFOA and PFOS half-lives have been observed (Lau *et al* 2007; Yoo *et al.*, 2009), available tissue distribution data which includes muscle for both compounds is limited to the rat. As muscle is the primary beef tissue consumed in the US, estimates of bovine whole body and individual tissue concentrations were based on rat pharmacokinetic data. These steady-state whole body concentrations (C) were estimated via a one-compartment pharmacokinetic model constructed using Berkeley Madonna software (University of California, Berkeley, California) and elimination rate constants ($k_e$=ln2/half life) based on half-lives of 2.6 days (average of male and female rat half-lives) for PFOA and 100 days for PFOS (Lau *et al.*, 2007). Steady state concentrations were estimated by assuming a constant PFOS or PFOA dose (D), a daily dosing

interval (T) and simulating an exposure duration of five half-lives which assured that the estimated whole body concentration was stable (Eqn. 3).

$$dC/dt = \frac{D}{T} - (ke * C) \qquad (3)$$

Muscle and sera concentrations were subsequently estimated using the muscle:whole body (0.13 PFOA, 0.19 PFOS) and blood:whole body (1.5 PFOA, 1.5 PFOS) concentration ratios observed in PFOA and PFOS radio-labeled rat distribution studies (*Supporting Information Tables S5, S6)* (Johnson et al., 1979; Kemper, 2003).

***Human Model Parameters.*** Estimation of Public Health Reference Values and Beef Consumption. Human PFOS and PFOA acceptable daily intakes (ADI) for subchronic and acute exposures were estimated via extrapolation from animal toxicity studies. EPA subchronic reference doses (RfDs) of 0.2 µg PFOA/kg bw day and 0.08 µg PFOS/kg bw day were used for human subchronic ADIs (Dinan and Crawford, 2009). While subchronic ADIs were derived from NOELs, the LOEL endpoints observed in these studies included increased levels of thyroid-stimulating hormone (males), reduced levels of high-density lipoproteins (females) and reduced T3 levels (males and females) for PFOS (Cynomolgus monkeys) and a variety of neonatal effects (eye opening, survival, bodyweight) and increased maternal liver weight, for PFOA (mice)( Lau *et al*., 2006;Seacat *et al*., 2002). For acute exposure, ADIs were derived from the 100 and 15 mg/kg lowest effect levels (LOEL) observed in PFOA and PFOS rat acute toxicity studies, respectively (Chang *et al*, 2008; Olsen and Andersen, 1983). The toxicity endpoints for these studies were liver hypertrophy, transient decreases in bodyweight and liver fatty acid composition (PFOA) and decreased serum TT4 concentrations (PFOS). Ten-fold uncertainty factors were used to account for intraspecies variation, and extrapolation of a LOEL to a no effect level (NOEL). A 3-fold uncertainty factor was used to account for interspecies toxicodynamic variation. Toxicokinetic uncertainty factors were estimated as the ratio of the test animal half-life:human half-life for each compound. This approach yielded acute toxicokinetic uncertainty factors

277 and 19.7 for PFOA and PFOS, respectively. This approach resulted in human acute ADIs of 1.2 µg PFOA/kg bw day and 2.5 µg PFOS/kg bw day (*Supporting Information Table S7*). Meat associated PFOS and PFOA consumption was estimated as the product of North American PFOX meat concentration ($Conc_{PFOX}$) and meat consumption (Cons) data (Trudel *et al*., 2008) (Eqn. 4). Relative source contributions (RSC) of 42 percent for PFOS and 15 percent for PFOA meat was estimated as the quotient of meat associated PFOX consumption and total PFOX exposure[5], respectively ((*Supporting Information Table S8*) (Eqn. 5). The portion of the acute or subchronic ADI allocated to meat consumption ($ADI_{meat}$) was estimated as the product of the PFOS or PFOA relative source contribution and the appropriate compound-exposure duration specific ADI (Eqn. 6).

$$meat\ associated\ PFOX\ consumption = Conc_{PFOX} * Cons \quad (4)$$

$$RSC_{PFOX} = \frac{meat\ associated\ PFOX\ consumption}{total\ PFOX\ exposure} \quad (5)$$

$$ADI_{meat} = RSC_{PFOX} * ADI \quad (6)$$

Human meat consumption statistics were obtained from the What We Eat in America portion of the Day one and Day two USDA National Health and Nutrition Examination Survey (Kordel et al., 2008) using SUDAAN Proc DESCRIPT. Mean (2.2 g/kg bw day) and upper 90$^{th}$ percentile (4.0 g/kg bw day) statistics were used for mean and high meat consumption estimates. PFOS and PFOA beef concentrations of concern (COC) were estimated as the portion of the ADI allocated to meat consumption divided by meat consumption (Cons) (Eqn. 7). These beef PFOS and PFOA concentrations of concern were compared to the estimated muscle concentrations to determine the magnitude of public health concern associated with the consumption of beef from exposed cattle.

$$COC = ADI_{meat}/Cons \quad (7)$$

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*Probabilistic Risk Evaluation*

The exposure scenario of greatest concern was further evaluated using a probabilistic model developed using Crystal Ball Software (Oracle Inc, Redwood Shores, CA). This probabilistic evaluation simulated PFOS and PFOA exposure and associated steady-state muscle concentration for five million cattle. The distribution of estimated PFOS and PFOA muscle concentrations were subsequently compared to the pertinent concentration of concern. For each simulation, values for soil concentration, water concentration, soil:water concentration factor, soil consumption, water consumption, forage consumption and half-life were Monte Carlo sampled from distributions for each of these variables (*Supporting Information Table S9*). Steady state whole-body PFOS and PFOA concentrations were estimated for each simulation by assuming 100 percent absorption of ingested PFCs. Muscle PFOS and PFOA concentrations for each simulation were estimated as in the deterministic model (*Supporting Information Table S4*).

*PFOS and PFOA Residue Analyses*

Several months after the rapid risk evaluation was completed, PFOS and PFOA residue analyses were completed on a limited number of muscle and sera samples from cattle which grazed on the PFC contaminated fields**.**

***Bovine Sample Collection.*** Samples were harvested at the Thompson-Bishop-Sparks State Diagnostic Laboratory in Auburn, AL. Fifteen 10 mL blood samples were collected from each animal in SST VacutainerTM tubes (Becton Dickinson, Franklin Lakes, NJ). The tubes were spun down to separate serum from cells. A 1 cc aliquot of serum was pipetted into labeled 1.5 cc microcentrifuge tubes. A 1kg muscle sample was collected from each animal. The muscle sample was sliced into 0.5cm thick pieces and placed into a labeled sealed bag. All samples were completely frozen prior to shipping.

Samples were shipped overnight to the United States Department of Agriculture (USDA), Food Safety and Inspection Service (FSIS), Western Laboratory, Alameda, CA in insulated shipping boxes containing completely frozen cold-packs. Samples were stored in a −10 °C laboratory freezer prior to further processing.

Sample Analysis. PFOS and PFOA were quantified in sera and muscle using USDA FSIS Chemistry Laboratory Guidebook Method R42, "Determination and Confirmation of PFOA and PFOS by UPLC/MS/MS" [21]. Briefly, PFOA and PFOS were extracted from serum with acidified acetonitrile and from muscle with a base digestion followed by a solid phase extraction. Quantitation was performed by LC/MS/MS with Ultra Performance Liquid Chromatography (UPLC) and triple quadruple mass spectrometer in an electrospray negative ion (ESI-) model (*Supporting Information Table S10*). Confirmation was based on comparison of sample LC retention time and product ion abundance ratios against those obtained for a positive control (recovery). The minimum method reporting limits for ppb PFOA and PFOS were 10 ppb in bovine serum and 20 ppb in bovine muscle.

The model's performance was evaluated by comparing the observed PFOS and PFOA concentrations with the estimated tissue concentrations. This provided a straight-forward approach to evaluate the accuracy of the model estimated PFOS and PFOA beef tissue concentrations.

## RESULTS AND DISCUSSION

Kordel and Herchen reported PFOA and PFOS soil to plant transfer factors for wheat, maize and rye grown in highly contaminated soils (Kordel *et al*., 2008). From these data, mean and maximum soil to plant transfer factors were calculated and multiplied by the mean and 95$^{th}$ percentile soil concentrations to estimate mean and high plant PFOS and PFOA concentrations from the biosludge treated fields of interest. The resulting estimated plant PFC concentrations were in the ng/g range (parts per billion); estimated PFOS concentrations were about 15% of the estimated PFOA concentrations (Table 1).

Cattle PFOS and PFOA exposures were estimated for ingestion of forage vegetation, water and soil (co-ingested with vegetation). Forage ingestion appears to be the most important source of PFC exposure, followed by soil and then water (Table 2). Mean and maximum estimated PFOA exposure was approximately six-fold greater than estimated PFOS exposure (Table 3). The estimated whole body and individual tissue concentrations resulting from this exposure were about three times greater for PFOS than PFOA. Even though the estimated PFOA cattle exposure associated with this incident was much greater than PFOS exposure, the longer biological half-life of PFOS (Lau *et al.*,2007) resulted in greater retention and higher tissue residue estimates. The bovine tissue distributions of PFOS and PFOA were based on rat distribution and excretion studies (*Supporting Information Tables S5, S6*) (Johnson, 1979; Kemper, 2003). The estimated high tissue concentrations for both PFCs were about 3-fold greater than the estimated mean concentrations.

PFOS and PFOA residues were measured in one muscle and sera sample from each of nine cattle that consumed forage from the PFC contaminated fields. Method limits of detection (MLOD) (instrument responses of three times that observed for controls) for PFOS and PFOA were 6.3 and 2.0 µg/kg for muscle and 8.1 and 2.9 ng/mL for sera, respectively. Reporting Limits (RLs) for PFOS and PFOA were 20 µg/kg for muscle and 10 ng/mL for sera. For determination of the mean concentration in the bovine samples, non-detects (instrument responses less than MLOD) were assigned a value of 0. Samples with analytical responses greater than the MLOD and less than the RL were assigned concentrations equivalent to the average of the MLOD and RL. For samples greater than the RL, the estimated concentrations were used (*Supporting Information Table S11*).

*Validation*

Comparison of the model estimated mean and high concentrations with the mean and maximum observed concentrations provided a quantitative approach for evaluating the accuracy of the model estimates and the validity of the rapid risk evaluation model (Table 4). Four and seven of the nine samples contained quantifiable PFOS residues in muscle and sera, respectively. However, only one of nine samples contained quantifiable PFOA residues in muscle or sera. For this reason, comparison of

estimated and observed PFOS residues provided a better means to evaluate the model's performance. The model estimated mean PFOS muscle and sera concentrations of 5.6 and 44 µg/kg are nearly identical (+/- 9%) to the observed mean concentrations of 5.5 µg/kg and 48 µg/kg, respectively. The model estimated high PFOS muscle concentration of 17 µg/kg falls within the estimated maximum concentration range of 6 – 20 µg/kg. The model estimated high PFOS sera concentration of 134 µg/kg is nearly identical (+/- 10%) to the observed maximum concentration of 122 µg/kg.

Even though we obtained only one quantifiable PFOA residue in each matrix, the estimated and observed PFOA concentrations were similar. The model estimated mean PFOA muscle and sera concentrations of 0.7 and 8.6 µg/kg were within a factor of four of observed mean concentration 1.2 µg/kg and 2.5 µg/kg, respectively. The model estimated high PFOA muscle concentration of 2 µg/kg falls within the estimated observed maximum concentration range of 2 – 20 µg/kg. The model estimated high PFOA sera concentration of 23.5 µg/kg is nearly identical (+/- 5%) to the observed maximum concentration range of 22.1 µg/kg. Given the similarity of the estimated and observed PFOS and PFOA tissue concentrations, we conclude that the model provides reasonable estimates of PFOS and PFOA beef tissue concentrations.

*Risk Evaluation*

The mean and high estimated PFOS and PFOA beef muscle concentrations were subsequently compared to the tissue concentrations of concern to evaluate the public health risk associated with consumption of beef from PFOS and PFOA exposed cattle associated with this environmental contamination incident. Beef concentrations of concern were greater for PFOS than PFOA for both acute and subchronic (Table 5). For both compounds, subchronic concentrations of concern were less than acute concentrations of concern. Acute concentrations of concern for PFOA and PFOS ranged from 45 to 483 µg/kg, respectively. Subchronic concentrations of concern for PFOA and PFOS ranged from 7 to 15 µg/kg, respectively. As indicated in Figure 1, the estimated PFOA and PFOS muscle concentrations were at least an order of magnitude less than the acute concentrations of concern. For subchronic consumption of beef, the estimated PFOA muscle concentrations were also less than the

concentrations of concern. The estimated PFOS concentration was also less than the PFOS muscle concentration of concern for the mean subchronic exposure scenario. However, for the high subchronic exposure scenario, the estimated high (worst case) PFOS muscle concentration was about twice the level of concern (Figure 2).

While this initial analysis indicated potential concern for subchronic exposure of PFOS contaminated meat from cattle with the highest water and forage consumption rates which consumed forage and water with the highest levels of contamination, an added level of consumer safety is afforded by the unlikelihood that a consumer would ingest meat from a single contaminated animal over an extended period of time. For example, contaminated ground beef would be diluted with significant quantities of non-contaminated ground beef during routine beef slaughter house procedures. The potential custom slaughter scenario (where consumers would repeatedly consume beef from a single contaminated animal for an extended period of time) was explored at multiple public meetings and failed to identify any such consumers in the contaminated area. This subchronic exposure scenario was further evaluated with a probabilistic model to estimate the exposure and risk associated with subchronic consumption of muscle tissue from PFC contaminated cattle. The model employed input distributions which encompassed the entire range of observed soil and water PFOS concentrations and variable distributions for forage, water and soil consumption which resulted in the simulation of a wide range of cattle PFOS exposures. The model also employed a PFOS half-life distribution which encompassed the range of half-lives reported for all non-human test animals (rats, chickens, monkeys) (Washington et al, 2009).. The predicted maximum PFOS muscle concentration was 24.2 µg/kg, which is about three times the 8 µg/kg PFOS beef muscle concentration of concern. Additional analysis of the probabilistic forecast, suggests that approximately three percent of cattle would exceed the concentration of concern (Figure 3).

For these analyses, we used plant/soil accumulation ratios that were generated from the analyses of soil and plants collected from historically contaminated sites (Kordel *et al*., 2008). These plant accumulation ratios were less than ten percent of the ratios reported by Stahl *et al.(*2009), which were

generated under laboratory conditions using freshly fortified soils. This suggests that for the determination of plant/soil accumulation factors, it is preferable to use aged rather than freshly fortified soils.

Trudel et al.(2008) reported a PFOS concentration range of 0.03 to 0.5 ug/kg and a PFOA concentration range of 0 to 1 µg/kg for North American meat. Fortunately, the subchronic and acute meat concentrations of concern are greater than these reported values. However, the estimated and observed beef contaminant concentrations associated with the biosludge contamination of agricultural fields in this study indicates that localized events could result in meat residues which are greater than those routinely consumed by the general population under certain high exposure scenarios.

***Uncertainty.*** As the model was developed to assist rapid risk evaluation and risk management decisions for a situation in which there were minimal data, a variety of assumptions and extrapolations were employed. Sensitivity analyses associated with the probabilistic analyses were conducted to identify the most important inputs, the inputs which had the greatest impact on the magnitude of the model estimates. The most significant input was the soil concentrations followed by the plant:soil accumulation factor (Figure 4). These inputs accounted for 61 and 37 percent of the variability in the estimated bovine tissue concentrations, respectively. Half-life accounted for only 1.5% of variability in the estimated tissue concentrations. This implies that accurate estimation of soil PFC concentrations and soil to plant accumulation rates are the most important inputs with respect to the accuracy of the model predictions. In the absence of cattle distribution and elimination data for PFOS or PFOA, we used values that were derived from rat studies. Assuming that the actual elimination kinetics for cattle fall within the range observed for the limited number of animal species tested to date, then the use of rat half-life values did not have a major impact on the model estimates. However, if cattle elimination kinetics are more similar to humans (reported PFOS half-life of 5.4 years) than the other animal species tested to date, we would expect significantly greater beef muscle resides; using a half-life distribution ranging from 100 days (rats) to 5.4 years (humans) in the probabilistic model resulted in maximum estimated PFOS muscle concentrations greater than 306 µg/kg and approximately seventy percent of

exposed cattle containing muscle residues greater than the 8 μg/kg level of concern (*Supporting Information Fig. S1*). However, as the estimated PFOA and PFOS beef residues were very similar to the observed residues, cattle PFC pharmacokinetics appear more similar to rats than humans. In light of this uncertainty, USDA is currently conducting PFOS and PFOA absorption, distribution, metabolism and excretion studies in cattle.

In estimating mean observed PFOA and PFOS concentrations in muscle and sera, observed residues which exceeded the MLOD but were less than the Reporting Limit were assigned a value that was half way between these two metrics. While such approaches are not uncommon in exposure and risk assessments, this adds a degree of uncertainty to the mean observed concentrations. Additionally, the model assumes that cattle are consuming PFC contaminated forage, water and soil throughout the year. If cattle spend a significant portion of the year in feedlots, on non-biosludge treated fields, or other non-field locations, then consumption of contaminated soil and/or contaminated forage (if feed is from a different locale) would likely be less and result in lower concentrations in meat. Furthermore, if our assumption of a relatively short half-life for PFOA in cattle is true, then PFOA residues would decrease fairly rapidly if cattle are moved to a non-contaminated location prior to slaughter. While both these scenarios would increase the magnitude of difference between estimated and observed residues, the model's approach of estimating residues associated with a "worst-case" scenario is likely appropriate for developing rapid response public health risk evaluation and risk management guidance. However, these uncertainties further suggest the unlikelihood that consumers will be exposed to meat containing PFOA and/or PFOS concentrations of public health concern.

Extrapolating animal toxicity data to estimate human No Effect Levels is accompanied by a degree of uncertainty. In this study, we used the relative animal to human PFOS and PFOA half-life ratios to account for toxicokinetic differences. As such, there is likely less uncertainty associated with this approach compared to using default uncertainty values (typically 10 for combined toxicokinetic and toxicodynamic uncertainty) in the absence of human and test animal data.

The rapid risk evaluation model provides a valuable approach for quickly estimating PFOS and PFOA beef tissue concentrations in the absence of readily available residue data in the tissues of concern. Comparison of these residue estimates with beef concentrations of concern provided a science-based approach to evaluate the validity of the model and its subsequent usefulness for determining impacts on public health. For the PFC environmental contamination scenario presented here, PFOS and PFOA in beef muscle do not appear to pose an imminent or long-term public health concern. This risk evaluation approach could be expanded to include a broader range of PFCs and estimates of cumulative exposure and subsequent public health risk impact. Model estimates can be easily updated when subsequent relevant data become available. This rapid risk evaluation approach is adaptable to other environmental contaminants and exposure scenarios of potential public health concern.

## SUPPORTING INFORMATION

Table S1. PFOA and PFOS soil concentrations

Table S2. PFOA and PFOS water concentrations.

Table S3. Estimation of PFOA and PFOS soil to plant accumulation factors

Table S4. Deterministic model inputs

Table S5. Rat PFOS tissue/whole body ratios

Table S6. Rat PFOA tissue/whole body ratios

Table S7. Estimation of acute human acceptable daily intakes

Table S8. PFOA and PFOS Relative source contributions for meat consumption

Table S9. Probabilistic model parameters

Table S10. Multiple reaction monitoring conditions

Table S11. Observed PFOA and PFOS tissue residues

Figure S1. Probabilistic model forecast incorporating human PFOS half-life in half-life input distribution


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Table 1. Estimated Plant (Cattle Forage) PFC Concentration

| Compound | Soil Concentration[1] (ng/g) | Vegetation:Soil Concentration Factor[2] | Estimated Plant Concentration[3] (ng/g) |
|---|---|---|---|
| Mean | | | |
| PFOS | 135 | 0.05 | 7 |
| PFOA | 158 | 0.35 | 55 |
| High | | | |
| PFOS | 305 | 0.05 | 16 |
| PFOA | 301 | 0.35 | 105 |

[1]Average (Mean) or 95th percentile (High) EPA measured PFC soil concentrations[7]

[2]Concentration factors based on Kordel and Herrchen[22]

[3]Dry weight

Table 2. Estimated Daily Cattle PFOS and PFOA Exposure

| | Forage | | Water | | Soil | | Forage + Water + Soil |
|---|---|---|---|---|---|---|---|
| | Estimated Plant Concentration[1] | Estimated Cattle PFC Consumption[2] | Water Concentration[3] | Estimated Cattle PFC Consumption[4] | Soil Concentration[5] | Estimated Cattle PFC Consumption[6] | Estimated Cattle PFC Consumption |
| Compound | (ng/g) | (ng/kg bw) | (ng/L) | (ng/kg bw) | (ng/g) | (ng/kg bw) | (ng/kg bw) |
| Mean | | | | | | | |
| PFOS | 7 | 144 | 11 | 11 | 135 | 59 | 214 |
| PFOA | 55 | 1098 | 599 | 551 | 158 | 70 | 1719 |
| High | | | | | | | |
| PFOS | 16 | 356 | 60 | 61 | 305 | 226 | 642 |
| PFOA | 105 | 2300 | 2150 | 2172 | 301 | 223 | 4694 |

[1]From table 1

[2]Cattle forage consumption: mean= 20 g/kg bw, high = 22 g/kg bw [9]

[3] EPA measured water PFC concentrations [8]

[4]Cattle water consumption: mean = 0.09 L/kg bw , high =1.01 L/kg bw[10]

[5] EPA measured soil PFC concentrations [7]

[6]Soil consumption: mean = 2.2 % of forage, high = 3.7% of forage [11]

Table 3. Estimated PFOS, PFOA Concentrations in Bovine Muscle and Sera

| | | Estimated Cattle PFOS, PFOA Tissue Concentrations | | |
|---|---|---|---|---|
| Compound | Estimated Cattle PFC Consumption[1] (ng/kg bw) | Whole Body[2] (µg/kg bw) | Muscle[3] (µg/kg bw) | Sera[3] (µg/kg bw) |
| Mean | | | | |
| PFOS | 214 | 29 | 5.6 | 44.0 |
| PFOA | 1719 | 6 | 0.7 | 8.6 |
| High | | | | |
| PFOS | 642 | 90 | 17.0 | 134 |
| PFOA | 4694 | 16 | 2.0 | 23.5 |

[1]From table 2

[2]Estimated whole body steady state concentration, elimination constant estimated from rat half-lives[1]

[3] Whole body:tissue ratios based on 14C-PFOA and 14 C-PFOS distribution studies[12,13]

Table 4. Estimated vs. Observed PFC Residues

| Compound | Estimated Muscle PFC Conc.[1] (µg/kg bw) | Observed Muscle PFC Conc. (µg/kg bw) | Estimated Sera PFC Conc.[1] (µg/kg bw) | Observed Sera PFC Conc. (µg/kg bw) |
|---|---|---|---|---|
| Mean | | | | |
| PFOS | 5.6 | 5.5 | 44.0 | 48.0 |
| PFOA | 0.7 | 1.2 | 8.6 | 2.5 |
| High | | | | |
| PFOS | 17.0 | 6<X<20[2] | 134.3 | 121.6 |
| PFOA | 2.0 | 2<X<20[2] | 23.5 | 22.1 |

[1]From Table 3

[2]Greater than limit of detection and less than limit of quantification

Table 5. Estimated Beef PFC Concentrations of Concern

| | Meat Consumption[1] (kg beef/kg BW day) | Portion of Human No-Effect Level or US EPA Reference Dose Allocated to Meat[2] (µg/kg BW day) | Meat Concentration of Concern[3] (µg/kg beef) |
|---|---|---|---|
| **Acute Exposure** | | | |
| Mean | | | |
| PFOS | 2.2E-03 | 1.04 | 483 |
| PFOA | 2.2E-03 | 0.18 | 83 |
| High | | | |
| PFOS | 4.0E-03 | 1.04 | 258 |
| PFOA | 4.0E-03 | 0.18 | 45 |
| **Subchronic Exposure** | | | |
| Mean | | | |
| PFOS | 2.2E-03 | 3.3E-02 | 15 |
| PFOA | 2.2E-03 | 3.0E-02 | 14 |
| High | | | |
| PFOS | 4.0E-03 | 3.3E-02 | 8 |
| PFOA | 4.0E-03 | 3.0E-02 | 7 |

[1]Mean and 90th percentile meat consumption.
N= 9,000; data from NHANES (2001-2006) Centers for Disease Control, National Center for Health Statistics [20]

[2]41% (PFOS) and 15% (PFOA) of exposure due to consumption of meat [5,19]

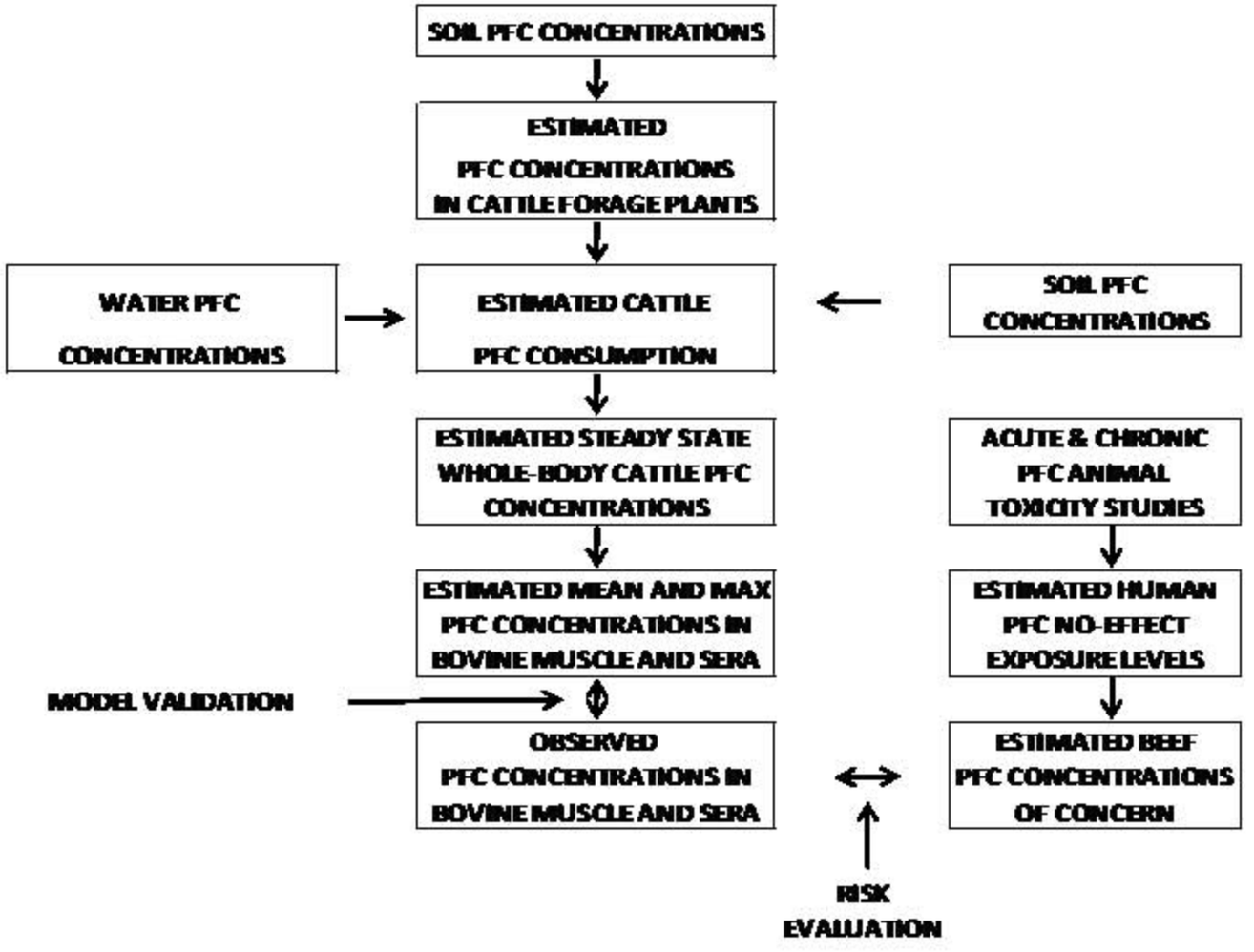
Figure Legends

Figure 1. Acute concentrations of concern vs. estimated Concentrations

Figure 2 Subchronic concentrations of Concern vs. Estimated Concentrations

Figure 3. Probabilistic Forecast: Distribution of estimated residues vs. concentration of concern

Figure 4. Sensitivity Analyses: Relative impact of model inputs on residue estimates


SOIL PFC CONCENTRATIONS
ESTIMATED PFC CONCENTRATIONS IN CATTLE FORAGE PLANTS
WATER PFC CONCENTRATIONS
ESTIMATED CATTLE PFC CONSUMPTION
SOIL PFC CONCENTRATIONS
ESTIMATED STEADY STATE WHOLE-BODY CATTLE PFC CONCENTRATIONS
ACUTE & CHRONIC PFC ANIMAL TOXICITY STUDIES
ESTIMATED MEAN AND MAX PFC CONCENTRATIONS IN BOVINE MUSCLE AND SERA
ESTIMATED HUMAN PFC NO-EFFECT EXPOSURE LEVELS
MODEL VALIDATION
OBSERVED PFC CONCENTRATIONS IN BOVINE MUSCLE AND SERA
ESTIMATED BEEF PFC CONCENTRATIONS OF CONCERN
RISK EVALUATION

Scheme 1

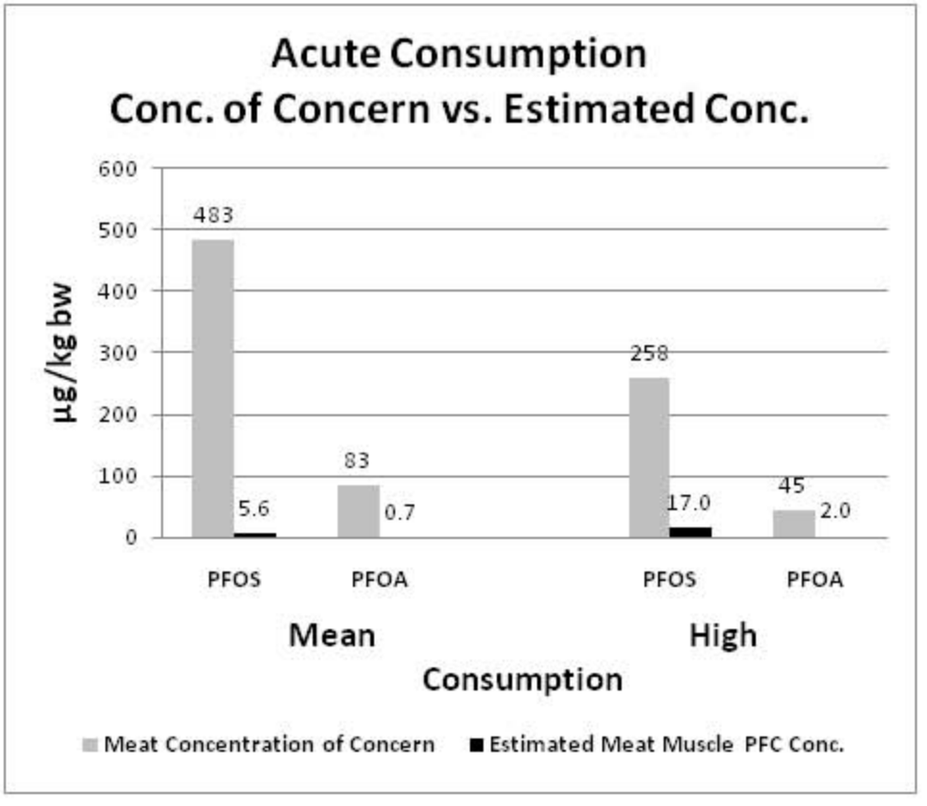

Acute Consumption
Conc. of Concern vs. Estimated Conc.
600
500
400
300
200
100
0
µg/kg bw
483
5.6
83
0.7
258
17.0
45
2.0
PFOS
PFOA
PFOS
PFOA
Mean
High
Consumption
Meat Concentration of Concern
Estimated Meat Muscle PFC Conc.

**Figure 1.**

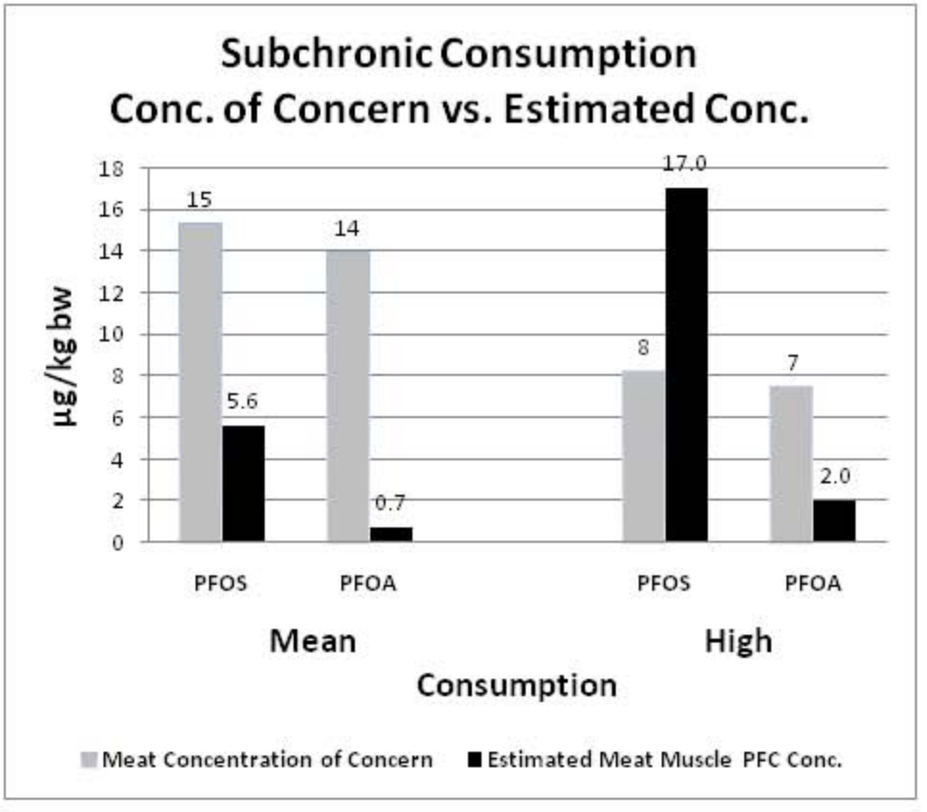

Subchronic Consumption
Conc. of Concern vs. Estimated Conc.
µg/kg bw
18
16
14
12
10
8
6
4
2
0
15
5.6
14
0.7
8
17.0
7
2.0
PFOS
PFOA
PFOS
PFOA
Mean
High
Consumption
Meat Concentration of Concern
Estimated Meat Muscle PFC Conc.

**Figure 2**

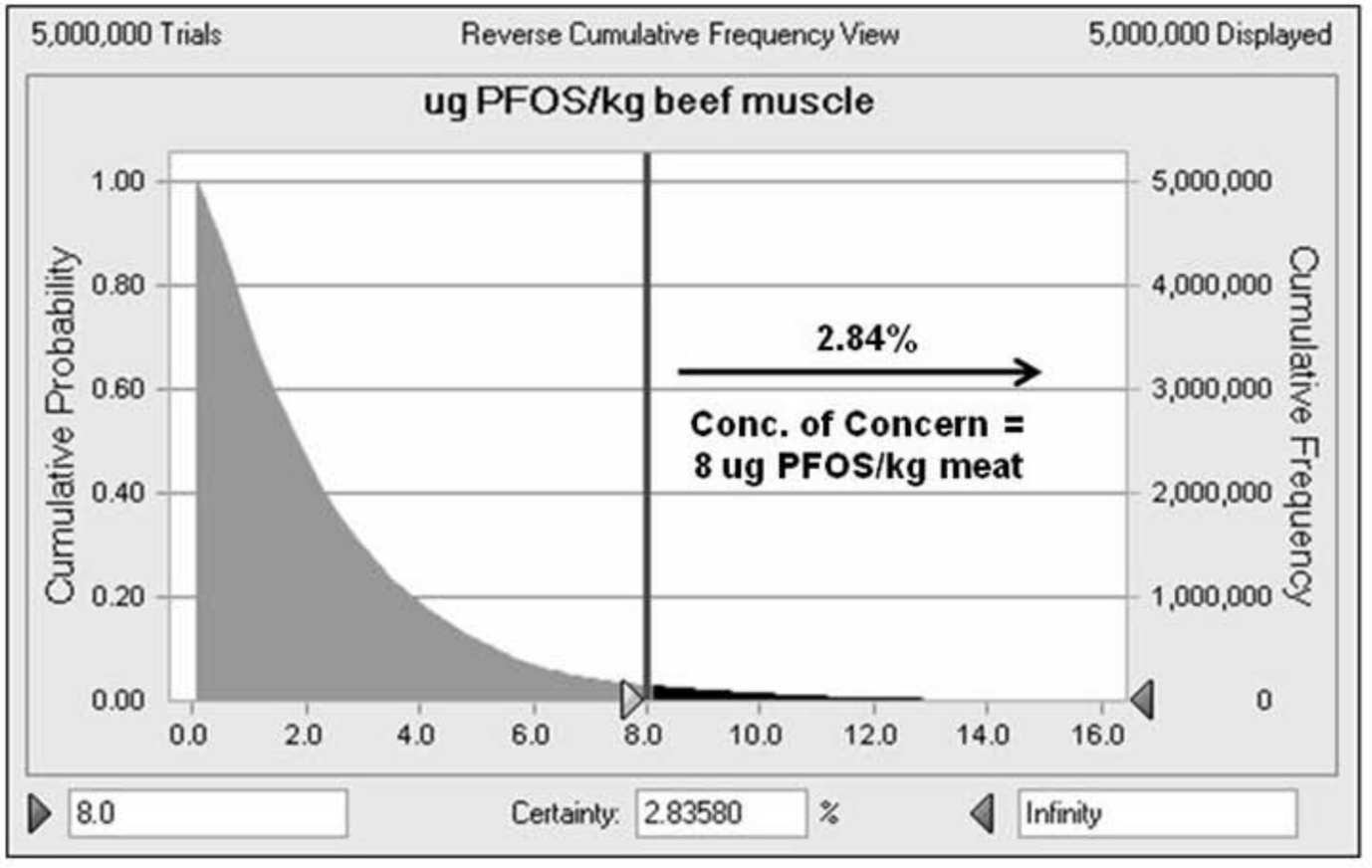

5,000,000 Trials
Reverse Cumulative Frequency View
5,000,000 Displayed
ug PFOS/kg beef muscle
Cumulative Probability
1.00
0.80
0.60
0.40
0.20
0.00
Cumulative Frequency
5,000,000
4,000,000
3,000,000
2,000,000
1,000,000
0
0.0
2.0
4.0
6.0
8.0
10.0
12.0
14.0
16.0
2.84%
Conc. of Concern =
8 ug PFOS/kg meat
8.0
Certainty: 2.83580 %
Infinity

**Figure 3.**

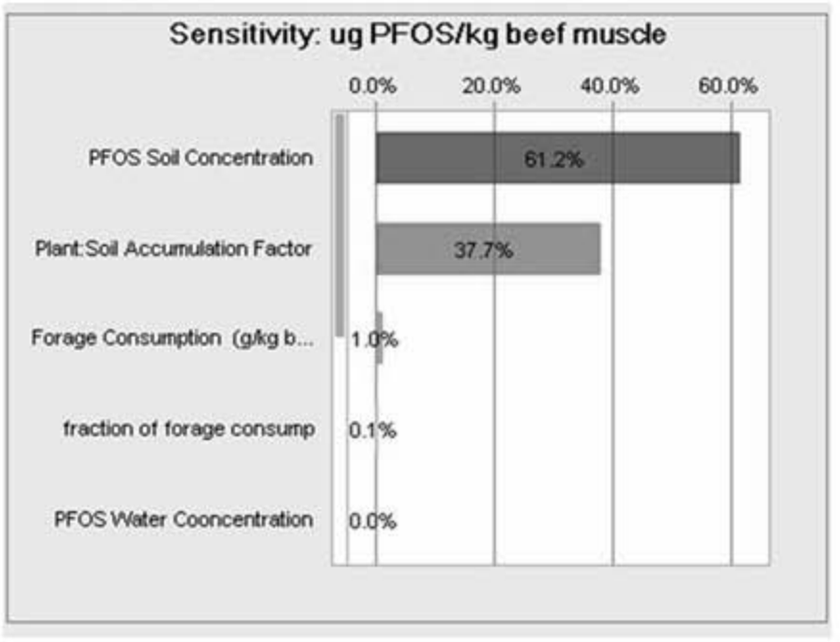

Sensitivity: ug PFOS/kg beef muscle
0.0%
20.0%
40.0%
60.0%
PFOS Soil Concentration
61.2%
Plant:Soil Accumulation Factor
37.7%
Forage Consumption (g/kg b...
1.0%
fraction of forage consump
0.1%
PFOS Water Cooncentration
0.0%

**Figure 4**

# SUPPORTING INFORMATION: Consumption of PFOA and PFOS Contaminated Beef: Rapid Risk Evaluation

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Table S1. PFOA and PFOS soil concentrations

| | EPA Region IV PFOA Soil Concentrations (ng/g) | EPA Region IV PFOS Soil Concentrations (ng/g) |
|---|---|---|
| | 190 | 127 |
| | 269 | 189 |
| | 120 | 81 |
| | 249 | 122 |
| | 87 | 58 |
| | 139 | 73 |
| | 312 | 203 |
| | 233 | 164 |
| | 183 | 202 |
| | 255 | 325 |
| | 153 | 177 |
| | 264 | 245 |
| | 94 | 118 |
| | 133 | 160 |
| | 119 | 88 |
| | 123 | 99 |
| | 54 | 61 |
| | 105 | 35 |
| | 64 | 31 |
| | 87 | 36 |
| | 185 | 82 |
| | 236 | 82 |
| | 84 | 203 |
| | 60 | 149 |
| | 317 | 408 |
| | 0.17 | 4.5 |
| Mean | 158.2757692 | 135.4807692 |
| 95th ptile | 301.25 | 305 |
| 5th ptile | 55.5 | 32 |
| max | 317 | 408 |

Table S2. PFOA and PFOS water concentrations.

| | EPA Region IV PFOA Water Concentrations (ng/L) | EPA Region IV PFOS Water Concentrations (ng/L) |
|---|---|---|
| | 0 | 0 |
| | 29.5 | 0 |
| | 134 | 11.6 |
| | 13.6 | 0 |
| | 94.8 | 0 |
| | 594 | 14.1 |
| | 1100 | 83.9 |
| | 993 | 16.5 |
| | 396 | 14.6 |
| | 750 | 66.3 |
| | 16.815 | 53.6 |
| | 0 | 13.2 |
| | 0 | 0 |
| | 0 | 0 |
| | 0 | 0 |
| | 0 | 0 |
| | 0 | 0 |
| | 2230 | 0 |
| | 0 | 0 |
| | 0 | 0 |
| | 16.85 | 0 |
| | 0 | 0 |
| | 0 | 0 |
| | 758 | 0 |
| | 2070 | 0 |
| | 0 | 0 |
| | 0 | 0 |
| | 0 | 0 |
| | 0 | 12 |
| | 149 | 151 |
| | 393 | 25.05 |
| | 6410 | 0 |
| | 0 | 21.1 |
| | 30.1 | 31.7 |
| | 24.1 | 31.5 |
| | 0 | 0 |
| | 0 | 0 |
| | 0 | 0 |
| | 26 | 0 |
| | 321 | 0 |
| | 204 | 0 |
| | 67.9 | 0 |
| | 0 | 0 |
| | 32.2 | 0 |
| | 1250 | 0 |
| | 1160 | 0 |
| | 11000 | 0 |
| | 176 | 38.2 |
| | 90.5 | 0 |
| | 35.7 | 0 |
| | 0 | 0 |
| Mean | 599.3346078 | 11.45784314 |
| 95th ptile | 2150 | 59.95 |
| 5th ptile | 0 | 0 |
| Median | 26 | 0 |
| max | 11000 | 151 |

Table S3. Estimation of PFOA and PFOS soil to plant accumulation factors

| Plant | PFOA | PFOS |
|---|---|---|
| wheat | 0.147 | 0.001 |
| maize | 0.022 | 0.028 |
| rye | 0.872 | 0.13 |
| mean | 0.347 | 0.053 |

Soil to Plant accumulation factors (plant concentration/soil concentration) for three types of potential cattle forage grown on highly contaminated soil. Data from Kordel and Herchen.

Table S4. Deterministic model inputs

| Variable | Units | Distribution | Parameters |
|---|---|---|---|
| Soil Consumption fraction of forage consumption | unitless | Uniform | min: 0.014; max:0.037 |
| Forage Consumption | g/kg bw day | Uniform | min: 18; max:25 |
| Water Consumption | L/kg bw day | Uniform | min: 0.08; max:0.1 |
| Soil Concentration | ng/kg | Custom | min: 4.5; mean 135.5; median 120; max:408 |
| Plant:Soil Concentration Factor | unitless | Uniform | min: 0.02; max:0.48 |
| Half-life | days | Uniform | min: 100; max:150 |
| Water Concentration | ng/L | Custom | min: 0; mean 11.5; median 0; max:151 |

Table S5. Rat PFOS tissue/whole body ratios

| Tissue | 14C conc ug/g | relative concentration (tissue/whole body) |
|---|---|---|
| Liver | 20.56 | 13.707 |
| Plasma | 2.21 | 1.473 |
| Kidney | 1.09 | 0.727 |
| Lung | 1.06 | 0.707 |
| Spleen | 0.51 | 0.340 |
| bone marrow | 0.46 | 0.307 |
| Rbc | 0.45 | 0.300 |
| Adrenals | 0.41 | 0.273 |
| Testes | 0.36 | 0.240 |
| Skin | 0.35 | 0.233 |
| Muscle | 0.29 | 0.193 |
| Fat | 0.2 | 0.133 |
| Eye | 0.16 | 0.107 |
| whole body | 1.5 | 1.000 |

Mean rat bodyweights: beginning = 288 g; terminal = 450 g
Estimation of whole body concentration:
57.2% of dose remaining
original dose = 4.2 mg/kg bw
final conc = 0.572*4.2 = 2.4 mg/kg if no weight gain
dilution of 14C due to weight gain=450/288=1.56 dilution factor
estimated final whole body concentration = 2.4/1.5 = 1.5

Table S6. Rat PFOA tissue/whole body ratios

| | PFOA concentrations (µg/g) | | | Relative Concentration | | | |
|---|---|---|---|---|---|---|---|
| | Dose | | | Dose | | | |
| Tissue | 1 mg/kg | 5 mg/kg | 25 mg/kg | 1 mg/kg | 5 mg/kg | 25 mg/kg | mean |
| whole blood | 0.357 | 1.103 | 5.771 | 1.519149 | 1.105764 | 1.803438 | 1.476117 |
| Muscle | 0.035 | 0.102 | 0.476 | 0.148936 | 0.102256 | 0.14875 | 0.133314 |
| whole body | 0.235 | 0.9975 | 3.2 | 1 | 1 | 1 | 1 |

Male rat 14C PFOA tissue distribution data from EPA Public Docket AR226-1499

Table S7. Estimation of acute human acceptable daily intakes

| | Rat LOEL mg/kg | Uncertainty Factors | | | | Human ADI mg/kg |
|---|---|---|---|---|---|---|
| | | LOEL to NOEL | Intra-species | Toxico-dynamics | Toxico-kinetics | |
| PFOA | 100 | 10 | 10 | 3 | 277 | 0.001203 |
| PFOS | 15 | 10 | 10 | 3 | 19.7 | 0.002538 |

[1]Olsen and Andersen,1983

[2]Chang et al, 2008

Toxicokinetic uncertainty factors= (half-life humand/half-life test animal)

Table S8. PFOA and PFOS Relative source contributions for meat consumption

| | | | | | |
|---|---|---|---|---|---|
| **US Meat Consumption (NHANES)** | | | | | |
| Mean | 2.2 | g meat/kg bw day | | | |
| **Concentration in meat (table 3, Trudel et al. 2008)** | | | | | |
| PFOS | | intermediate = | 0.3 | ng/g | PFOS |
| PFOA | | intermediate = | 0.2 | ng/g | PFOA |
| **meat associated intake** | | | | | |
| PFOS | | mean = | 660 | pg/kg bw day | PFOS |
| PFOA | | mean = | 440 | pg/kg bw day | PFOA |
| **Total intake (table 9, fromme et al, 2009)** | | | | | |
| PFOS | | mean = | 1560 | pg/kg bw day | PFOS |
| PFOA | | mean = | 2857 | pg/kg bw day | PFOA |
| **Fraction of total exposure due to meat (relative source contribution)** | | | | | |
| PFOS | | mean = | **0.423** | **PFOS** | |
| PFOA | | mean = | **0.154** | **PFOA** | |

Table S9. Probabilistic model parameters

| Variable | Units | Parameters |
|---|---|---|
| Soil Consumption | | |
| fraction of forage consumption | unitless | mean: 0.022; high:0.037 |
| Forage Consumption | g/kg bw day | mean: 20; high:22 |
| Water Consumption | L/kg bw day | min: 0.92; max:1.01 |
| Plant:Soil Concentration Factor | unitless | min: 0.02; max:0.48 |
| Half-life | days | min: 100; max:150 |
| Soil Concentration | | |
| PFOA | ng/kg | mean: 159; 95th p'tile: 301 |
| PFOS | ng/kg | mean: 135.5; 95th p'tile: 305 |
| Water Concentration | | |
| PFOA | ng/L | mean 599; 95th p'tile 2150 |
| PFOS | ng/L | mean 11.5; 95th p'tile 60 |
| Tissue Distribution | | |
| Muscle Conc/Whole Body Conc | | |
| PFOA | unitless | 0.13 |
| PFOS | unitless | 0.19 |
| Sera Conc/Whole Body Conc | | |
| PFOA | unitless | 1.5 |
| PFOS | unitless | 1.5 |

Table S10. Multiple reaction monitoring conditions

| Compound | Serum RT (min) | Muscle RT (min) | Precursor Ion (m/z) | Cone (V) | Product Ion (m/z) | Collision (eV) |
|---|---|---|---|---|---|---|
| PFOA | 2 | 0.62 | 412.9 | 20 | 168.9 | 16 |
| | | | | 20 | 218.9 | 20 |
| | | | | 20 | **369** | 12 |
| PFOS | 2.2 | 0.65 | 498.9 | 70 | **98.9** | 40 |
| | | | | 70 | 129.9 | 40 |
| | | | | 70 | 169.1 | 38 |
| mPFOA | NA | 0.62 | 417 | 20 | 372 | 10 |
| mPFOS | NA | 0.65 | 503 | 70 | 80 | 40 |

Note: Quantitation ion is in **Bold**

Table S11. Observed PFOA and PFOS tissue residues

| Decatur Animal # | Muscle PFOA | Serum PFOA | Muscle PFOS | Serum PFOS |
|---|---|---|---|---|
| 1 | 0 | 0 | 13.2 | 73.9 |
| 2 | 0 | 0 | 13.2 | 82.1 |
| 3 | 0 | 22.1 | 13.2 | 104.3 |
| 4 | 11.0 | 0 | 0 | 10.8 |
| 5 | 0 | 0 | 10.0 | 121.6 |
| 6 | 0 | 0 | 0 | 23.8 |
| 7 | 0 | 0 | 0 | 15.7 |
| 8 | 0 | 0 | 0 | 0 |
| 9 | 0 | 0 | 0 | 0 |
| Mean | 1.2 | 2.5 | 5.5 | 48.0 |
| Max | 11.0 | 22.1 | 13.2 | 121.6 |

| | MLOD (ppb) | | MLOQ* (ppb) | | Mean (ppb) MLOD,MLOQ | |
|---|---|---|---|---|---|---|
| Tissue | PFOA | PFOS | PFOA | PFOS | PFOA | PFOS |
| Muscle | 2.0 | 6.3 | 20 | 20 | 11.0 | 13.2 |
| Sera | 2.9 | 8.1 | 10 | 10 | 6.5 | 9.1 |

*Method Reporting Limit

Figure S1. Probabilistic model forecast incorporating human PFOS half-life in half-life input distribution