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Transfer model for PFOS in dairy cows, version 1.0.0 - model documentation.

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Summary

The fundamentals of a model for the transfer of PFOS from feed to milk, meat and other tissues of dairy cows are presented. The model, which is available as a webtool application (https://feedfoodtransfer.nl/), can be used to compare simulated concentrations with regulatory limits for these food matrices.

1 Introduction

Perfluorooctanesulfonic acid (PFOS) belongs to the poly- and perfluoroalkyl substances (PFASs), a group of synthetic chemicals used in many products and previously emitted by industry due to its adverse effects on human health. However, PFOS is still present in the environment where it accumulates due to its non-degradable character and therefore poses a risk for human health via the consumption of contaminated crops and water. Another route of human exposure is via the consumption of dairy cow meat and milk that is contaminated by transfer of PFOS via feed. Although the hazards of (chronic) exposure to PFOS are still ambiguous, regulatory limits have been set in the European Union for meat and offal, whereas for milk only an indicative value was established. This report describes a transfer model to predict the concentrations of PFOS in meat, liver, kidney and milk from dairy cows after exposure to feed contaminated with PFOS. The estimated concentrations can be compared to the regulatory limits that have been defined by regulatory agencies in various countries. The model is available as a webtool application (https://feedfoodtransfer.nl/).

2 Model description

2.1 General overview

The distribution of PFOS to edible tissues such as meat, liver, kidney and milk is described by a physiologically based kinetic (PBK) model. The PBK model connects several compartments including gut lumen, liver, adipose tissue, muscle (meat), lung, kidney, mammary gland (udder) and a rest compartment with a plasma compartment (see figure 1). With this model concentrations of PFOS can be simulated over time in plasma and the included tissues. Since the exposure to PFOS is via feed, the dose will enter the system via the gut lumen whereafter it distributes throughout the tissues taking into account the partitioning. Biotransformation of PFOS in the liver (or other tissues) is absent as reported previously (EFSA, 2014). PFOS excretion via urine is negligible, but it is excreted via milk and faeces (Kowalczyk, 2013; Lupton, 2014; Noorlander, 2025 (in preparation)). Enterohepatic circulation is not physiologically captured by this model, however faecal excretion is estimated and incorporated as a rate removed from plasma (Noorlander, 2025 (in preparation)). The data underlying this model come from an animal study performed at WFSR in 2022 with 4 cows with origin Holstein-Friesian and mixes of them with other breeds. NB, in this model total PFOS is simulated, which means that this is the sum of linear and branched PFOS.

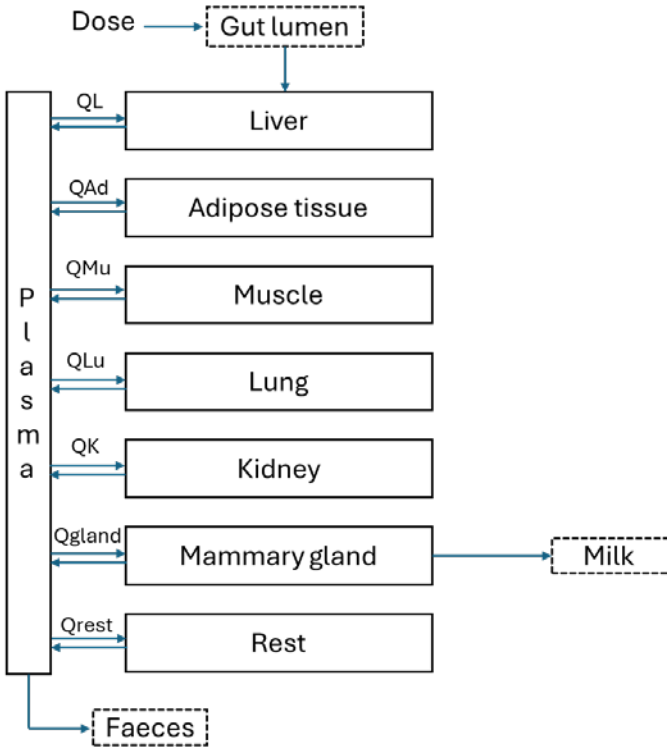

Figure 1. *Schematic overview of the dairy cow PBK-model for PFOS. Absorption takes place in between the gut lumen and liver compartments. Afterwards PFOS distributes over the tissues via the plasma flow (Q) and is subsequently excreted via the milk and faeces.*

2.2 Model equations

The model was based on differential equations to describe the change in the amount of PFOS in the different compartments (µg/h). Concentrations in tissues were calculated by dividing the amount of PFOS in the tissues by the volume of the tissues (see equation 1)

$$Ci = \frac{Ai}{Vi} \quad (1)$$

Where C*i* is the concentration of PFOS in µg/L in tissue *i*, A*i* is the amount of PFOS in µg in tissue *i* and V*i* is the volume in L or kg of tissue *i*.

For adipose tissue, muscle, kidney, lung and rest compartment the following equation applied:

$$\frac{dAi}{dt} = Qi \times \left(Cplasma - \frac{Ci}{Pi}\right) \quad (2)$$

Where t is time in hours, Q*i* the blood flow in L/h to tissue *i*, Cplasma the concentration PFOS in plasma, and P*i* the partition coefficient of PFOS in tissue *i* (unitless).

Exposure to PFOS was implemented as an event that occurred every 24 hours. Specifically, every 24 hours, a dose, *D* [µg], was added to the gut lumen compartment. ka is the absorption rate constant for PFOS from gut lumen to liver per hour.

$$\frac{dAlumen}{dt} = D - ka \times Alumen \quad (3)$$

The change in the amount of PFOS in liver over time was described following equation 4.

$$\frac{dAliver}{dt} = QLiver \times \left(Cplasma - \frac{Cliver}{Pliver}\right) + ka \times Alumen \quad (4)$$

The change in the amount of PFOS in the mammary gland over time was described by equation 5.

$$\frac{dAgland}{dt} = Qgland \times \left(Cplasma - \frac{Cgland}{PMilk}\right) - Qmilk \times Cgland \quad (5)$$

Where PMilk is the partition coefficient of PFOS from milk to plasma and Qmilk is the milk production in L/h.

The amount of PFOS in milk over time is described by equation 6:

$$\frac{dAmilk}{dt} = Qmilk \times Cgland \quad (6)$$

The plasma compartment for PFOS is described by equation 7:

$$\frac{dAplasma}{dt} = \sum_{n}\left(Qn \times \frac{Cn}{Pn} - (QCP \times Cplasma)\right) - Aplasma \times ke1 \quad (7)$$

Where QCP is the cardiac output in L/h corrected for plasma based on haematocrit and ke is the faecal excretion rate per hour.

The amount of PFOS in faeces over time is described by equation 8:

$$\frac{dAfaeces}{dt} = Aplasma \times ke \quad (8)$$

2.3 Model assumptions

The following assumptions were made in the presented model:

- There is a 100% absorption of PFOS from the gut lumen to the liver.
- PFOS is not metabolised in the liver (or any other tissue).
- The concentration PFOS in the mammary gland is equal to the concentration in milk.
- The muscle compartment represents meat meaning concentration PFOS modelled in muscle equals concentration PFOS in meat.
- PFOS is not excreted in the urine, therefore glomerular filtration and subsequent renal resorption back to the plasma are not included.
- The model is built for total PFOS, i.e. the sum of linear and branched PFOS.
- Excretion via the faeces is modelled from the plasma compartment with a generic elimination rate, thereby circumventing the incorporation of an enterohepatic circulation, which requires extensive model modification.
- For all tissues, the density is assumed to be 1 kg/L.

2.4 Generic parameters

The physiological parameters such as the tissue volume fractions and the blood flow fractions used in this PBK model were obtained from the literature (Table 1).

Table 1. Physiological parameters of dairy cattle

Parameter	Value	Unit	Source
BW	624	kg	a
Tissue volume fractions			
VAd	0.184	-	b, c
Vgland	0.022	-	b, c
VK	0.0024	-	b, c
VL	0.013	-	b, c
VLu	0.0083	-	b, c
VMu	0.34	-	b, c
VPlasma	0.038*(1-Htc)	-	b, c
Vrest	0.84 –(volume fractions above)	-	
Cardiac output	5.45	L/h/kg	d
Htc	0.45		a
Blood flow fractions			
QAd	0.068	-	b, c
Qgland	0.165	-	b, c
QK	0.016	-	b, c
QL	0.35	-	b, c
QLu	0.028	-	b, c
QMu	0.1899	-	b, c
Qrest	1 – (blood flow fractions above)	-	
Qmilk	1.25	L/h	a

[a] Noorlander et al., 2025 (in preparation)

[b] Noorlander et al., 2024

[c] Lautz et al., 2020

[d] Lin et al., 2020

The distribution of PFOS in the different tissues was calculated by the partition coefficients obtained from literature (Table 2). The partition coefficient of the 'rest of the body' compartment wads fitted with plasma, muscle, liver and kidney data from four dairy cows in the animal study described by Noorlander et al., 2025 (in preparation).

Table 2. Partition coefficients of PFOS in dairy cattle

Parameter	Value	Source
PAd	0.2	a
PK	0.33	b
PL	1.3	b
PLu	0.00485	b
PMu	0.05	b
PMilk	0.005	b
Prest	0.15	Fitted to data in b

[a] Lupton et al., 2025

[b] Noorlander et al., 2025 (in preparation)

Kinetic parameters of PFOS that were obtained from the literature are mentioned in Table 3. The excretion rate (ke) is fitted to the total body burden of PFOS and the excretion via milk in Noorlander, 2025 (in preparation).

Table 3. Kinetic parameters of PFOS

Parameter	**Value**	**Unit**	**Source**
ka (absorption)	2.12	$hr^{-1}kg^{-1}$ $BW^{-0.25}$	a
ke (excretion)	0.002	hr^{-1}	b

[a] Chou et al., 2022

[b] Noorlander et al., 2025 (in preparation)

3 Software details

The transfer model simulations were developed and run using the R modelling language and using the deSolve package. The model code is publicly available online (https://github.com/rivm-syso/pfos-cow). Specifications on the programming packages are listed below:

Name software: R (tested with v. 4.5.0)
Manufacturer: The R Foundation for Statistical Computing
Place of manufacture: online
Year of manufacture: 2022
Description: A programming language for statistical computing

Name software: DeSolve (tested with v. 1.40)
Manufacturer: Karline Soetaert, Thomas Petzoldt and R. Woodrow Setzer
Place of manufacture: online
Year of manufacture: 2023
Description: Package to solve systems of differential equations
url: https://cran.r-project.org/web/packages/deSolve/index.html

Name software: dplyr (tested with version 1.1.4)
Manufacturer: Hadley Wickham, Romain François, Lionel Henry, Kirill Müller, Davis Vaughan, Ryan Dickerson, Posit Software, PBC
Place of manufacture: online
Year of manufacture: 2023
Description: A fast, consistent tool for working with data frame like objects, both in memory and out of memory.
url: https://cran.r-project.org/web/packages/dplyr/index.html

4 Model applicability

The transfer model presented in this report can be used to simulate the transfer of PFOS to milk, muscle, liver and kidney of dairy cows after exposure to PFOS via feed. As such, the model enables comparison of the estimated concentration to regulatory limits of these food matrices. Similarly, the model can be used to estimate the wash-out period needed to comply with regulatory limits in case the concentrations exceeded such regulatory limits.

An example of a model application is given in Figure 2 for milk and muscle (meat) and Figure 3 for liver and kidney. Exposure to PFOS (2 µg/kg dry matter (dm) grass during summer) was simulated for an exposure duration of 66 days. Contaminated grass intake was 15 kg grass per day. After the 66 days of exposure to contaminated feed, an additional 110 days were simulated in which only clean feed (i.e. feed not containing PFOS) was provided. Note that the model was fitted for a milk production of 32 L/day.

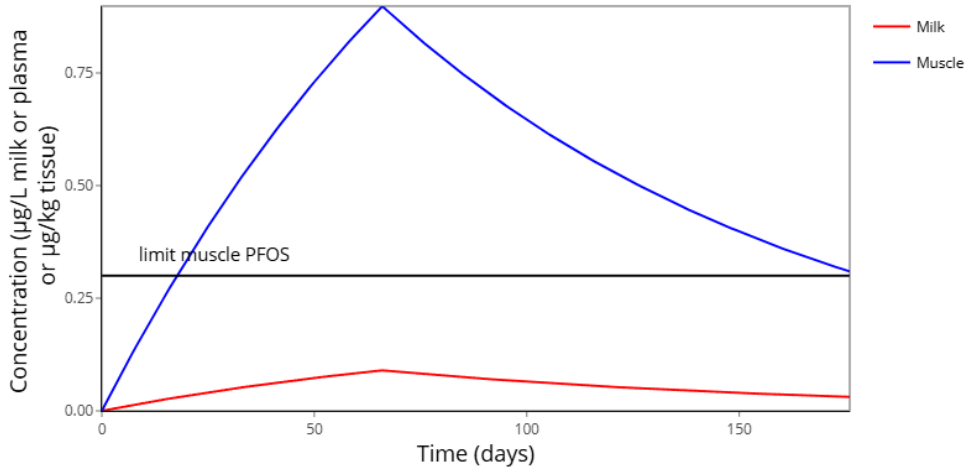

Figure 2. *Simulated PFOS concentration in milk and muscle of dairy cows fed grass containing 2 µg/kg dm PFOS during 66 days followed by clean feed for 110 days. The dairy cows were fed 15 kg dm grass per day and had a milk production of 32 L/day.*

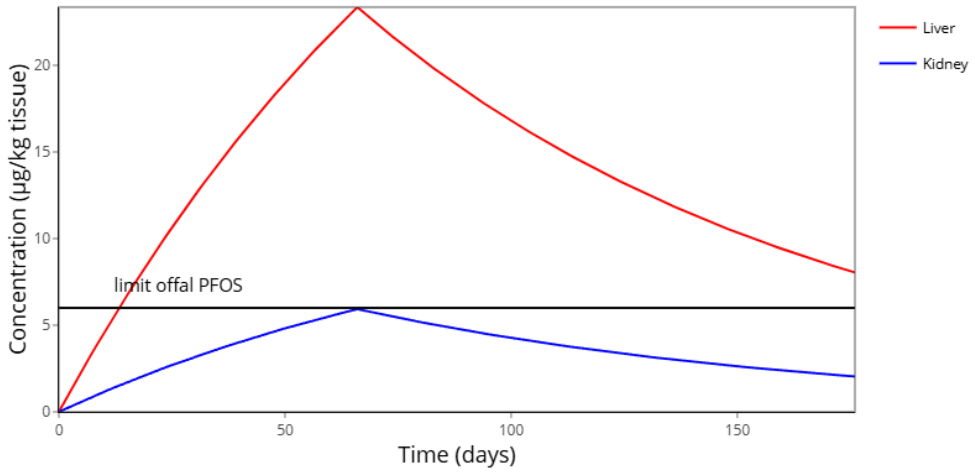

Figure 3. *Simulated PFOS concentration in liver and kidney of dairy cows fed grass containing 2 µg/kg dm PFOS during 66 days followed by clean feed for 110 days. The dairy cows were fed 15 kg dm grass per day and had a milk production of 32 L/day.*

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