Food Safety and Inspection Service
Protecting Public Health and Preventing Foodborne Illness
Development of a PFOS Plasma Depletion Model in Dairy Cattle

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Introduction

• Perfluoroalkyl substances (PFAS) include perfluorooctanesulfonic acid (PFOS), perfluorooctanoic acid (PFOA), etc.

• In 2018, FDA (U.S. Food and Drug Administration) notified USDA that a dairy herd of approximately 5,000 animals had been exposed to PFAS via drinking water and forage. FDA determined that milk from the herd was adulterated due to PFOS levels.

• USDA/FSIS (responsible for regulating meat, poultry, and egg products) was concerned about the safety of beef from the dairy herd.
Objective

• This study: to better understand perfluorooctanesulfonic acid (PFOS) plasma depletion dynamics in dairy cattle

• Part of broader project that includes:
  – Developing and validating analytical methods to measure PFAS concentrations in cattle tissues
  – Investigating the relationship between cattle plasma and muscle PFOS concentrations as possible ante-mortem approach to estimate PFOS concentrations in beef
Data, analysis, and results are preliminary.

Measurements obtained to date are plasma concentrations of the PFOS linear isomer.

Plasma branched PFOS isomer concentrations are currently being quantified.

The analysis will be updated based on the total concentration of linear and branched isomers.
• PFOS (linear isomer) was quantified in plasma from blood samples collected every 2 weeks (0 - 153 days) from 8 animals (3 lactating, 5 young) after removal from exposure to PFOS at a contaminated dairy operation.

• PFOS (linear isomer) plasma depletion model was developed based on 92 PFOS plasma concentrations of the 8 animals.
Methods

• To account for the lack of independence of repeated measures within cows over time, longitudinal data analysis was performed using generalized estimating equations (GEE).

• Animal class (lactating or young) was identified by an indicator variable (young = 0,1).
• A difference in plasma depletion rates between young and lactating animal classes was evaluated by including the young x days interaction term in the models.

• Four depletion model forms were considered: log-linear, log-quadratic, log-cubic, and second-order.
Log-Linear

\[ \ln(C_{it}) = \ln(C_0) + b_i \text{cow}_i + b_1 \text{days} + b_2 \text{young}_i \times \text{days} \]
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Log-Quadratic

\[ \ln(C_{it}) = \ln(C_0) + b_i \text{cow}_i + b_1 \text{days} + b_2 \text{days}^2 + b_3 \text{young}_i \times \text{days} \]
Log-Cubic

\[
\ln(C_{it}) = \ln(C_0) + b_i \text{cow}_i + b_1 \text{days} + b_2 \text{days}^2 + b_3 \text{days}^3 + b_4 \text{young}_i \times \text{days}
\]
Second-Order

\[
\frac{1}{C_{it}} = \frac{1}{C_0} + b_{icow_i} + b_1\text{days} + b_2\text{youngix days}
\]

\[
\frac{1}{C_t} = \frac{1}{C_0} + b_1\text{days} := \ln \left( \frac{C_0-C_t}{C_0C_t} \right) = \ln(b_1) + \ln(\text{days})
\]

- If \(C_t > C_0\), \(\ln(C_0-C_t)\) is undefined
Results

- Based on regression diagnostics and fit criteria, the log-cubic model was selected.

- The limited data provided no evidence that the depletion rate differs between lactating and young dairy cows (interaction term n.s. in all models).

- Preliminary PFOS plasma depletion model:

  \[ \ln(C_{it}) = b_0 + b_{cowi} + b_1days + b_2days^2 + b_3days^3 \]
Comparison of Plasma PFOS (linear isomer) Concentrations Observed and Predicted by the Log-Cubic Depletion Model
Out-of-Sample Performance

- Independent of the data used to estimate the depletion model, paired PFOS (linear isomer) plasma concentration data for 19 animals were collected on-farm and at necropsy after 14 days post-exposure.

- An out-of-sample prediction under the depletion model was accurate for the 14-day post-exposure withdrawal period.
• The preliminary results suggest that PFOS plasma depletion dynamics in dairy cattle are complex: first- and second-order kinetics fail to describe the observed data.

• Potential applications of this model include development of risk management strategies to permit the recovery of unadulterated beef from PFOS exposed cattle.
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Food Safety and Inspection Service: Questions