Appendix A

Procedure for Extrapolating Steady State Concentrations
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Procedure for Extrapolating Steady State Concentrations

1. Take the natural log of the concentrations (ppm) measured on or after the last day of feeding. Conduct a linear regression analysis where day is the independent variable and ln (concentration) is the dependent variable. The slope of this line is the depuration rate, $kd \ (d^{-1})$.

2. Estimate the tangent, $dC/dt$, for each point of the uptake curve using an exponential fit of the uptake data.

3. Estimate the uptake rate, $ku$, using each point during uptake and the last day of feeding using the following equation:

$$
k_u = \frac{\frac{dC}{dt} + kd \times Ct}{CIR}
$$

where

- $ku$ = Uptake rate based on some time $t \ (kg^{-1})$,
- CIR = Chemical intake rate (mg/d),
- Ct = Concentration at some time $t \ (mg/kg)$, and
- $kd$ = Depuration rate ($d^{-1}$).
4. Average each value of $k_{ut}$ to get the best overall estimate of $ku$.

5. Estimate the steady state concentration, $C_{ss}$ (mg/kg) using the following equation:

$$C_{ss} = \frac{ku}{kd} \times CIR.$$ 

6. Estimate the biotransfer factor (BTF) ([mg/kg]/[mg/d]) using the following equation:

$$BTF = \frac{C_{ss}}{CIR}.$$ 

7. Estimate the half-life of the chemical using the following equation:

$$t_{1/2} = \frac{\ln(2)}{kd}$$

where

- $t_{1/2}$ = half life of the chemical (d), and
- $kd$ = depuration rate (d⁻¹).

8. Estimate the time required to reach steady state using the following equation:

$$t_{ss} = 5 \times t_{1/2}$$

where

- $t_{ss}$ = time to reach steady state (d), and
- $t_{1/2}$ = half life of the chemical (d).

9. Compare the raw data to the steady-state prediction by plotting the two where the y-axis is concentration and the x-axis is time. Estimate concentrations during uptake using the following equation:

$$C_t = C_{ss} \times \left(1 - e^{-kd \times t}\right).$$
10. Compare the kinetic model’s prediction to the actual data. Calculate concentrations during uptake using the equation provided in Step 9. Calculate concentrations during depuration as follows:

\[ C_t = C_{last} \times e^{-kd \times (t - t_{dosed})} \]

where

- \( C_t \) = Concentration at time \( t \) (mg/kg milk),
- \( C_{last} \) = Predicted concentration on last day of dosing (mg/kg milk),
- \( kd \) = Depuration rate (d\(^{-1}\)),
- \( t \) = Time, \( \geq \) days dosed (d), and
- \( t_{dosed} \) = Days dosed (d).
Appendix A

Reference