

Estimation of "Safe" Reference Level (ppb) of PFOS in Plasma

Basic Factors:

- LOAEL in Rhesus Monkeys = 0.5 mg/kg/day over 90 days.
- PFOS is cumulative, the excretion kinetic being quite low (30.2% in urine and 12.6% in feces 89 days after an i.v. dose in rats [rats may have significantly more urinary excretion capability than humans]).
- Absorption from the G.I. tract is almost complete (>95%) within 24 hours after administration.
- Significant enterohepatic re-circulation occurs.

Safety Factors:

- 10 for LOAEL to NOAEL
- 10 for sub-chronic to chronic
- 100 for interspecies extrapolation
- 10 for exposure of children (Food Quality Safety Act & Water Act)

note bene:

I might be inclined to keep or reduce interspecies S.F. and increase LOAEL to NOAEL and/or subchronic to chronic.

Applying 100,000-fold safety factor to sub-chronic Rhesus study gives RfD of 5 nanograms/kg/day. For a 70 kg human, this is converted to 0.35 micrograms/day.

note bene:

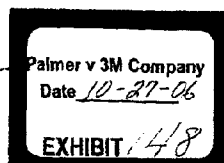
Please recall that FDA uses 5.0 micrograms/day from all sources as a risk level for N-Ethyl FOSE. We can compare PFOS and N-Ethyl FOSE risk values stated here on a molar basis:

- 5.0 micrograms/day N-Ethyl FOSE = 8.5 nanomoles/day
- 0.35 micrograms/day PFOS = 0.7 nanomoles/day

Since our basis is a 90-day study in Rhesus monkeys, what is the estimated plasma level of PFOS associated with this RfD of 0.35 micrograms per day? I can only think to do this by multiplying 0.35 micrograms per day by 90 days to get a total dose of 31.5 micrograms. Of this, let's assume 10% is in plasma (may actually be a little less). So, 3.15 micrograms in plasma gives a concentration of 1.5 ppb, assuming that the average human has 3 liters of plasma (60% of blood volume, which is 5 liters in the normal human, assuming normal hematocrit of 40%).

Therefore, I derive with 1.05 ppb as a reference level in plasma for chronic PFOS exposure from all sources.

While this may seem extreme, it follows the approach used by federal agencies. The safety factors used could be significantly reduced with the results of additional studies.



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Exhibit
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State of Minnesota v. 3M Co.,
Court File No. 27-CV-10-28862