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**Internal Correspondence**

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**Subject:** Draft Drinking Water Health Advisory (DWHA) - PFOS

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Mike –

The attached document presents the derivation of a draft lifetime Drinking Water Health Advisory (DWHA) for perfluorooctanesulfonate (PFOS). This represents the concentration of PFOS in drinking water that is not expected to cause any adverse non-cancer effects over a lifetime of exposure, with a margin of safety. The draft DWHA is based on a reference dose (RfD) which was derived using a conservative, composite uncertainty factor (UF) of 1000 based on the no observed effect level in a six-month primate study and supported by a robust database of human and animal health-effects data. The DWHA assumes lifetime exposure to PFOS through the consumption of two liters of contaminated water per day. The DWHA also assumes that drinking water represents 20 percent of the total daily exposure to PFOS. In other words, if drinking water was determined to be the only source of exposure, the DWHA level could be five times higher. The level derived in this process, 1.0 μg PFOS per liter, does not represent an absolute value above which health risk is imminent. It can best be described as a *de minimus* risk level for lifetime exposure for non-cancer effects and incorporates a significant margin of safety.

If you have questions or would like to discuss, please let me know.

John

**Lifetime Drinking Water Health Advisory (DWHA) for PFOS**

## Background[1]

The DWHA for PFOS was calculated using standard EPA methodology. Briefly, the following three equations were used:

$$RfD = \frac{(NOAEL)\ or\ (LOAEL)}{(UF)} = mg/kg\ body\ weight - day$$

$$DWEL = \frac{(RfD)\ (70\ kg)}{2\ L/day} = mg/L\ or\ \mu g/L$$

$$Lifetime\ DWHA = DWEL\ x\ RSC = mg/L\ or\ \mu g/L$$

Where:

**RfD** = Chronic Reference Dose [the estimate (with uncertainty spanning an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious effects during a lifetime]

**NOAEL** = No Observed Adverse Effect Level [the exposure level at which there are no statistically or biologically significant increases in the frequency or severity of adverse effects between the exposed population and the appropriate control; some effects may be produced at this level but they are not considered to be adverse, nor to be a precursor to specific adverse effects]

**LOAEL** = Lowest Observed Adverse Effect Level [the exposure level at which there are statistically or biologically significant increases in the frequency or severity of adverse effects between the exposed population and the appropriate control]

**UF** = Total Uncertainty Factor (chosen using EPA guidance). The total UF is composed of five sub-factors that attempt to account for uncertainty with regard to: 1) interhuman variability; 2) extrapolation of results from

experimental animal to human; 3) extrapolation from subchronic to chronic exposure; 4) extrapolation from LOAEL to NOAEL; and 5) incomplete database to complete database.

A modifying factor (**MF**) may also be applied to account for areas of scientific uncertainty not accounted for in the five sub-UFs.

The standard EPA default factor for each of the five sub-UFs = 10; that for the MF = 1. Sub-UFs <10 may also be used when existing data reduce or eliminate the need to account for a particular area of uncertainty. ***The choice of appropriate sub-UFs and the MF is accomplished on a case-by-case basis using professional judgment by experienced risk assessors.***

**DWEL** = Drinking Water Equivalent Level [the concentration of a substance in drinking water that is not expected to cause any non-carcinogenic health effects in humans over a lifetime of exposure]

**RSC** = Relative Source Contribution [is the proportion of exposure to a chemical from drinking water relative to other sources such as food and air](in the absence of any other data the EPA default value = 20% is used)

**Lifetime Drinking Water Health Advisory (DWHA)** = The concentration of a chemical in drinking water that is not expected to cause any adverse noncarcinogenic effects over a lifetime of exposure, with a margin of safety.

## [1]References

Cicmanec, J.L *et al.* (1996). Noncancer risk assessment: present and emerging issues. In: Fan, A.M. and Chang, L.W. (editors) *Toxicology and Risk Assessment: Principles, Methods, and Applications*. Marcel Dekker, New York, pp. 293-310. *(copy of paper attached)*

Dourson, M.L. *et al.* (1996). Evolution of science-based uncertainty factors in noncancer risk assessment. *Regulatory Toxicology and Pharmacology* **24**: 108-120. *(copy of paper attached)*

Environmental Protection Agency (1999). Integrated Risk Information System (IRIS). WWW address: http://www.epa.gov/ncea/iris.htm

Environmental Protection Agency (1999). Office of Water. Drinking Water Regulations and Health Advisories.

## I. Lifetime Drinking Water Health Advisory (DWHA) for PFOS

### Step 1. RfD Calculation

$$RfD = \frac{(NOAEL)\ or\ (LOAEL)}{(UF)} = mg/kg\ body\ weight - day$$

**NOAEL = 0.15 mg/kg-day** [NOAEL from 6-month monkey oral capsule study]

**UF = 900 (rounded up = 1000)** [total UF = 900 (10x3x10x1x3). Individual sub-UFs were as follows [also refer to Appendix]:

**Interhuman (person-to-person variability) = 10** [standard EPA default]

**Extrapolation from experimental animal-to-human (interspecies variability) = 3** [used non-human primate]

**Extrapolation to chronic exposure (chronicity) = 10** [based on exposure duration longer than subchronic but significantly less than chronic (6 months in a non-human primate); PFOS also appears to accumulate in the body on repeated exposure due to poor elimination]

**LOAEL to NOAEL = 1** [standard default - NOAEL used]

**Incomplete database = 3** [significant data accumulated on chemical; results of the 2-year bioassay are still pending]

**Modifying Factor = 1** [human data available; significant data accumulated on chemical; sensitive endpoint established in studies; uncertainties accounted for in other sub-factors]

**Therefore:**

$$RfD = \frac{0.15\ mg/kg-day}{1000} = 0.00015\ mg/kg-day = (0.2\ \mu g/kg-day)$$

**Note:** The precision associated with the RfD is usually one significant figure, therefore, RfD should be rounded to = 0.2 μg/kg-day

## II. Lifetime Drinking Water Health Advisory (DWHA) for PFOS

### Step 2. DWEL Calculation

$$DWEL = \frac{(RfD)\ (70\ kg)}{2\ L/day} = mg/L\ or\ \mu g/L$$

$$DWEL = \frac{(0.2\ \mu g/kg-day))\ (70\ kg)}{2\ L/day} = 7\ \mu g/L$$

## III. Lifetime Drinking Water Health Advisory (DWHA) for PFOS

### Step 3. Lifetime DWHA Calculation

$$Lifetime\ DWHA = DWEL\ x\ RSC = mg/L\ or\ \mu g/L$$

$$\boxed{Lifetime\ DWHA = (7\ \mu g/L)(0.2) = 1.0\ \mu g/L\ (ppb)}$$