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FROM: Gloria Post, Ph.D., DABT, Research Scientist GP

SUBJECT: Updated Drinking Water Guidance for Perfluorooctanoic Acid (PFOA)

DATE: October 3, 2017

Drinking water guidance values developed by NJDEP for PFOA and other contaminants are intended to be protective for chronic (lifetime) exposure. This memorandum provides an update of the drinking water guidance for perfluorooctanoic acid (PFOA) of 40 ng/L (0.04 µg/L) developed by the Division of Science, Research and Technology in 2007. An update of the 2007 guidance is appropriate because a large body of relevant health effects information from both human and animal studies has become available since it was developed.

The New Jersey Drinking Water Quality Institute (DWQI) has conducted a detailed evaluation of the relevant scientific information that is currently available and developed a Health-based Maximum Contaminant Level (MCL) of 14 ng/L (0.014 µg/L) (DWQI, 2017a). The DWQI also evaluated the Practical Quantitation Level for PFOA and the ability of available treatment technology to remove PFOA from drinking water. The DWQI concluded that achievement of the Health-based MCL is not limited by the analytical or treatment removal considerations. Therefore, the DWQI recommended a Maximum Contaminant Level (MCL) of 14 ng/L to NJDEP Commissioner Martin (DWQI, 2017a).

The DWQI recommendations have been reviewed by the Division of Science, Research and Environmental Health (DSREH). DSREH scientists are in agreement with the DWQI recommendation of a heath based drinking water value of 14 ng/L, and they also agree that PFOA can be quantitated and removed from drinking water to levels below the health based value of 14 ng/L.

It is our understanding that Commissioner Martin has accepted the DWQI recommendation of a PFOA MCL of 14 ng/L, and that NJDEP plans to propose this as a regulatory MCL. An updated drinking water guidance for PFOA is needed at this time in order to provide current and health-

protective advice to New Jersey public water systems with detections of PFOA until the New Jersey PFOA MCL is finalized. Therefore, it is recommended that the drinking water guidance for PFOA be updated to 14 ng/L at this time.

The basis for the 2007 guidance of 40 ng/L and the current guidance of 14 ng/L are briefly summarized below.

Basis of 2007 guidance (40 ng/L)

Although the key primary scientific literature was reviewed as appropriate, NJDEP did not conduct a comprehensive literature search on health effects of PFOA when developing the 2007 guidance due to the need for a rapid response. Instead, the 2007 guidance was based on No Observed Adverse Effect Levels (NOAELs) or Lowest Observed Adverse Effect Levels (LOAELs) for administered doses and serum PFOA levels (internal doses) in experimental animals at various life stages that were identified in the USEPA (2005) draft risk assessment for PFOA. While NOAELs and LOAELs were identified, USEPA (2005) did not develop Reference Doses (RfDs), slope factors, or a health-based drinking water level for PFOA.

Because the half-life of PFOA is much longer in humans (several years) than in the animal species used in the toxicological studies (several hours to 30 days), the 2007 guidance was based on comparisons between effect levels in animal studies and human exposures on the basis of serum levels rather than external dose.

For non-carcinogenic effects, Target Human Serum Levels (analogous to RfDs, but on a serum level basis) were derived by applying uncertainty factors to the measured or modeled serum levels at the NOAELs or LOAELs identified by USEPA (2005). The default Relative Source Contribution factor (RSC) of 20% was applied to the Target Human Serum Levels to account for contributions to serum PFOA from non-drinking water exposures.

For carcinogenic effects, NJDEP noted that PFOA was classified as having "suggestive evidence of carcinogenic potential" by USEPA (2005) and as "likely to be carcinogenic to humans" by the USEPA Science Advisory Board (2006). The serum level resulting in a one in one million (10^{-6}) risk level was estimated by linear extrapolation from the modeled serum level in animals at a dose resulting in an approximate 10% tumor incidence.

The mean ratio of approximately 100:1 between serum PFOA levels and drinking PFOA water concentrations in exposed communities was used to convert the serum PFOA levels for non-carcinogenic and carcinogenic effects identified above to the corresponding drinking water concentrations (Post et al., 2009). The range of drinking water concentrations for the seven toxicological endpoints assessed (six non-carcinogenic endpoints and carcinogenicity) was 40 – 260 ng/L, and drinking water concentrations for five of these endpoints fell within a similar range (40, 50, 60, 70, and 80 ng/L). The most sensitive endpoints, resulting in a drinking water concentration of 40 ng/L, were decreased body weight and hematological effects in the adult female rat in a chronic dietary study (Sibinski, 1987). This value was determined to be protective for carcinogenic effects, as the drinking water concentration at the 10^{-6} cancer risk level was estimated as 60 ng/L. Therefore, the guidance of 40 ng/L was considered to be protective for both non-carcinogenic and carcinogenic effects.

Basis of updated guidance (14 ng/L)

The updated guidance of 14 ng/L is based on the Health-based MCL and MCL recommended by the DWQI (2017a). In developing the Health-based MCL for PFOA, DWQI (2017b) conducted a literature search in 2015 that identified over 2000 publications related to PFOA, with subsequent updated searches to identify additional relevant publications. Of these studies, only 244 were published in 2005 or earlier, while more than 1700 were published in 2006 or later and were therefore not considered by USEPA (2005) or by NJDEP in developing its 2007 PFOA guidance of 40 ng/L.

It was noted that a large body of relevant health effects information not considered in development of the 2007 guidance has become available. Of particular importance are toxicology studies reporting developmental effects in mice, and epidemiology studies reporting associations of PFOA with numerous health effects in the general population and in communities with contaminated drinking water. Developmental effects of PFOA in mice were first reported in 2006, while earlier developmental studies were from rats. The rat is not a suitable model for developmental effects of PFOA because of very rapid excretion of PFOA (half-life 2-4 hours) in females. In contrast, the mouse is an appropriate model for developmental effects of PFOA because female mice, like humans, excrete PFOA slowly. In humans, PFOA exposure levels prevalent in the general population have been associated with health effects including increased serum cholesterol and liver enzymes, decreased response to vaccines, and decreased birth weight. Drinking water exposure to PFOA was also associated with testicular and kidney cancer. In addition, the DWQI noted that PFOA persists in the body for many years after exposure ends (half-life of several years) and that relatively low exposures in drinking water substantially increase serum PFOA levels. The DWQI concluded that the information presented above supports a public health protective approach in developing a Health-based MCL and a need for caution regarding exposure through drinking water.

Both non-carcinogenic and carcinogenic effects were evaluated for Health-based MCL development. Delayed mammary gland development and increased liver weight were the most sensitive non-carcinogenic endpoints with serum PFOA data needed for dose-response analysis, and Target Human Serum Level were developed for these endpoints. The Target Serum Levels were developed by applying appropriate uncertainty factors to serum BMDLs (lower confidence limit on Benchmark Dose) developed through Benchmark Dose modeling. A clearance factor (1.4×10^{-4} L/kg/day) which relates serum PFOA concentrations to human PFOA doses was applied to the Target Human Serum Levels to develop Reference Doses. This clearance factor predicts a ratio of drinking water:serum levels of 114:1 from average water consumption, consistent with observations in communities using drinking water contaminated with PFOA.

For delayed mammary gland development, the Target Human Serum Level is 0.8 ng/ml, which is below the median serum PFOA level in the U.S. general population, and the Reference Dose for this endpoint is 0.11 ng/kg/day. Because the use of delayed mammary gland development as the basis for quantitative risk assessment is a currently developing topic, a Health-based MCL using this endpoint as its primary basis was not recommended. However, it was concluded that an uncertainty factor for sensitive endpoints is needed to protect for this and other effects that occur at similarly low doses.

A Health-based MCL protective for increased relative liver weight was derived based on a study in which male mice were exposed to PFOA for 14 days (Loveless et al., 2006). For increased relative liver weight, the Target Human Serum Level is 14.5 ng/ml and the Reference Dose is 2

ng/kg/day. This Target Human Serum Level and Reference Dose incorporate uncertainty factors to protect sensitive human subpopulations, to account for toxicodynamic differences between human and experimental animals, and to protect for more sensitive endpoints that occur from developmental exposures (delayed mammary gland development, persistent hepatic toxicity, and others). Default values for drinking water exposure assumptions (2 L/day water consumption; 70 kg body weight) and Relative Source Contribution factor (20%) were used to develop a Health-based MCL of 14 ng/L based on the Reference Dose for increased relative liver weight.

A cancer slope factor of 0.021 $(mg/kg/day)^{-1}$ was developed based on increased incidence of testicular tumors in a chronic rat study. This slope factor was used to develop a Health-based MCL protective for cancer effects at the 1×10^{-6} (one in one million) lifetime cancer risk level of 14 ng/L, identical to the Health-based MCL based on non-cancer endpoints.

Therefore, the Health-based MCL recommended by the DWQI and accepted by NJDEP was 14 ng/L.

In conclusion, it is recommended that the drinking water guidance for PFOA be updated to 14 ng/L.

Please let me know if you have any questions or need additional information.

c: Dan Kennedy, Assistant Commissioner, Water Resource Management

Citations

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