Technical Analysis of New Jersey’s Proposed Health-Based Maximum Contaminant Level (MCL) for Perfluorooctane Sulfonate (PFOS)

by

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submitted January 2018

Executive Summary

The RfD (reference dose) for PFOS (perfluorooctane sulfonate) derived by the NJDWQI (New Jersey Drinking Water Quality Institute) is the most stringent and protective in the U.S., based on a rigorous analysis of all available PFOS animal and epidemiologic toxicological studies. However, in its use of adult default exposure values to determine a maximum contaminant level (MCL), younger children would not be protected since younger children dose intakes would exceed the allowable RfD. This is disconcerting since existing PFOS serum levels in children in the normal population are already within or near the serum PFOS levels associated with immunotoxic effects found in epidemiologic studies. In addition, other toxic effects found associated with children and PFOS exposure may lead to increased potential for later disease manifestation. It is essential, therefore, that the NJDWQI depart from the typical use of adult default exposure values and use children’s values. Using appropriate children exposure values, we recommend a MCL for PFOS of 5 ng/L.

Alternatively, we recommend a MCL such that the combination of PFOS and PFOA concentrations in water supplies be no higher than 13 ng/L, MCL [PFOA + PFOS] \leq 13 ng/L.

Introduction

The presence of PFOS and PFOA (perfluoro-octanoic acid) in New Jersey is of public health concern because relatively high concentrations have been found in public water supplies (PWS), in some instances at levels greater than the existing 14 ng/l MCL for PFOA and the proposed 13 ng/l MCL for PFOS. Ten of 80 PWS tested by the New Jersey DEP (Department of Environmental Protection) had PFOS at levels ≥ 20 ng/l with 7 PWS containing PFOS at levels exceeding 40 ng/l (NJDEP 2017). Testing of 175 New Jersey PWS, including 165 large community systems and 10 small community systems completed under the UCMR3, found 6 PWS with PFOS levels exceeding 40 ng/L and 18 PWS with PFOA levels exceeding 20 ng/L (UCMR3 2017, NJDWQI 2017). Ingestion of any level of PFOS and PFOA contaminated water could further increase residents’ PFOS blood serum levels beyond that already found in epidemiologic studies to be associated with adverse health effects (immunotoxicity) in the general U.S. population.
A large number of animal studies indicate a wide range of PFOS toxicity effects. These include decreased body weight, increased liver weight with microscopic lesions in monkeys and rats, increased incidence of hepatocellular adenomas in rats, developmental effects on rats and mice including neonatal mortality, decreased gestation length, lower birth weights, and developmental delays. For post-gestation and lactational exposure these include: developmental neurotoxicity, changes in thyroid and reproductive hormones, altered lipid and glucose metabolism, and decreased immune function (USEPA 2016b).

Among non-cancer endpoints the NJDWQI concludes that, for adult animals, the most sensitive endpoints (lowest LOAELs based on serum PFOS concentrations) are described in 9 studies and include: “endocrine/metabolic effects (e.g., decreases in thyroid hormone and increased incidence of thyroid follicular cell adenomas), changes in immune parameters (e.g., increased relative number of macrophages and decreased plaque forming cell response), and increased liver weight and liver histopathology” (NJDWQI 2017). For post-natal or gestational exposures, NJDWQI concludes the most sensitive non-cancer endpoints (lowest LOAELs based on serum PFOS concentrations) are described in 11 studies and include: “decreased body weight, changes in endocrine/metabolic parameters (i.e., fasting levels of serum glucose and insulin, markers of insulin resistance, and thyroid hormone levels), increased liver weight, changes in lung morphology, and increased mortality” (NJDWQI 2017).

NJDWQI examined these 20 toxic endpoints in terms of the timing of biological significance and suitability for dose-response analysis, and determined 4 endpoints suitable to calculate a (POD) point of departure. The immunotoxic effect shown in the Dong et al. (2009) study was chosen as the most sensitive POD (point of departure) at 674 ng/ml.

The immunotoxic endpoint chosen to develop an MCL based on decreased plaque forming cell response, a predictor of immunosuppression, in animal studies is supported by epidemiologic studies that found associations between PFOS and PFOA blood serum levels in humans and decreases in immune function.

A study by Grandjean and Budtz-Jørgensen (2013) found an association between increases in serum PFOS and PFOA levels and decreases in serum antibody concentrations against tetanus and diphtheria toxoids. In this study regression modeling of PFOA and PFOS concentrations as independent variables along with potential confounders of sex, age, and booster type at age 5 and 7, with antibody concentrations as outcome, allowed determination of benchmark response (BMR) and benchmark dose (BMD). The lower one-sided 95% confidence limit of the BMD, the BMDL (benchmark dose level), was determined in this study to be approximately 0.33 ng/ml for PFOA and 1.3 ng/ml for PFOS, based on the linear slope model of the regression. The study notes strong correlation between PFOS and PFOA, making mutual adjustment in the regression difficult. However, the BMDL developed provides a strong epidemiologic basis using an immunosuppression endpoint to develop a MCL.

A study in Norway evaluated the effect of prenatal exposure to PFAS (perfluoroalkyl substances) on responses to pediatric vaccines and immune-related health outcomes in
children up to 3 years of age (Granum et al. 2013). In this study blood samples were taken from the mothers at time of delivery and children at 3 years age. The study found an inverse association between the level of anti-rubella antibodies in the children’s serum at age 3 years and the concentrations of four PFAS compounds (PFOS, PFOA, PFNA, and PFHxS). The strength of the association between rubella antibody-levels and PFAS concentrations were PFNA>PFOA>PFHxS>PFOS.

A cross-sectional study of 1191 children 12-19 years old using NHANES data (1999-2000 and 2003-2004) found that increased exposure to several PFAS compounds was associated with lower levels of mumps and rubella antibody concentrations, especially among seropositive individuals (Stein et al. 2016). This study found that a doubling of PFOS serum concentration was associated with a 7.4% (95% CI: -12.8, -1.7) decrease in mumps antibodies. A doubling of PFOS serum concentration was also associated with a 13.3% decrease in rubella antibodies; this association occurred among seropositive individuals. Decreases in rubella antibodies were also found to be associated with PFOA and PFHxS. The authors found that children with higher PFOS levels were less likely to be sensitized to allergens, but children with higher PFOS levels were more likely to be sensitized to mold (IQR OR 1.33, 95% CI: 1.06, 1.69).

A small study in Denmark evaluated reduced antibody responses to perfluorochemical exposures (Kielsen et al. 20016). Twelve adults were boosted with tetanus and diphtheria toxoids with antibody responses and followed in a subsequent one-month period. Participants had been vaccinated with diphtheria and tetanus toxoids in childhood, but no boosters had been received within the last 5 years. The study found that at a doubling of PFOS exposure, based on serum obtained from participants 10 days post-vaccination, the relative increase in the diphtheria antibody concentration decreased by an average of about 12%, p = 0.044. Significant diptheria antibody concentration reductions were also found for PFNA, PFDA, PFUnDA, and PFDnDA.

A study of 411 adults in the mid Ohio region of Ohio and West Virginia, where the drinking water supply had been contaminated with PFOA (Dupont plant), evaluated antibody response and PFOS and PFOA levels in blood serum following vaccination with influenza vaccine. The study found that elevated PFOA serum concentrations were “associated with reduced antibody titer rise, particularly to A/H3N2 influenza virus, and an increased risk of not attaining the antibody threshold considered to offer long-term protection” (Looker et al. 2014). However, in this study no association was found between PFOS serum levels and reductions in antibody rise.

The National Toxicology Program concluded that “exposure to PFOS is presumed to be an immune hazard to humans based on a high level of evidence that PFOS suppressed the antibody response from animal studies and a moderate level of evidence from studies in humans”. NTP also concludes that “PFOS is suspected to suppress infectious disease resistance and NK cell activity in humans, and these conclusions are based on moderate level of evidence from animal studies and low or inadequate level of evidence from human studies” (NTP 2016).

Reference Dose and Uncertainty Factors - Immunotoxicity Endpoint
Human epidemiologic data have current limitations and are not used as a quantitative basis for a health-based RfD and MCL. However, a RfD based on quantitative epidemiologic data for an immunotoxic effect should be taken into account. In our review of the New Jersey 2016 proposed standard for PFOA we derived a MCL based on the Grandjean and Budtz-Jørgensen (2013) study where benchmark calculations based on regression modeling enabled a determination of a BMDL. Based on that study’s BMDL we calculated a 0.03 MCL for PFOA (Oliaei and Kriens 2016). Using the same methodology, we derive a MCL for PFOS as follows:

The lower one-sided 95% confidence limit of the BMD, the BMDL (benchmark dose level) determined in the Grandjean and Budtz-Jørgensen (2013) study, is approximately 1.3 ng/ml for PFOS, based on the linear slope model of the regression. Based on the immunotoxic effects shown in this study we propose a 1.3 ng/ml BMDL for PFOS as the target human serum level. An uncertainty factor of 10 for human variation in susceptibility is applied. A clearance factor of $8.1 \times 10^{-5} \text{ L/kg/day}$ derived by USEPA for PFOS (USEPA 2016b) is applied to the target human serum Level to calculate an RfD.

$$\text{RfD} = \frac{1.3 \text{ ng/ml} \times 1000 \text{ ml/L} \times 8.1 \times 10^{-5} \text{ L/kg/day}}{10} = 0.01 \text{ ng/kg/day}$$

Using NJDWQI default adult exposure values of 70 kg body weight, 2 L/day water intake, and a relative source contribution of 0.2, the MCL is:

$$\text{MCL} = \frac{0.01 \text{ ng/kg/day} \times 70 \text{ kg} \times 0.2 \text{ RSC}}{2 \text{ L/day}} = 0.07 \text{ ng/L} \text{ (round to 0.1 ng/L)}$$

Absent application of epidemiologic data, NJWQI’s rigorous methodology and criteria used to select a BMDL, or NOAEL if applicable, is scientifically sound and conservative. Of the 4 final studies chosen by NJWQI for dose-response modeling, the Dong et al 2009 study of decreased plaque forming cell response, predictive of immunotoxicity, resulted in the lowest (most sensitive) point of departure (POD). As discussed in the report, the NOAEL of the study was used as the POD, or 674 ng/L, since BMDS software modeling would not calculate a BMDL for this study’s dose-response data (NJDWQI 2017). After application of uncertainty factors the target human serum level calculated was the lowest among the 4 final studies, and resulted in the lowest RfD of 1.8 ng/kg/day.

This RfD is considerably more protective than the USEPA RfD of 20 ng/kg/day based on animal developmental effects (e.g. decreased pup body weight) (USEPA 2016b). However, because of potential increased susceptibility during pregnancy and lactation EPA used drinking water intake and body weight exposure values at the 90% distribution for lactating women, moderating the calculation (versus use of adult default weight and intake) to 70 ng/l for a lifetime health advisory (HA) or “MCL” for this target population.

Although the RfD determined by NJDWQI is a significant departure from the much less
protective RfD of 20 ng/kg/day developed by USEPA, we disagree with the UF (uncertainty factor) used to determine the target human serum level. NJDWQI applied a UF of unity (1.0) for sub-chronic versus chronic testing used in Dong et al (2009) even though this study of 60 days is of sub-chronic duration. Sub-chronic duration is > 30 day to ≤ 90 days. A UF of 10 is normally applied when sub-chronic is used instead of chronic testing to estimate a NOAEL.

NJDWQI asserts that an uncertainty factor to extrapolate sub-chronic to chronic is not needed because the immunotoxicity studies of sub-chronic duration did not show a greater effect (response) at longer duration (but within the sub-chronic duration period) among the three studies reviewed. NJDWQI notes that for the same PFOS serum concentration of $1 \times 10^5$ ng/ml, plaque forming cell response decreased by the same 60% in two studies despite the difference in duration between these two studies, Zheng et al (2009) at 7 days duration and Dong et al (2009) at 60 days duration. NJDWQI asserts, therefore, that the decrease in plaque forming cell response does not progress at longer exposure duration. Although suggestive of a lack of progression over time, these tests are of very short duration (7-60 days) and would not fully explain whether this premise holds true at longer chronic durations of 6 months or more. Further, the mechanistic basis for the immunotoxic effect of PFOS is unknown, and whether further long-term exposures accelerate this effect.

Omission of a UF for sub-chronic-to-chronic in risk assessment should not be done on the basis of results taken solely from short term studies, especially without an understanding of the mechanism of toxicity. A UF should be applied. In lieu of some (limited) evidence of no increase in effect in dose-response between the 7-day and 60-day short-term sub-chronic studies applying a UF of 3 versus 10 is reasonable.

As indicated by NJDWQI, “serum PFOS levels in the general U.S. population are currently near or within the range of central tendency serum PFOS levels in the studies that found associations with decreased immune response (NJDWQI 2017). Median and 95% serum PFOS concentrations are 5.2 ng/ml and 19 ng/ml, respectively, in the general U.S. population (CDC-NHANES 2017). Decreases in vaccine response were found at serum levels 6 – 27 ng/ml (Grandjean et al. 2012; Granum et al. 2013; Kielsen et al. 2016; Stein et al., 2016), within the range of serum levels in the general population. Therefore, contribution of any additional PFOS from exposure to contaminated drinking water, irrespective of the MCL level chosen, may be inadequate to assure protection for these toxicity effects (immunotoxicity), especially in sensitive individuals and vulnerable segments like infants and children. This uncertainty is broadly reflected in applying UFs to calculate MCLs.

Derivation of RfD and MCL – Adding an Uncertainty Factor to Adjust Sub-chronic to Chronic

A UF of 3 should be applied to extrapolate from sub-chronic to chronic testing in the Dong et al. (2009) study, to calculate a RfD and MCL, as follows:
A UF\textsubscript{human} of 10 was used to account for increased sensitivity in sensitive sub-populations versus the average human population, and for general physiological and metabolic variation within the human population. A UF of 3 was used to account for interspecies (rodent to human) toxicodynamic differences. No UF is needed for toxicokinetic differences since the POD (point of departure), in this case the NOAEL, is based on blood serum PFOS levels. A UF of 3 is applied to estimate the NOAEL for chronic testing from sub-chronic testing used. Since individual UFs are as log-units the product of 3 x 3 is taken as 10. Therefore, the total UF applied is 100.

Target Human Serum Level = POD (NOAEL) \frac{674 \text{ ng/ml}}{UF 100} = 6.74 \text{ ng/ml}

The RfD (reference dose) is calculated as: target human serum level x clearance factor, where the clearance factor is the constant 1.8 x 10\textsuperscript{-5} derived by USEPA (EPA 2016b).

Reference dose (RfD) = 6.74 \text{ ng/ml} \times 1000\text{ml/L} \times 0.000081 \text{ L/kg/day} = 0.55 \text{ ng/kg/day}

Summary of variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOAEL (POD)</td>
<td>674 \text{ ng/ml}</td>
</tr>
<tr>
<td>total UF</td>
<td>100 (10 UF\textsubscript{human}, 3UF\textsubscript{sub-chronic-chronic}, 3UF\textsubscript{interspecies toxicodynamic})</td>
</tr>
<tr>
<td>Target human serum level</td>
<td>6.74 \text{ ng/ml}</td>
</tr>
<tr>
<td>RSC</td>
<td>0.20</td>
</tr>
<tr>
<td>clearance factor</td>
<td>0.000081 \text{ L/kg/day}</td>
</tr>
<tr>
<td>default adult body weight</td>
<td>70 kg per NJDWQI</td>
</tr>
<tr>
<td>default adult water intake</td>
<td>2.0 \text{ L/day per NJDWQI}</td>
</tr>
</tbody>
</table>

To compare with NJDWQI in its derivation, the MCL is calculated using adult default exposure values of weight and intake:

\[
\text{MCL} = \frac{0.55 \text{ ng/kg/day} \times 70 \text{ kg} \times 0.2}{2 \text{ L/day}} = 3.85 \text{ ng/L (rounded to 4 ng/L)}
\]

Adjusting the total UF to 100, the MCL calculated using NJDWQI variables should be 4 \text{ ng/L}.

Children Exposure and Risk

There is evidence that young children are exposed to differential intakes of PFOS and PFOA because of age-specific behaviors, such as hand-to-mouth behavior, resulting in greater ingestion of house dust and dust on surfaces/products containing perfluorochemicals such as upholstered furniture, clothing, bedding, automobile fabrics, and carpets. These exposures are
generally in addition to normal PFOS exposures from food and water, packaging, and a range of consumer products.

Using NHANES data, Lorber and Egeghy found that incidental ingestion of dust is far less important among adults than children (Lorber and Egeghy 2011). Children dust intakes are highly variable due to the distribution of dust PFOA concentrations in homes; the 95th percentile intake from dust ingestion is about three times the intake from food ingestion (Lorber and Egeghy 2011). In another study by Egeghy and Lorber, the authors estimated that under typical exposure conditions, where exposure media concentrations are representative of background conditions, the median PFOS intake (sum of the median route-specific intakes) for 2-year-old children under typical exposure conditions was 50 ng/day (Egeghy and Lorber 2011). In the typical scenario for 2-year olds the contribution from ingested dust and ingested water were found to be nearly the same at 36% and 42%, respectively. Alternatively, for adults the contributions to PFOS daily intakes were much different, 6% for dust ingestion and 72% for food.

Under a typical scenario Egeghy and Lorber estimated a median total PFOS intake at 160 ng/day for adults. Under a contaminated environment scenario (contaminated water supply) they estimate median total PFOS intakes of 640 ng/day in 2-year olds and 2200 ng/day in adults. In either the typical scenario or a contaminated water scenario the authors estimated that the contribution of water to total PFOS intake is about the same in adults as in 2-year olds, about 20%. Using the authors median PFOS intake data and median weight for 2-year olds of about 13 kg (Table 8-12, Exposure Factors Handbook 2011), we calculate the median PFOS daily dose to 2-year olds at 3.85 ng/kg/day, and the median daily PFOS dose to adults (using a default 70 kg adult weight) at 2.29 ng/kg/day under the typical scenario. The 2-year old children PFOS daily exposure dose is therefore about 70% higher than adults. **Both adults and children (2-year olds) median daily dose under the typical exposure scenario would exceed the allowable reference dose (RfD) of 1.8 ng/kg/day proposed by NJDWQI for PFOS, double the proposed RfD in 2-year olds.**

In addition to greater environmental exposures than adults, children are burdened with PFOS at birth. “Evidence shows that PFOS is distributed within the body and can be transferred from pregnant women to their unborn children and offspring” (USEPA 2016b). PFOS has been quantified in umbilical cord blood, suggesting maternal transfer (Apelberg et al. 2007; Cariou et al. 2015; Tao et al. 2008; Völkel et al. 2008; Von Ehrenstein et al. 2009; USEPA 2016b). One study found PFOS at a mean of 1.28 ng/ml in 99 of 100 samples of cord blood (Cariou et al. 2015).

PFOS is also transferred to children via breast milk. Cariou et al. 2015 found PFOS in 82% of breast milk samples at a mean concentration of 0.04 ng/ml. In a study of 70 human breast milk samples in patients from Germany and Hungary PFOS concentrations ranged from 0.028 to .309 ng/ml (Völkel et al. 2008; USEPA 2016b). PFOS transfer to infants during breast feeding lowers the mother’s PFOS blood serum levels. In a study by Mondal et al. (2014) of 633 women and 49 infants each month of breast feeding was found to lower maternal serum PFOS levels by 3%.
and increase infant serum levels by 4%. Using the Cariou et al. (2015) mean breast milk PFOS concentration of 0.04 ng/ml and an upper percentile daily milk intake of 951 ml/day (table 15-3, USEPA 2008), we calculated daily PFOS intake from breast milk to breast fed infants 0 < 1 years at about 38 ng/day. Based on a 90th percentile body weight of 10.8 kg for infants 6 < 12 months age (table 8-3 USEPA 2008), **the daily dose intake for this infant group of 0 < 1 years from breast milk is estimated at 3.5 ng/kg/day.**

In summary, age-specific behaviors (e.g. hand-to-mouth) and exposures from placental transfer and breastfeeding, in addition to normal exposures from ingested water and food, increase the PFOS body burdens in young children.

**Children Toxicity Studies**

Epidemiologic studies have shown many associations between PFOS and PFOA exposure and health effects in children. A systematic review by Rappazzo et al. (2017) summarized the epidemiologic evidence (literature) for relationship between prenatal/childhood perfluorochemical exposure and health outcomes in children. They conclude: “there is evidence for positive associations between PFAS (perfluoroalkyl substances) and dyslipidemia, immunity (including vaccine response and asthma), renal function, and age at menarche”, as described below (Rappazzo et al. 2017).

A study by Geiger et al. (2014) in adolescents from NHANES data, found increases in PFOA, PFOS, or total PFAS serum concentrations positively associated with high total cholesterol (>170 mg/dL) and high LDL-C. Results in a study of 12,476 children and adolescents found that PFOA was significantly associated with increased total cholesterol and LDL-C, and PFOS was significantly associated with increased total cholesterol, HDL-C, and LDL-C (Frisbee et al. 2010). Several other studies support dyslipidemia effects from exposure to PFCs in children (Rappazzo et al. 2017).

Delayed onset of puberty has been associated with altered risk of adult disease: diabetes mellitus, heart disease, bone disease, substance abuse, and asthma" (Rappazzo et al 2017). A C8 cross-sectional analysis of 3076 boys and 2931 girls found later age of puberty in both boys and girls associated with serum PFOS and PFOA levels (Lopez-Espinosa et al. 2011). For boys in that study “there was a relationship of reduced odds of reached puberty (raised testosterone) with increasing PFOS (delay of 190 days between the highest and lowest quartile)”. In girls, “higher concentrations of PFOA or PFOS were associated with reduced odds of postmenarche (130 and 138 days of delay, respectively)”. Delayed onset of puberty associated with PFOS and PFOA levels in epidemiologic studies is supported by animal studies. For example, PFOA was found to cause delayed mammary gland development in female mice offspring (White et al. 2011).

A limited number of studies have shown associations between renal function and serum PFC levels. Decrements in estimated glomerular filtration rate (eGFR) were found to be associated with increases in PFOA and PFOS concentrations in a large community study of 9660 children
age 1<18 years (Watkins et al. 2013). The study population was children and adolescents highly exposed to PFOA from contaminated water supplies, but exposed to levels typical of PFOS, PFNA, and PFHxS in the normal population. Another cross-sectional analyses of NHANES 2003-2010 data of 1960 adolescents aged 12-19 years found PFOS and PFOA associated with a reduction in kidney function and increased uric acid levels (Kataria et al. 2015). The authors found that adolescents in the highest PFOA and PFOS quartile had a lower eGFR (estimated glomerular filtration), 6.84 mL/min/1.73 m² (95 % CI: 2.19 to 11.48) and 9.69 mL/min/1.73 m² (95 % CI: -4.59 to 14.78), respectively, compared to the lowest quartile. However, the authors note that reverse causality and residual confounding could explain their findings.

As described in the Introduction, three epidemiologic studies found suppression of vaccine-mediated antibody response to be associated with PFOS and PFOA exposure in children. The study by Grandjean and Budtz-Jørgensen (2013) found an association between increases in serum PFOS and PFOA levels and decreases in serum antibody concentrations against tetanus and diphtheria toxoids in young children (follow-up of a Faroese birth cohort). A study in Norway of 99 participants found an inverse association between the level of anti-rubella antibodies in children’s serum at age 3 years and the concentrations of PFOS, PFOA, PFNA, and PFHxS (Granum et al. 2013). A recent large cross-sectional study by Stein et al (2016) of 1191 children 12-19 years old using NHANES data (1999-2000 and 2003-2004) found that a doubling of PFOS serum concentration was associated with a 7.4% (95% CI: -12.8, -1.7) decrease in mumps antibodies. A doubling of PFOS serum concentration was also associated with a 13.3% decrease in rubella antibodies; this association occurred among seropositive individuals (Stein et al. 2016).

PFOS serum levels in children associated with these immunosuppressive effects, found in these studies, are within or close to the PFOS serum levels found in the normal population.

**Calculation of MCL Based on Children-Specific Exposure Variables**

Some of the PFOS toxic endpoints to children have lasting effects and may subject children to later disease development. Deriving a MCL based on adult weights and water intakes results in a RfD imposed on children in excess of the maximum allowable 1.8 ng/kg/day. The uncertainty factor for sensitivity in the human population applied in the derivation accounts only for human variability in sensitivity to effect. To assure protection of children it is important that children-specific weight and water intake exposure values be used in the MCL calculation.

Body weight and water intakes of children ages 1-6 are used herein to determine a MCL. We use a mean body weight for this group of 16.8 kg and water intakes of 0.69 L/day mean, 1.19 L/day 90th percentile. Mean weight for the group 1-6 were determined using EPA 2011 Exposure Factor Handbook data for these ages, taking smaller increments of age groups and gender, combined by weighting the means of group increments, and pooling variances to determine means and standard deviations. We determined a 1.19 L/day composite water intake rate for children 1-6 at the 90th percentile, based on the lognormal distribution of water intakes for this combined age group, shown in the graph below.
To compare the difference in MCLs derived by NJDWQI with that derived herein using children weight and water intakes, we use the same RfD of 1.8 ng/kg/day derived by NJDWQI (which excludes applying the uncertainty factor of 3 we used to estimate NOAEL chronic from sub-chronic testing).

Summary of variables used and values
RfD 1.8 ng/kg/day
RSC 0.20
children body weight 16.8 kg
children intake 1.19 L/day 90th percentile

Children Group (age 1-6)

MCL = \( \frac{1.8 \text{ ng/kg/day} \times 16.8 \text{ kg} \times 0.2 \text{ RSC}}{1.19 \text{ L/day}} = 5.08 \text{ ng/L (round to 5 ng/L)} \)

(Using a mean water intake of 0.69 L/day results in a MCL of 8.8 ng/L)

The MCL for PFOS should be 5 ng/l.

If a UF of 3 to estimate chronic NOAEL from sub-chronic is included the MCL becomes:

MCL = \( \frac{0.55 \text{ ng/kg/day} \times 16.8 \text{ kg} \times 0.2 \text{ RSC}}{1.19 \text{ L/day}} = 1.55 \text{ ng/L (round to 2 ng/L)} \)

Other states have recognized children and infants as a more vulnerable population segment. Vermont used a 95th percentile body weight-adjusted water intake rate of 0.175 L/kg/day for the first year of life in its MCL calculation to determine a MCL of 20 ng/l. The MCL is applied as a
sum combination, [PFOS + PFOA] ≤ 20 ng/l (Vermont 2016). In 2017 the Minnesota Department of Health (MDH) updated its earlier Health Risk Limit (HRL) for PFOS in drinking water. MDH used the USEPA RfD of 20 ng/kg/day based on animal developmental effects but incorporated a database uncertainty factor of 3 in recognition of immunotoxicity shown in animal studies. This resulted in a RfD of 5.1 ng/kg/day. MDH modeled two scenarios and found a breast-fed infant exposure scenario as most limiting, and determined a PFOS limit of 27 ng/L (MDH 2017).

**Conclusion**

NJDWQI’s evaluation of animal and epidemiologic PFOS toxicity studies was comprehensive and rigorous. The New Jersey Department of Environmental Protection has been progressive in efforts to protect public health from PFOS, PFOA, and other perfluorochemical exposures. We concur with the process used to derive a PFOS reference dose, concluding with the Dong et al (2009) study showing an immunotoxic effect in test animals.

However, all population segments must be protected. Our analysis finds that at the proposed 13 ng/l MCL, PFOS daily intakes by body weight posed to young children 1-6 would be more than double the PFOS dose of 1.8 ng/kg/day deemed allowable by NJDWQI. This is disconcerting since existing serum PFOS levels in children in the population are already within or near serum PFOS levels associated with immunotoxic effects found in epidemiologic studies. The developing fetus, infants, and young children are particularly sensitive to PFOS and PFOA exposures during early sensitive periods. Early PFOS exposures in children, even at low doses of 1.8 ng/kg/day, may affect risk for later disease manifestation. To assure protection of children’s health NJDWQI should depart from using adult default exposure values and use children-specific exposure values in its MCL derivation, as described in this review.

**We recommend an MCL of 5 ng/L, as calculated above based on children exposure values.**

**Alternatively, due to PFOS and PFOA co-occurrence in water supplies and additivity concerns, we recommend that the combination of PFOS and PFOA concentrations in water supplies be no higher than 13 ng/L.** [PFOS + PFOA] ≤ 13 ng/L

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