MEMORANDUM

TO: Barker Hamill, Assistant Director for Water Supply Operations

THROUGH: Alan Stern, Dr.P.H., DABT, Chief, Risk Analysis Section, DSRT
Eileen Murphy, Ph.D., Director, DSRT

FROM: Gloria Post, Ph.D., DABT, Research Scientist, Risk Analysis Section, DSRT

SUBJECT: Guidance for PFOA in Drinking Water at Pennsgrove Water Supply Company

This memorandum is written to assist the Bureau of Safe Drinking Water in its response to the request from the Pennsgrove Water Supply Company for guidance in assessing the public health implications of the recent detections of perfluorooctanoic acid (PFOA) in that system’s drinking water. Approaches for development of health-based drinking water guidance for PFOA based on both non-cancer and cancer endpoints are discussed below.

This assessment was developed in order to provide preliminary guidance within a reasonable time frame, and the recommendations will be reevaluated in the future as additional relevant information becomes available. Although key primary scientific literature was reviewed as appropriate, this assessment takes as its starting point the findings of the USEPA (2005) draft risk assessment for PFOA and the final recommendations of the USEPA Science Advisory Board (SAB) on the draft USEPA risk assessment (USEPA, 2006). Therefore, this memorandum does not represent a comprehensive review of the toxicological literature on PFOA. Technical review of the approach and recommendations presented here was provided by Dr. Alan Stern of DSRT and Dr. Perry Cohn of DHHS.

The goal of the USEPA (2005) risk assessment was to evaluate the significance of exposure to PFOA that is prevalent throughout the general population, as evidenced by the consistent detection of PFOA in the blood of people in all age groups. USEPA did not attempt to develop a human Reference Dose or cancer slope factor, nor did they develop criteria for PFOA in air, water, or soil. For this reason, the USEPA risk assessment and the SAB review address the external doses of PFOA which result in adverse effects in experimental animals and the blood levels of PFOA associated with these external doses. The animal blood levels are then compared to levels of PFOA found in the blood of the general human population in order to develop margins of exposure (MOEs) between general human exposure and levels of concern in animals. However, the USEPA and the SAB did not address the levels of exposure from environmental
media such as water, food, or air which would result in a given human blood level, and this information is needed in order to develop health-based guidance for PFOA in drinking water. A recently completed study (Emmett et al., 2006) provides data on the relationship between PFOA in drinking water and the human blood level of PFOA, and these data were used in the development of the health-based guidance values for PFOA as discussed below.

**Background - Use of human and animal blood levels rather than ingested dose**

The risk assessment approach for PFOA developed in this memorandum is based on a target human blood PFOA level rather than on a target external (ingested) dose of PFOA, the approach used for assessing most other chemicals. The reason for the use of blood levels rather than external dose is that the kinetics of PFOA are very different in humans and experimental animals because the half-life of PFOA in humans is much longer than in the animals. For this reason, a given external dose (in mg/kg/day) of PFOA results in very different internal doses (as indicated by blood levels) in humans and animals. Therefore, a human health criterion should not be based directly on the external dose found to yield effects (or no effects) in test animals. The USEPA (2005) draft PFOA risk assessment uses the approach of evaluating No Observed Adverse Effect Levels (NOAELs), Lowest Observed Adverse Effect Levels (LOAELs), and tumor occurrence based on the blood levels in the animals rather than on the external dose they received, and this approach was endorsed by the Science Advisory Board (2006) report reviewing the USEPA draft PFOA risk assessment.

In order to derive health-based drinking water guidance for PFOA using a risk assessment approach based on blood levels, the relationship between external dose and blood levels in humans must be known. The approaches described below all depend on use of the data of Emmett et al. (2006), who studied the relationship between exposure and blood levels in several hundred individuals who drank water contaminated with PFOA in Little Hocking, Ohio. Emmett et al. (2006) found that there is a concentration factor of approximately $100$ between drinking water and blood – that is, a person drinking water with 1 ppb PFOA would be expected to have a PFOA blood level of approximately 100 ppb. The background blood level of PFOA in the general population, in all age groups, is about 5 ppb. (The geometric mean is 4.6 ppb and the 90th percentile value is 9.4 ppb, USEPA (2005)).

Interestingly, two earlier efforts to model the relationship between exposure to PFOA in drinking water and blood levels of PFOA gave similar results. Hinderliter and Jepson (2001) used simple, conservative compartmental kinetic modeling to develop a table which predicts a concentration factor of 300 between drinking water and blood. Gray (2005) used pharmacokinetic modeling to predict a concentration factor of approximately 100 in adult women and approximately 150 in adult men.

Additional data on the relationship between exposure to PFOA in drinking water and PFOA levels in blood, as well as human health effects of PFOA, will be available in the future from the C8 Health Project. This project was authorized and funded through the settlement of the Class Action, Jack Leach, et al. v. E.I. du Pont de Nemours and Co. Blood samples have been gathered from over 68,000 individuals from Ohio and West Virginia who drank water contaminated with PFOA for at least three years. (C8 Health Project).
Approaches based on non-carcinogenic effects of PFOA
USEPA (2005) identified LOAELs or NOAELs for non-cancer effects in male non-human primates, male and female adult rats, and for developmental effects in male and female rats exposed prenatally, during lactation, and post-weaning. They calculated Margins of Exposure (MOEs) for these endpoints. (Additionally, developmental effects were seen in rabbits by Gortner (1983) but those data were not used by USEPA (2005) in its assessment because information on blood levels in rabbits was not available.) In the assessment presented here, the endpoints identified by USEPA (2005) were evaluated as the basis for human health-based drinking water guidance values for PFOA. As stated above, the blood levels identified in the USEPA (2005) draft risk assessment and reviewed by the USEPA SAB (2006) are used, rather than reviewing the primary scientific literature and identifying the NOAELs, LOAELs, and blood levels independently.

In the assessments presented below, the uncertainty factors typically used in Reference Dose development are applied to the PFOA blood level identified by USEPA (2005) at the NOAEL or LOAEL in the experimental animal, rather than to the administered dose. The uncertainty factor of 10 for interspecies extrapolation typically includes a factor of 3 for toxicokinetic difference and a factor of 3 for toxicodynamic differences between humans and experimental animals. The USEPA (2005) draft risk assessment and the risk assessment presented in this memorandum are both based upon comparison of blood levels in experimental animals and humans. For this reason, the question arose as to whether toxicokinetic differences are already considered, and whether an interspecies uncertainty factor of 3 rather than 10 would be appropriate. However, the Science Advisory Board (2006) addressed this issue and stated that they did not believe that overall uncertainty about the interspecies differences in PFOA toxicity was sufficiently reduced to justify modifying the default interspecies uncertainty factor of 10. Therefore, the interspecies uncertainty factor of 10 was used in the assessments presented here.

As stated above, a 100-fold concentration factor between drinking water and blood was used, based upon the results of Emmett et al. (2006). Finally, as per the policy of USEPA and New Jersey DEP in development of human health-based drinking water values for a non-carcinogenic endpoint, a Relative Source Contribution (RSC) is applied to account for non-drinking water sources of exposure to the contaminant. The default value for this factor is 20% (meaning that non-drinking water sources are assumed to provide 80% of total exposure), and 20% is also the lowest recommended value, even if more than 80% of the recommended exposure comes from sources other than drinking water. The relative contributions of drinking water versus non-drinking water exposures to PFOA are not fully characterized at this time. Therefore, for PFOA, the default value of 20% is an appropriate RSC, and was used in this assessment.

Health-based guidance values based on the NOAELs or LOAELs identified by USEPA for adult female rats, adult male rats, non-human primates, and developmental effects in male and female rats are presented below. The basis for these assessments is summarized in Table 1 (attached).

Adult female rats
The NOAEL for female rats identified by USEPA (2005), from a chronic (2 year) dietary exposure study (Sibinski, 1987), was 1.6 mg/kg/day (30 ppm in diet). At 16.1 mg/kg/day, decreased body weight gain and decreased erythrocytes, hemoglobin concentration, and hematocrit occurred.
In the study of Sibinski (1987), blood levels were not measured, and the blood levels and daily area under the curve (AUC) in the female rats receiving 1.6 mg/kg/day are estimated by USEPA (2005) from a pharmacokinetic model. This model is based on pharmacokinetic parameters obtained from two other studies in adult female rats administered a single dose of PFOA. The half-life of PFOA in female rats is very short, measured at approximately 3-16 hours depending on the dose, and in the USEPA pharmacokinetic model, 3.2 hours is used as the half-life. (USEPA, 2005). Because of the very short half-life of PFOA in female rats, steady-state is not reached if PFOA is given as a bolus dose, and blood levels will thus fluctuate throughout the day. As stated above, the rats in the Sibinski (1987) study were exposed through the diet, so that exposure was more constant than if dosing was by gavage, although daily fluctuations in blood level almost certainly occurred. The predicted daily AUC for female rats dosed chronically at 1.6 mg/kg/day is 44 ug x hr/ml, which is equivalent to a mean daily blood concentration of about 1800 ppb. Standard uncertainty factors for a NOAEL from a chronic study of 100, including 10 for interspecies extrapolation and 10 for intraspecies extrapolation, were applied to the blood concentration at the NOAEL of 1800 ppb, resulting in a target blood level in humans of 18 ppb.

Using the 100-fold concentration factor between drinking water and blood discussed above, the drinking water concentration estimated to result in an increase in PFOA blood level of 18 ppb (ug/L) is 0.18 ppb, assuming drinking water is the only source of exposure. Application of the Relative Source Contribution factor of 20% discussed above gives a drinking water concentration of 0.04 ppb.

**Adult male rats**

For adult male rats, the LOAEL identified by USEPA (2005) was 1 mg/kg/day for body weight reduction in the F1 generation in a two-generation reproductive study using gavage, and a NOAEL was not established (York, 2002; Butenhoff et al., 2004). Liver and kidney weights were also increased, both as absolute weight and as their ratio to body weight and to brain weight at this dose. The half-life of PFOA in male rats is much longer than in female rats, and a half life of 119 hours was assumed by USEPA (2005). At a dose of 1 mg/kg/day, the blood concentration was predicted by USEPA (2005) to be 42,000 ug/ml. An uncertainty factor of 1000 for a LOAEL from a chronic study (10 for LOAEL to NOAEL, 10 for intraspecies, and 10 for interspecies) was applied, resulting in a target human blood level of 42 ppb. The corresponding drinking water concentration, based on a 100-fold concentration factor between drinking water and human blood levels and a relative source contribution factor of 20%, is 0.08 ppb.

A NOAEL of 0.06 mg/kg/day and a LOAEL for increased liver weight and hepatocellular hypertrophy in a subchronic study in male rats (Palazzolo, 1993) of 0.64 mg/kg/day, which is similar, but slightly lower to the one discussed above, was also identified by USEPA (2005). USEPA discounted these liver effects by stating that PFOA’s effects on the liver in male rats (cancer and non-cancer) occur solely through a mechanism involving activation of the peroxisome proliferator alpha receptor (PPAR-alpha) and that this mechanism is not relevant to humans.

However, the Science Advisory Board (USEPA, 2006) disagreed with the EPA’s conclusions regarding the relevance of liver toxicity and liver tumors induced by PFOA. The reasons they provided were as follows: 1) PFOA’s liver toxicity in rats is has not been proven to occur solely through the PPAR mechanism. For example, a strain of mice that lacks PPAR-alpha (knockout mice) showed increased liver weight in response to PFOA, but not in response to a well-
characterized prototype PPAR-alpha agonist (WY-14643). 2) The PPAR mechanism of liver toxicity may be relevant to humans. In particular, there is uncertainty as to whether the PPAR-alpha agonists cause liver toxicity in human fetuses, infants, and children, and 3) Some of the key steps in the proposed PPAR-alpha mechanism of action (liver cell proliferation and apoptosis) in rats have not been shown to occur after exposure to PFOA. For these reasons, the liver effects observed in male rats may actually be relevant to humans, contrary to USEPA’s interpretation. Because, as discussed above, this assessment uses as its starting point the endpoints identified by USEPA (2005), a drinking water criterion based on this endpoint was not calculated.

Non-human primates
For non-human primates, a LOAEL of 3 mg/kg/day was observed in both of two subchronic studies, a 13 week study in Rhesus monkeys based on clinical signs of toxicity (Goldenthal, 1978) and a 6 month study of cynomolgus monkeys based on increased liver weight and possibly mortality (Thomford, 2001; Butenhoff et al, 2002). No NOAEL was established in either study. USEPA based its assessment on the cynomolgus monkey study because it was longer in duration, included more animals, and had better serum PFOA data. PFOA levels in serum were measured in the cynomolgus monkey study and were 77,000 ppb at the 3 mg/kg/day dose. In the case of non-human primates, it is judged appropriate to use an intraspecies uncertainty factor of 3 rather than 10 because of the closer relationship between non-human primates and humans, particularly because pharmacokinetic differences are already at least partially considered. A composite uncertainty factor of 3000 is applied, including 10 for intraspecies, 3 for interspecies, 10 for less than chronic duration, and 10 for LOAEL to NOAEL, giving a target human blood concentration of 26 ppb. The corresponding drinking water concentration, based on a 100-fold concentration factor between drinking water and human blood levels and a Relative Source Contribution factor of 20%, is 0.05 ppb.

Rat developmental/reproductive endpoints
Endpoints were also identified by USEPA (2005) from the oral rat two-generation developmental/reproductive study using gavage doses of 1, 3, 10, and 30 mg/kg/day (York, 2002; Butenhoff et al. 2004). In this study, male and female rats (F0 generation) were dosed for six weeks prior to and during mating, and the dosing of the females continued through gestation, delivery, and lactation. Exposure of the F1 generation was continued through the post-weaning period, and effects were seen during lactation and post-weaning. During lactation, there was a reduction in body weight on a litter basis (males and females not evaluated separately) at 30 mg/kg/day. During the post-weaning period, effects on body weight of males occurred at 10 mg/kg/day and at 30 mg/kg/day in females. Additionally, during the post-weaning period, mortality was increased and sexual maturation was delayed at 30 mg/kg/day in both sexes. Thus, the NOAEL was 3 mg/kg/day in male offspring and 10 mg/kg/day in female offspring, based on the post-weaning body weight effects. An overall NOAEL for developmental effects is therefore 3 mg/kg/day.

Development of health-based drinking water concentration based on these effects is complicated by several factors, as is the case with most multi-generational studies. It is not clear whether the critical time period for the effects seen in the post-weaning period is during pregnancy, lactation, or after weaning. Furthermore, for exposure during the prenatal period, it is uncertain whether the area under the curve (AUC, related to mean blood level) or the maximum blood concentration in the pregnant female is more relevant to toxicity. Development of the drinking water guidance value for these endpoints is based on the pharmacokinetic information presented by USEPA
(2005) for the pregnant mother, and for the male and female pups in the post-weaning period. (Information is not available for the development of criteria based on exposure during lactation.) As shown below, these endpoints are not more sensitive than the endpoints for adults discussed above.

**Pregnant female**
Since the mean daily blood concentration in the pregnant female is several-fold lower than the maximum blood concentration from a single daily gavage dose, the predicted mean daily blood concentration used here as a conservative choice. As mentioned above, the NOAEL for developmental effects provided by USEPA was 3 mg/kg/day. The AUC for the pregnant rat dose with 3 mg/kg/day is given by USEPA (2005) as 83 ug x hr/mL, which is equivalent to a mean daily blood concentration of about 3500 ug/L. Applying an uncertainty factor of 100 appropriate for a NOAEL in a developmental study gives a target human blood level of 35 ug/L. The corresponding drinking water concentration, based on a 100-fold concentration factor between drinking water and human blood levels and a Relative Source Contribution factor of 20%, is **0.07 ppb**.

**Post-weaning period**
For evaluation of drinking water exposure during the post-weaning period, serum concentrations for post-weaning male and female pups are used. The AUC was determined for each of the five post-weaning weeks 4 through 8. For males dosed with the NOAEL of 3 mg/kg/day, the lowest value provided by USEPA (2005) for AUC, 202 ug x hr/ml, was seen at 4 weeks post-weaning, the first time point at which it was measured, and the AUC increased dramatically at weeks 5 and later. The week 4 value is used here, as a conservative assumption, and is equivalent to a mean blood PFOA concentration of about 9200 ug/L. Applying an uncertainty factor of 100 appropriate for a NOAEL in a developmental study gives a target human blood level of 92 ug/L. The corresponding drinking water concentration, based on a 100-fold concentration factor between drinking water and human blood levels and a Relative Source Contribution factor of 20%, is **0.18 ppb**.

For female pups, the NOAEL was 10 mg/kg/day, and the AUC was more consistent throughout the post-weaning period than in males. The lowest AUC value, 308 ug x hr/ml, was measured at week 7 post-weaning and is conservatively used here, although effects were observed at earlier time periods at which the AUC was higher. This AUC is equivalent to a mean blood concentration of about 13,000 ug/L. Applying an uncertainty factor of 100 appropriate for a NOAEL in a developmental study gives a target human blood level of 130 ug/L. The corresponding drinking water concentration, based on a 100-fold concentration factor between drinking water and human blood levels and a Relative Source Contribution factor of 20%, is **0.26 ppb**.

**Approach based on carcinogenic effects of PFOA**
Another approach for developing human health-based drinking water guidance for PFOA is based on carcinogenicity. Two chronic dietary studies of PFOA have been conducted in rats. In the first study (Sibinksi, 1987), groups of 50 male and female Sprague-Dawley rats were fed 0, 30, or 300 ppm in the diet for two years. In this study, the incidence of Leydig cell adenomas was increased in males in a dose related fashion, as follows: Controls - 0/50; 30 ppm (1.3 mg/kg/day) – 2/50 (4%); and 300 ppm (14.2 mg/kg/day) – 7/50 (14%). The incidence in the 300 ppm group was statistically significant increased (p<0.05) compared to controls. The incidence of mammary
fibroadenomas in female rats in this study was also significantly increased in both dose groups as follows: Controls - 10/47 (21%); 30 ppm (1.6 mg/kg/day) – 19/47 (40%); and 300 ppm (16.1 mg/kg/day) – 21/49 (43%). The significance of these mammary tumors has been debated, and is dependent upon the choice of historical control group to which the data is compared (e.g. Sprague-Dawley rats in general or in the laboratory at which the study was conducted.)

The second study (Biegel et al., 2001) was a follow-up mechanistic study in which male Sprague-Dawley rats were fed 300 ppm PFOA (mean dose of 13.6 mg/kg/day) for two years. Two controls groups were used: an ad libitum fed (AL) group and a pair-fed (PF) group in which the food intake was controlled to match the food intake of the PFOA exposed group. In this study, there was a significant increase in Leydig cell adenomas (AL – 0/80; PF – 2/76, Treated – 8/76), hepatic adenomas and carcinomas (AL – 2/80, PF – 3/79, Treated – 10/76), and pancreatic adenomas and carcinomas (AL – 0/80, PF- 1/79, treated – 8/76).

Thus, PFOA was found to induce liver adenomas, Leydig cell adenomas, and pancreatic acinar cell tumors in male Sprague-Dawley rats and mammary cell fibroadenomas in female rats, although USEPA (2005) questioned the significance of the mammary tumors compared to historical background incidences. USEPA (2005) interpreted the liver, Leydig cell, and pancreatic acinar cell tumors as constituting a “tumor triad” known to be caused by a class of chemicals which are peroxisome proliferator-activated receptor-alpha (PPAR-α) agonists. USEPA (2005) states that the relevance to humans of tumors caused by this group of chemicals is uncertain. Additionally, they state that there are no adequate human studies of PFOA’s carcinogenic potential since the occupationally exposed cohorts are still quite young. Based upon this, USEPA (2005) concluded that PFOA was best described as having “suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential”.

The USEPA Science Advisory Board (2006) disagreed with USEPA (2005) as to the most appropriate descriptor for the carcinogenicity of PFOA. They concluded that the PFOA cancer data are consistent with the USEPA cancer guidelines descriptor “likely to be carcinogenic to humans” which applies to chemicals which have been shown to cause tumors in more than one species, sex, strain, site, or exposure route, regardless of the existence of evidence in humans. Most SAB panel members felt that the animal data are much stronger than the type of data which would warrant a “suggestive” descriptor. This conclusion was based on the following: 1) existence of two positive cancer studies in animals for PFOA, 2) data suggesting that PPAR-α activation may not be the sole mechanism of liver carcinogenesis (discussed above in regard to liver toxicity of PFOA), 3) disagreement about the appropriateness of comparison to historical controls rather than concurrent controls in evaluating the mammary tumor date, and 4) disagreement about the USEPA (2005) assumptions about the mode of action for the Leydig cell and pancreatic acinar cell being related to PPAR-alpha agonist activity, and the USEPA comparison of mammary tumors to historical, rather than concurrent, controls. Furthermore, most SAB (2006) members recommended that a cancer risk assessment for each of the PFOA-induced tumors be developed, where data permit.

The approach recommended by USEPA for low-dose extrapolation for cancer risk assessment when the mode of action has not been fully characterized is the use of linear extrapolation from a point of departure. This approach is most appropriate for PFOA, since, as discussed above, the mode of action is not known.
Health-based drinking water guidance based on carcinogenicity can be developed using the data from Biegel et al. (2001), in which male Sprague-Dawley rats were given 300 ppm PFOA in their diets and the mean ingested dose was 13.6 mg/kg/day. As discussed above, in this study, only one dose of PFOA was used, although a similar incidence of Leydig cell tumors, but not liver or pancreatic tumors, was seen in the earlier Sibinski (1987) study.

Blood levels were not measured in this study, but can be estimated from the pharmacokinetic model provided by USEPA (2005), just as they were estimated in the non-cancer assessments presented above. Based on the USEPA (2005) model, the steady state blood level in male rats ingesting 13.6 mg/kg/day is 572 mg/L or 572,000 ug/L.

In these rats, statistically significant tumor incidences, compared to pair-fed controls, were as follows:

- Liver adenoma/carcinoma combined: Control – 4%, PFOA – 13%.
- Leydig cell adenoma: Control – 3%, PFOA – 11%.
- Pancreatic acinar cell adenoma/carcinoma: Control – 1%, PFOA – 11%.

The incidence of all three of these tumor types in the rats ingesting 13.6 mg/kg/day was approximately 10% above the percentage incidence in the pair-fed controls.

Assuming a linear dose-response relationship between blood concentration and cancer risk, and using the USEPA (2005) estimate of a blood concentration of about 570 ppm at the 10% tumor incidence level as a point of departure, the blood concentration expected to correspond to a 10^-6 cancer risk is 5.7 ppb. Based upon the 100-fold concentration ratio between drinking water and blood concentration, a drinking water concentration of 0.06 ppb would correspond to a blood concentration of 5.7 ppb. For development of drinking water guidance based on a carcinogenic endpoint, a relative source contribution factor is not used, since the drinking water guidance is intended to protect at a certain risk level (e.g. 10^-6) resulting from exposure through drinking water, without consideration of other potential sources of exposure. Therefore, **0.06 ppb** is the health-based drinking water concentration based upon a one in one million risk level.

**Discussion of uncertainties**

As discussed above, the health-based drinking water guidance values developed in this document for several non-cancer endpoints and for the cancer endpoint are based on comparisons between target blood levels of humans exposed to PFOA and actual or predicted blood levels of experimental animals administered PFOA. This approach involves more assumptions than the traditional risk assessment approach based upon administered dose.

The blood levels used for some of the endpoints from experimental animals were not directly measured, but are based on pharmacokinetic modeling provided by USEPA (2005). Uncertainty is particularly great for the blood levels in the adult female rat which has a very short half life for PFOA. In the female rat, PFOA levels would not reach steady state with daily bolus dosing, and the maximum blood concentration is predicted to be several-fold higher than the average daily blood concentration. It should be noted, however, that the fluctuation in blood levels are expected to be less in the dietary study used in the assessment of adult female rats (Sibinski, 1987) than in a bolus study because the entire dose is not received at one time but, rather, is spread out throughout the day.
Additionally, for male rats, data from the subchronic dietary study of Palazzolo (1993) suggests that the relationship between the steady-state blood concentration and the daily dose may be less-than-linear in the dose range of the identified NOAELs and LOAELs. Therefore, the predicted blood levels used as the basis for the assessments for male rats presented here may actually be somewhat higher than actual, so that the drinking water guidance values derived here likely are higher than they would be if the blood data of Palazzolo (1993) had been used.

Furthermore, the drinking water-to-blood concentration factor in humans of 100 is based on a study (Emmett et al., 2006) in which most of the subjects were exposed to the same concentration of PFOA, rather than to a range of exposure concentrations. The assessment presented above also assumes that the daily drinking water intake in the population of concern is similar to the intake in the population study by Emmett et al., 2006. The results of the C8 Health Project are anticipated to provide additional data on the relationship between PFOA in drinking water and PFOA in blood from a large number of subjects over a range of PFOA concentrations.

**Summary**

The health-based drinking water guidance developed in this assessment based on non-cancer endpoints and on cancer at the 10^-6 risk level all fall within the same general range, with most of the values falling into a narrow range from 0.04 to 0.26 ppb. The basis for the various health-based drinking water values are summarized in Table 1 (attached). As discussed above, the findings of USEPA (2005) and its Science Advisory Board (2006) were used as the starting point for developing these health-based drinking water values. The drinking water concentration based on the cancer endpoint is 0.06 ppb, which falls within the range of the non-cancer based drinking water concentrations. Since the lowest drinking water value based on non-cancer effects is below the drinking water concentration based on a 10^-6 cancer risk, there is no need to incorporate an additional uncertainty factor for potential carcinogenic effects into the non-cancer risk assessment.

**Recommendation**

It is recommended that 0.04 ppb be used as preliminary health-based guidance for PFOA in drinking water. This value is the lower end of the range of values derived based on several non-cancer and cancer endpoints in different species, most of which cluster within a factor of two of this value. This drinking water concentration is expected to be protective for both non-cancer effects and cancer at the one in one million risk level. The recommendations provided here will be reevaluated as additional data on PFOA’s effects and kinetics in humans and animals become available.

NJDEP’s analytical Practical Quantitation Limit (PQL) for PFOA is 0.004 ppb or 4 ppt, as discussed in the accompanying report NJDEP Bureau of Safe Drinking Water report “Determination of Perfluorooctanoic Acid (PFOA) in Aqueous Samples”. This PQL is below the health-based value of 0.04 ppb recommended above. Therefore, the PQL is not the limiting factor for the health-based concentration recommended in this memorandum.

Please let me know if I can be of further assistance with this issue.
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<td>13.6 mg/kg/day (300 ppm (~10% tumor incidence)) (LOAEL or NOAEL not applicable)</td>
<td>572,000 ug/L (USEPA model)</td>
<td>Not applicable – Target human blood level is based on linear extrapolation from 10^-4 tumor incidence to 10^-6 incidence.</td>
<td>5.7</td>
<td>0.06</td>
</tr>
</tbody>
</table>
References


Cc: Joe Aiello, Office of Quality Assurance, DEP  
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