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EWG urges North Carolina Science Advisory Board to develop a health-protective standard for PFOA in groundwater

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Regarding: NCSAB recommendations for perfluorooctanoic acid (PFOA) Maximum Allowable Concentration in groundwater

Dear Dr. Jordan,

Environmental Working Group (EWG) is a non-profit public health and environmental research and advocacy organization based in Washington, DC. We focus much of our research on human and environmental health risks from chemical contamination. With this letter, we urge the North Carolina Science Advisory Board on Toxic Air Pollutants (NCSAB) to reconsider their recommendation setting a Maximum Allowable Concentration (MAC) for highly toxic and persistent contaminant perfluorooctanoic acid (PFOA) in groundwater in the range of 0.9 – 1.6 parts per billion (micrograms per liter, or $\mu\text{g/L}$) and to rely on the latest scientific information for developing a PFOA water standard that would provide a sufficient margin of safety for the citizens of North Carolina.

Due to PFOA's widespread use in commerce and in manufacturing of everyday consumer products from cookware and food packaging to clothing as well as the extraordinary persistence and toxicity of this chemical, PFOA is now known as a pervasive global contaminant (EPA 2010a). It has been slated for removal from emissions and products by 2015, under an agreement between the U.S. Environmental Protection Agency and eight major manufacturers (EPA 2006).

This regulatory scrutiny and phase-out of PFOA could not be timelier. As demonstrated by an extensive body of research, PFOA is linked to developmental toxicity, immunotoxicity, alterations in the hormonal levels, metabolic disturbances and an elevated risk of cancer. It is laudable that, in the absence of the federal standard for PFOA in drinking water, state environmental health agencies have embarked on the process of developing their own standard for this toxic contaminant. Yet, long-term exposure to PFOA in drinking water in the concentration range proposed by the draft NCSAB recommendations would result in the pollutant building up in the body to levels at which adverse health effects are observed in human epidemiological studies.

The current draft developed by the NCSAB has three key shortcomings that undermine the scientific validity of the current MAC recommendation and that could put public health at risk:

1. If the MAC were finalized at the proposed level, North Carolinians drinking water polluted to this extent would have far higher body burdens of PFOA than other Americans. Drinking water polluted with PFOA at the level proposed as the MAC would

result in PFOA building up in the body to levels 20-40 fold higher than the current average in the general population, 90-160 ppb as compared to the general average of 4 ppb PFOA in the American population (Calafat 2008). This amount in the body would be higher than levels associated with reproductive and developmental effects, as well as effects on the immune system, hormone levels, and metabolism in human epidemiology studies. The NCSAB draft does not take into account the fact that PFOA concentrates in the body to 100 times the amount in drinking water (Emmett 2006).

2. The NCSAB draft does not take into account the extensive body of human epidemiological data on PFOA toxicity that reports a risk for reproductive and developmental effects at current levels of exposure in the general population. The MAC proposed by NCSAB could result in exposures far above those found to be potentially harmful in epidemiology studies.
3. The MAC proposed by the NCSAB is more than 30 times higher than that which would be established using standard U.S. EPA protocols for accounting for uncertainties in understanding the full range of health risks from exposures to this toxic, persistent compound. In particular, the NCSAB's unwarranted choice of inappropriately low uncertainty factors for interspecies (animal-to-human) and study type (subchronic-to-long term) conversions results in a MAC far above what is normally considered to be adequately protective of human health.

EWG strongly disagrees with the draft's assumption that "humans are likely to be less sensitive to toxic properties of PFOA than rodents" (draft recommendations, p. 16). This assumption is not supported by the available data; instead, studies are finding evidence of human health effects of PFOA at the levels found in the general population (Apelberg 2007; Fei 2009; Joensen 2009).

Below we provide to you details and specific suggestions on the steps to remedy the shortcomings of the current draft as well as EWG estimates of appropriate PFOA MAC in the range of 0.03-0.05 µg/L that is based on the latest research and U.S. EPA regulatory procedures for developing drinking water contaminant standards.

1. If the MAC were finalized at the proposed level, North Carolinians drinking water polluted to this extent would have far higher body burdens of PFOA than other Americans.

As demonstrated by the seminal study from the University of Pennsylvania, PFOA ingested with drinking water builds up in the human body to levels 100-fold higher than found in the contaminated water source (Emmett 2006). Due to this tendency of PFOA to accumulate and persist in the body, at the drinking water levels of PFOA proposed in the current draft, body burden levels in exposed residents of North Carolina may end up as high as 90-160 ppb, 20-40 times above the average levels in the general American population (Calafat 2008). As described below, these levels of PFOA have been associated with adverse health effects in human epidemiological studies. Thus, proposed MAC would place the health of the North Carolina citizens at risk from this toxic chemical.

2. For the development of MAC, NCSAB should take into account the extensive body of human data on PFOA toxicity at the levels observed in the general population.

The most recent research findings have found evidence of adverse health effects at the levels of PFOA that are found in the general population and so far scientists do not know what internal concentration of PFOA may be safe.

Key studies are listed below:

- A recent study found an association between PFOA levels in the blood and delayed time to pregnancy, a well-established indicator of fertility problems. Analyzing data from a cohort of 1,240 women enrolled in a Danish longitudinal study, a team of scientists based at the University of California-Los Angeles found that women with elevated blood levels of PFOA experienced more difficulties in conceiving and were twice as likely to be diagnosed with infertility as women with lower PFOA body burdens. For women with more than 3.9 parts per billion (ppb) of PFOA in their bodies the risk of infertility increased by 60 to 150 % (Fei 2009). This PFOA concentration is 20-40 fold lower than the levels that could build up in exposed people due to the proposed MAC.
- Study by Danish scientists associated PFOA with lower sperm quality in otherwise healthy young men (Joensen 2009). This study included 105 Danish men (median age 19 years) from the general population; the median levels of PFOA in this population were 4.9 ppb. Researchers observed that men with high levels of perfluoroalkyl acids (PFAAs) had a median of 6.2 million normal spermatozoa in their ejaculate compared to 15.5 million normal spermatozoa counts among men with low PFAA levels. The authors of the study suggested that “high levels of PFAAs may contribute to the otherwise unexplained low semen quality seen in many young men” (Joensen 2009). PFOA concentration in this study population was 18-32 fold lower than the levels that could build up in exposed people due to the proposed MAC.
- An association of the PFOA with serum lipids was reported in a multi-year study of 69,000 West Virginians and Ohioans whose drinking water was contaminated by a fluorochemical manufacturing plant in Washington, W. Va., along the Ohio River (Steenland, Tinker, Frisbee 2009; West Virginia University School of Medicine 2008). These findings of elevated cholesterol and other lipids in people exposed to PFOA in drinking water are in agreement with the increased lipid levels in PFOA-exposed workers in fluorochemical plants (Costa 2009; Sakr, Kreckmann 2007; Sakr, Leonard 2007). The authors of the study concluded: “If a causal relation between perfluorinated compound levels and cholesterol exists, there could be potentially serious consequences in the form of increased risk of cardiovascular disease” (Steenland, Tinker, Frisbee 2009).
- In the same study, known as the C8 Health Project, greatly decreased concentrations of estradiol were observed in women and in girls with higher serum levels of PFOA (West Virginia University School of Medicine 2008). Adverse effects on the immune system have also been noted (Frisbee 2008). The immune system changes included a significant decrease in serum levels of two immune defense proteins, immunoglobulins IgA and IgE, which correlated with increasing PFOA serum levels (C8 Science Panel 2009). The levels

of PFOA that could build up in the bodies of North Carolina citizens due to the proposed MAC would be in the range where changes in key biological markers are observed in the C8 Health Project study population.

- The latest publication from the C8 Health Project found that PFOA is significantly associated with elevated levels of uric acid in serum (Steenland, Tinker, Shankar 2009); similar results have been reported in cross-sectional studies of PFOA-exposed workers (Costa 2009; Sakr, Kreckmann 2007). Increased uric acid is a risk factor for hypertension; it may also be associated with stroke and diabetes (Heinig 2006; Steenland, Tinker, Shankar 2009).

These studies are only the latest addition to the rapidly growing body of data indicating that the levels of PFOA in the general population pose a risk to human health. We agree with the NCSAB opinion that currently published human studies cannot be used to derive a quantifiable dose-response relationship (draft recommendations, p. 13). Yet, we strongly disagree with the draft's decision to rely exclusively on animal studies for estimating MACs without taking human data into consideration.

Additionally, human PFOA toxicity studies outlined above clearly demonstrate that the assumption about lower sensitivity of humans to PFOA compared to animals is unwarranted. They also demonstrate that chronic PFOA exposure is associated with the type of health effects that may be easily missed in short-term (subchronic) animal studies, such as the effects on the immune system, metabolism, and fertility, as well as increased risk of cancer. In people these effects would lead to long-term, chronic health problems that carry a heavy burden of suffering as well as high financial costs.

3. NCSAB should incorporate uncertainty factors into the PFOA standard development that will result in a MAC that protects public health, using a total uncertainty factor of 1000 and deriving a Maximum Allowable Concentration estimate of PFOA in groundwater in the range of 0.03-0.05 µg/L. The uncertainty factor used in the current draft is 33 times less protective than what EPA advises for the development of drinking water standards.

The current draft identified three studies for selection of critical endpoints and the points of departure for the development of MAC. These studies are:

- A reproductive toxicity study in rats where animals were orally dosed with PFOA for 2 months (males) to 4 months (females) (Butenhoff 2004).
- A small scale study in male cynomolgus monkeys which involved only 4 animals in the lowest exposure group and lasted 6 months (Butenhoff 2002)
- A developmental toxicity study in mice where female mice were dosed with PFOA during pregnancy (gestation day 1 through 17) and critical developmental endpoints were examined in newborn pups (Lau 2006).

These three studies selected by NCSAB for quantitative assessment and derivation of the benchmark internal concentration dose are an important contribution in the PFOA research field. However, none of these studies was developed with the specific goal of determining the safe drinking water concentration of PFOA. Thus, data from these studies need to be treated with appropriate consideration of their limitations as well as their strengths.

Assessment of public health risks from drinking water contaminants relies on an inherently difficult extrapolation from animal studies to humans which is the reason why the U.S. Environmental Protection Agency (EPA) has developed a series of guidelines for conducting animal studies that are suitable for regulatory purposes (National Research Council 2006; U.S. EPA 2010). For a life-time exposure, chronic animal studies “conducted for a period of at least 12 months” serve as a key source of data (U.S. EPA 1998).

A subchronic (less than a year) toxicity study can be used for deriving short-term drinking water health advisories (Donohue 2002; U.S. EPA 2002, 2009). If a chronic toxicity study is not available, data from subchronic exposure study can be used with the application of appropriate uncertainty factors to derive safe drinking water concentrations from experimental animal data. As described by EPA guidance document, uncertainty factors are generally 10-fold and are intended to account for, among several consideration, “the uncertainty in extrapolating animal data to humans (i.e., interspecies variability)” and “the uncertainty in extrapolating from data obtained in a study with less-than-lifetime exposure to lifetime exposure (i.e., extrapolating from subchronic to chronic exposure)” (U.S. EPA 2002).

The draft NCSAB assessment chose an uncertainty factor of 3 for account for interspecies extrapolation, on an unfounded assumption that “humans are likely to be less sensitive to toxic properties of PFOA than rodents.” Nowhere in the draft document did NCSAB provide a scientific rationale and support for this statement. In fact, as demonstrated by a growing body of science, we are now finding health effects at the PFOA levels found in the general populations (average of 4 ppb in the American population, as determined by the researchers at the Centers for Disease Control and Prevention (Calafat 2007)). No animal studies have been even conducted at the PFOA levels so low. This human data, combined with the fact that PFOA has a much longer half-life in people compared to rodents (Olsen 2007) requires an application of a 10-fold safety factor, not an unjustifiable 3-fold factor that was chosen by the draft.

The study type uncertainty factor was selected by the draft to be at 1, which is inappropriate since the three studies used for the selection of the points of departure are not chronic studies. In Butenhoff (2004) study, rats were dosed with PFOA for no longer than 40 days. Butenhoff (2002) study suffered from the small group size, with only 4 animals in the group exposed to the lowest concentration (3 mg/kg/day) of PFOA and the study lasted 6 months. Finally, in Lau (2006) study, the duration of exposure was only 17 days of gestation, a far cry from the guideline 1-year study.

Another shortcoming of all three studies is that the true LOAEL (lowest observed adverse effects level) was not, in fact, identified in any of the publications because of the study design limitations. In each case, adverse health effects were noted at the lowest dose tested (1 mg/kg in

Butenhoff 2003; 3 mg/kg in Butenhoff 2002 and 1 mg/kg in Lau 2006). The current draft incorrectly classifies these lowest tested doses as LOAEL without noting the limitation that the true LOAEL could have been significantly lower but was simply not tested in those studies. Although the available data can be utilized for calculation of the benchmark dose, it is important to remember that these datasets likely underestimate the full extent of PFOA toxicity because of the high dose range tested.

Furthermore, human studies outlined in point 2 above demonstrate that PFOA accumulation and persistence in the body places humans at a type of long-term risks that mice and rats, with much faster PFOA elimination, might not experience. These data demonstrate that a 1-fold uncertainty factor for extrapolation from subchronic animal studies to a safe dose for human life-long exposure is inappropriate. Combined, all of these factors mean that a full, 10-fold uncertainty factor should be applied for study type extrapolation since the draft aims to start from a subchronic animal study and estimate a PFOA drinking water concentration for life-time exposure.

In sum, with the correctly updated uncertainty factors (10 for interspecies, as demonstrated above; 10 for intraspecies, as used in the draft; and 10 for study type, as demonstrated above), the total uncertainty factor should be 1000, not 30 as used in the current draft. Therefore, starting from the range of points of departure calculated in the draft with the benchmark dose methodology (31-58 µg/ml, p. 17 of the draft recommendations), the final Maximum Allowable Concentration estimate of PFOA in groundwater would be in the range of 0.03-0.05 µg/L.

In conclusion, EWG urges NCSAB to remedy the severe gaps in the current draft that, should the currently proposed standard be accepted, would pose a significant health risk for the citizens of North Carolina. We strongly advise the Board to incorporate the appropriately protective uncertainty factor of 1000 into the MAC estimates and to develop new guidelines for Maximum Allowable Concentration of PFOA in groundwater that would be in line with the latest scientific research. We will be pleased to continue working with NCSAB on the issues of PFOA safety for humans and the environment and provide our feedback on the future steps in this important process.

With best regards,

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