Agency for Toxic Substances and Disease Registry (ATSDR)
Toxicological Profile for Perfluoroalkyls
Draft for Public Comment

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"ATSDR needs to protect people and the environment from contamination with perfluoroalkyls"

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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 potential health risks from chemical contamination of food, water, consumer products, and the environment.

EWG appreciates this opportunity to comment on the Agency for Toxic Substances and Disease Registry (ATSDR) draft toxicological profile for perfluoroalkyl compounds. We are very concerned, however, with several significant shortcomings of the proposal, most notably that the Agency has decided not to develop minimum risk levels (MRLs) for this entire class of extraordinarily problematic chemicals.

For several critical perfluoroalkyl compounds, including perfluorooctanoic acid (PFOA) and perfluorooctane sulfonic acid (PFOS), there is a rich scientific literature that both supports the need and provides the basis for establishing an MRL. Several states, including New Jersey, North Carolina and Minnesota, have developed risk-based levels for PFOA in drinking water (MDH 2007; NCDENP 2008; NCSAB 2009; NJDEP 2007). The Agency's decision not to publish an MRL forces state agencies and public health officials across the country to employ their limited resources on developing their own guidance levels for PFOA and PFOS.

Perfluoroalkyls contaminate food, water, wildlife, consumer products, and have been detected in every corner of the globe. They have been found in the blood of virtually all Americans tested over the last decade (Calafat 2007). In the human body, these chemicals are persistent, bioaccumulative and toxic to numerous organs.

PFOA and PFOS are associated with a broad range of developmental effects, including developmental delays, and organ abnormalities (Lau 2007); liver toxicity (Guruge 2006); suppression of the immune system and predisposition to allergies (DeWitt 2008; Fairley 2007; Peden-Adams 2008; Yang 2002; Yang 2000); behavioral effects (Johansson 2008); altered hormonal function (Biegel 1992; Bookstaff 1990; Cook 1992; Liu 2007) as well as liver, pancreatic, testicular, and mammary cancers (Sibinski 1987).

EPA researchers have recently developed provisional drinking water guideline levels for PFOA and PFOS (U.S. EPA 2009c), and the agency is currently engaged in developing drinking water standards for both chemicals (Hegstad 2009). EPA Administrator Lisa Jackson recently announced that perfluorinated chemicals are one of the six chemicals or chemical classes of concern that EPA is considering for "action plan development" for targeted risk management (U.S. EPA 2009b). It makes no sense for ATSDR to claim that it is currently impossible to estimate minimal risk levels for people while the EPA is engaged in that very task – and both agencies are looking at the same basic set of data. Perfluoroalkyl chemicals present a significant, well-characterized risk to human health. There is no reason to delay setting MRLs for both PFOS and PFOA.

With this letter, we make three key points regarding the Agency's proposal:

- The latest science points to the health risks associated with the PFOA and PFOS levels found in the general population;
- Determining minimal risk levels for two perfluoroalkyls, perfluorooctanoic acid (PFOA) and perfluorooctane sulfonic acid (PFOS), is scientifically feasible;
- The Agency must develop minimal risk levels in order to protect human health from multiple sources of PFOA and PFOS exposure.

Details and rationale for these recommendations are provided below.

1. Latest science points to the health risks associated with the PFOA and PFOS levels found in the general population.

In its draft, ATSDR states (p. 22): " *It could be proposed that measured serum levels of perfluoroalkyls in the populations for whom health data are available be considered body burdens corresponding to no-observed-adverse-effect levels (NOAELs) or perhaps lowest-observed-adverse-effect levels (LOAELs) if the alterations reported in workers are considered adverse.*"

EWG strongly disagrees with this statement. Instead, the Agency should determine NOAELs and LOAELs using standard scientific practice that incorporates safety margins to account for uncertainties and variable susceptibility in the population and that are based on the most recent scientific findings, which, in this case, have found evidence of adverse health effects at the levels of PFOA and PFOS that are found in the general population.

Key studies are listed below:

- A recent study found an association between PFOA and PFOS 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).

- Study by Danish scientists associated PFOA and PFOS 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; the median levels of PFOS were at 24.5 ppb. Researchers observed that men with high combined levels of PFOS and PFOA had a median of 6.2 million normal spermatozoa in their ejaculate compared to 15.5 million normal spermatozoa counts among men with low PFOS-PFOA. The authors of the study hypothesized that "high levels of PFAAs may contribute to the otherwise unexplained low semen quality seen in many young men" (Joensen 2009).

- An association of the PFOA and PFOS 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, that correlated with increasing PFOA serum levels (C8 Science Panel 2009).

- The latest publication from the C8 Health Project found that both PFOA and PFOS were 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 and PFOS in the general population cannot be considered LOAELs or NOAELs. On the contrary, present levels of contamination are associated with a range of adverse health effects. To declare current body burden of perfluoroalkyls as either LOAEL or NOAEL would be irresponsible and indefensible from the scientific perspective. We strongly urge the Agency to re-consider this important point and make the final decision that will protect the health of the American public and help in setting standards for these contaminants rather than condone the persistent perfluoroalkyl pollution in people and the environment.

2. Determination of the minimal risk levels for two perfluoroalkyls, perfluorooctanoic acid (PFOA) and perfluorooctane sulfonic acid (PFOS), is scientifically feasible.

In its draft, the Agency decided not to derive the minimal risk levels (MRLs) for perfluoroalkyls (p. 21), citing insufficient human data and large differences in the metabolism of perfluoroalkyls in humans and various laboratory species as the reasons for not developing the MRLs. This decision seems to be in contradiction with another, very clear, statement in the ATSDR draft that "*inspection of the animal database would suggest that there are studies, particularly by the oral route, of PFOS and PFOA in animals that established dose-response relationships that could be used for MRL derivation.*" (p. 23)

Currently, EPA is engaged in developing drinking water standards for PFOA and PFOS; both chemicals have been listed in the final Contaminant Candidate List 3 (CCL3) of water contaminants that may require regulation under the Safe Drinking Water Act (U.S. EPA 2009a). Furthermore, EPA Administrator Lisa Jackson recently announced that perfluorinated chemicals are one of the six chemicals or chemical classes of concern that EPA is considering for "action plan development" for targeted risk management (U.S. EPA 2009b).

In light of these simultaneous developments at EPA, EWG finds it incomprehensible that ATSDR refuses to acknowledge that robust and sufficient data are available to develop MRLs for PFOA and PFOS. The recommendation to develop NOAELs and LOAELs was also given to ATSDR by one of the four peer reviewers of the initial draft, Dr. Edward Emmett, a recognized expert in this field and the author of several studies of perfluoroalkyls in people (Emmett 2006). EWG is very concerned that ATSDR's decision leaves public health at risk and would slow down rather than facilitate human and environmental health protection.

Below we highlight several studies that jointly provide sufficient toxicological data for determining minimal risk exposure levels for people. The list below primarily addresses the case of PFOA; however, a similar dataset is available for PFOS (see item 6) and we urge the Agency to take a focused look at both of these highly toxic chemicals.

1. Research by EPA scientists demonstrating developmental toxicity at low doses of PFOA exposure in mouse developmental studies (Lau 2007; Lau, Butenhoff 2004). These developmental effects include full litter resorptions, postnatal mortality, decreased birth weight, delayed growth and development, effects on mammary gland development; increased pup liver weight, structural changes in the uterus and metabolic effects in adulthood after prenatal exposures (reviewed in (Post 2009)). Some of these developmental changes are observed at doses as low as 0.1 mg PFOA/kg body weight/day (LOAEL) (Abbott 2007).

2. In follow up studies, EPA scientists observed that in mice, developmental exposure to even lower doses of PFOA, 0.01 mg/kg/day, lead to significant increases in body weight and levels of serum insulin and leptin hormones in mid-life (Hines 2009). These results indicate that fetal exposure to PFOA, similar to fetal exposure to other toxic chemicals, may predispose towards obesity in adulthood (Hines 2009).

3. Chronic dietary exposure to PFOA has been associated with liver, pancreatic, testicular, and mammary cancers in laboratory animals (Sibinski 1987). These results prompted the U.S. EPA's Science Advisory Board to classify PFOA as a "likely human carcinogen" (SAB 2006).

4. Chronic dietary exposure to PFOA in adult female rats was associated with decreased body weight and blood changes; this study reported NOAEL at 1.6 mg/kg/day dose of PFOA (U.S. EPA 2005).

5. A study in Cynomolgus monkeys linked oral PFOA exposure with sudden mortality; this study reported a LOAEL of 3 mg/kg/day of PFOA (U.S. EPA 2005).

6. For PFOS, U.S. EPA scientists recently identified the subchronic toxicity study in Cynomolgus monkeys (Seacat 2003) as acceptable and "critical" for the derivation of the Provisional Health Advisory value for PFOS contamination of drinking water (U.S. EPA 2009c). In this study, effects of PFOS on liver, thyroid hormones and serum lipids have been observed, with a NOAEL of 0.03 mg/kg/day (U.S. EPA 2009c).

Overall, the existing data provide a strong foundation for deriving MRLs for PFOA and PFOS. EWG urges the ATSDR to recognize that this important next step is scientifically feasible and should be done to provide the necessary guidance to state agencies and public health officials across the country.

3. The Agency should develop minimal risk levels in order to protect human health from multiple sources of PFOA and PFOS exposure.

Perfluoroalkyl chemicals are found in a wide range of consumer products, including water, stain and grease repellants, cookware, food wrap, carpeting, furniture and clothing. Perfluoroalkyls contaminate food because of bioaccumulation in the food supply (Martin 2004; Tittlemier 2007) and due to leaching from food packaging materials (Begley 2008; Begley 2005; Deon 2007). Furthermore, according to recently published EPA research, degradation of perfluorochemical-based polymers, like those used in grease-proof food packaging or waterproofing clothing, releases stable short-chain perfluoroalkyl compounds that are exceptionally persistent in the environment (Renner 2009; Washington 2009).

Children and infants are at particular risk from widespread presence of perfluoroalkyl pollutants. Scientists have found that children tend to have elevated exposure to PFOA, PFOS, perfluorohexansulfonate (PFHxS) and related perfluoroalkyls (Emmett 2006; Olsen 2004). Moreover, PFOA and PFOS have been found in maternal and umbilical cord blood, so there is transplacental exposure whereby these pollutants cross the placenta and transfer from mother's body to the fetus (Apelberg, Goldman 2007; Fei 2007; Inoue 2004; Midasch 2007). Perfluoroalkyls have been also found in breast milk, so infants are exposed to these chemicals via lactational transfer (Karrman 2007; Kuklenyik 2004; Tao 2008; Volkel 2008).

Two large cohort studies have found an association between PFOA levels in umbilical cord or maternal blood and smaller weight and size in newborn infants, indicating the human health risks of gestational

exposure to perfluoroalkyls (Apelberg, Witter 2007; Fei 2007). Low birth weight is a well-known indicator of potentially serious medical problems later in life (Lau and Rogers 2004).

In addition to other sources of exposure, perfluoroalkyl contamination of drinking water is a problem that needs urgent attention from the federal agencies. EWG's review of water quality data from both scientific literature and government dockets found that PFOA and PFOS pollute drinking water sources in at least 11 states and the District of Columbia (EWG 2009). The true number of states with PFOA- and PFOS-contaminated water is probably higher, since no nation-wide surveillance has been conducted as of now. Meanwhile, research by scientists in the New Jersey Department of Environmental Protection demonstrates both the feasibility and the great need for developing the MRLs for PFOA in drinking water (Post 2009).

It is a standard ATSDR practice to develop MRLs as an integral part of toxicological profiles for hazardous substances. EWG analyzed the existing ATSDR toxicological profiles and the list of MRLs that the Agency has developed in the past (ATSDR 2009a, b). Specifically, the latest update of ATSDR's Toxicological Profile Information Sheet, published on October 19, 2009, includes 190 entries for Finalized Toxicological Profiles (ATSDR 2009b). For comparison, the last list of MRLs, last updated on January 14, 2009, included 173 entries (ATSDR 2009a).

Based on this review, EWG confirmed that for the majority of cases, ATSDR has developed an MRL, making the present decision not to develop MRLs for perfluoroalkyls very unusual. We agree that for some perfluoroalkyls, such as six- and four- carbon fluorinated chemicals, the data are currently limited. This is, indeed, a problem that should be resolved by the manufactures who should be responsible for generating and publishing data for these chemicals as soon as possible. However, we already know enough about PFOA and PFOS to carry out comprehensive risk assessments for these chemicals on the basis of extensive toxicological data from animal studies and the growing number of human epidemiological studies.

In conclusion, EWG urges ATSDR to strengthen and improve its draft toxicological profile for perfluoroalkyls by developing the minimal risk levels for PFOA and PFOS. The development of the MRLs will address a severe gap in our current public health policy and protect the health of millions of Americans who may be exposed to perfluoroalkyls from a variety of sources.

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