On behalf of the Natural Resources Defense Council (NRDC), we appreciate this opportunity to submit comments on ATSDR’s Toxicological Profile on Perfluoroalkyls, Draft for Public Comment (June 2018). We commend ATSDR on updating their toxicological profile on perfluoroalkyls and appreciate ATSDR’s extensive review and consideration of the peer-reviewed scientific literature. A strong body of science links the per- and polyfluoroalkyl substances (PFASs) class of chemicals to adverse health and environmental effects. Given that the science on PFASs is rapidly emerging and there is widespread exposure to these compounds, it is essential that ATSDR utilize the most up-to-date science and establish the most health protective benchmarks.

ATSDR provides a critical service to the public health community through its toxicological profiles of hazardous substances. By collecting, examining, summarizing and interpreting available information on a hazardous substance, ATSDR creates an extensive reference guide for health professionals and researchers. Additionally, minimal risk levels (MRLs) serve as an important screening tool to help the public health community determine areas and populations potentially at risk from exposure to a particular chemical.

This 2018 draft profile is a stronger tool than previous versions; however, there are several key improvements that should be made to more adequately protect the public from the health hazards associated with exposure to PFASs. We urge ATSDR to carefully consider the enclosed information, move quickly to incorporate our recommendations based on the latest science, and finalize the profile in a timely manner.

Our comments are summarized here and more details are provided below.

1. **We commend ATSDR on updating its toxicological profile on perfluoroalkyls to more accurately reflect current data on perfluoroalkyls and the hazards they pose to human health.** The science on perfluoroalkyls is emerging rapidly; including the identification of new sensitive targets of PFOA and PFOS, as well as data on the toxicology of perfluoroalkyls other than PFOA and PFOS. Health
benchmarks must reflect current data to be protective of public health. We commend ATSDR on updating its toxicological profile on perfluoroalkyls to incorporate recent data. ATSDR should continue to keep vigilant with new literature and be prepared to establish new health benchmarks in the future in a timely manner.

2. **We strongly support the additional derivations of minimal risk levels (MRLs) for PFNA and PFHxS.** An ever-growing body of evidence suggests the possibility of significant human exposures to PFASs other than PFOA and PFOS that are also hazardous to human health. Deriving MRLs for two additional perfluoroalkyls, PFNA and PFHxS, helps address this growing problem.

3. **We support the decision to derive MRLs for PFOA and PFOS from more sensitive health endpoints than were used in ATSDR's previous 2015 draft toxicological profile and the U.S Environmental Protection Agency's (EPA) current health advisory levels.** The acknowledgement of PFOA- and PFOS-associated immune and developmental effects more accurately reflects current data on PFOA and PFOS and results in MRLs that are more protective of human health. These new draft MRL values are an order of magnitude lower (more health protective) than previous draft MRLs. These new MRL values suggest that current advisory and regulatory levels for PFOA and PFOS are much too permissive and do not protect human health.

4. **Immunotoxicity should be the critical endpoint for deriving a MRL for PFOS.** The data linking PFOS exposure to immunotoxicity is robust and is currently the most sensitive endpoint for PFOS. ATSDR states concern that immunotoxicity is a more sensitive endpoint than developmental toxicity; however, it does not derive its MRL from this endpoint. Multiple studies find immunotoxic effects at doses below the proposed MRL (2.5-100 times). Therefore, the proposed MRL is not protective of these critical effects. The MRL for PFOS should be recalculated using the most sensitive endpoint, immunotoxicity, using study with the lowest NOAEL, not the highest, to be truly protective of the effects of PFOS on the immune system.

5. **Altered mammary gland development should be considered an adverse health effect and the critical endpoint for deriving a MRL for PFOA.** Studies show that perturbations during critical windows of development, including gestation, puberty and pregnancy, may lead to changes that cause problems later in life with breast feeding and increased risk for breast cancer. Altered mammary gland development has been linked to exposures to numerous endocrine disrupting chemicals, including atrazine, bisphenol A, dibutylphthalate, dioxin, methoxychlor, nonylphenol, and polybrominated diphenyl ethers. Based on the available evidence linking PFOA exposure to alteration of mammary gland development, this should be considered the critical endpoint for MRL derivation.
6. As documented in this profile, data also suggest potential toxicity for perfluorooalkyls for which ATSDR did not derive a MRL for. ATSDR should take action on these perfluorooalkyls to protect human health. Not providing a health benchmark or guidance on a chemical suggests that there is no risk associated with the chemical. However, almost every perfluorooalkyl in this profile has data linking its exposure to health hazards. Existing data, with appropriate uncertainty factors, should be used to derive MRLs for chemicals that are linked to health hazards. This may require the use of alternative models and/or approaches than ATSDR is currently using, or simply addressing data limitations with additional uncertainty factors. The following compounds, PFDeA, PFBA, PFHxA, PFBuS, PFDoA, and PFUA have toxicity data that should not be ignored.

7. ATSDR should use a class-based approach for PFASs that have insufficient data to calculate a MRL on their own. Although PFASs are a broad class of chemicals, they are related in their extreme persistence in the environment. Subgroups within the PFAS class, such as perfluorooalkyls, share even more chemical and toxicological properties. ATSDR should utilize toxicological information on chemicals with greater amounts of data, such as PFOA and PFOS, to estimate toxicity of perfluorooalkyls with data limitations.

8. Exposures to PFASs do not occur in isolation. The current profile is incomplete without an examination of the threat from concurrent exposures. A person is likely to be concurrently exposed to a multitude of PFAS chemicals throughout their lifetime. We recommend that ATSDR work with leading scientists to develop health benchmarks for combined PFAS exposures to provide more robust health protection. ATSDR should emphasize a class-based approach to PFASs and consider the impacts of multiple PFAS chemicals that target the same body systems regardless of detailed knowledge of the underlying mechanism of action. The agency should explore all types of data available, including emerging and existing methods, and always use the most sensitive toxicological endpoint to derive health benchmarks. This will allow ATSDR to develop health protective MRLs for groups of chemicals, including those with sparse toxicological data.

9. Greater transparency is required, especially with respect to the process of deriving MRLs. Decisions made while deriving MRLs must be explicitly stated for stakeholders and experts to properly review the profile and provide meaningful input in their comments. Please provide more detailed rational on the selection of critical endpoints, the selection of studies to base MRLs on, and why MRLs can’t be calculated for specific chemicals.

10. Decisions delayed are health protections denied. The environmental and public health threat of PFAS contamination and exposure is growing. We urge ATSDR to move quickly to consider and incorporate recommendations to improve the quality of this profile, so that this critical public health tool can be finalized and used in a timely manner.
Detailed Comments

1. **We commend ATSDR on updating its toxicological profile on perfluoroalkyls to more accurately reflect current data on perfluoroalkyls and the hazards they pose to human health.**

The scientific literature on PFASs has greatly expanded over the last decade. As documented by the profile, the number of health effects associated with exposure to legacy PFASs, such as PFOA and PFOS, has also grown; including the discovery of several that can occur at extremely low levels of exposure. Data on PFASs other than PFOA and PFOS is growing and similarly links other PFASs to a range of health hazards. Additionally, PFASs are highly persistent, mobile and bioaccumulative, resulting in their ubiquitous presence in the environment and human population.

Given the well documented potential for adverse effects and widespread exposure, it is essential that the public health community stays current with the scientific literature on this growing public health and environmental threat. Likewise, health benchmarks for PFASs must reflect current data to be protective of public health. We commend ATSDR on updating its toxicological profile on perfluoroalkyls to incorporate recent data. We also appreciate the addition of figures and tables to summarize the information in a more assessible manner. ATSDR should continue to keep vigilant with new literature and be prepared to establish new health benchmarks in the future.

2. **We strongly support the additional derivations of minimal risk levels (MRLs) for PFNA and PFHxS.**

The enormous PFASs class of chemicals is estimated to contain between 3,000 to 5,000 man-made chemicals. Entire new subclasses of PFASs are still being discovered in use and in the environment. The data that does exist on PFASs other than PFOA and PFOS suggests the possibility of significant human exposures and

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health hazards as well. The 2014 Helsingør\textsuperscript{6} and 2015 Madrid\textsuperscript{7} Statements, founded on extensive reviews of the scientific literature, provided consensus from more than 200 scientists on the potential for harm associated with the entire class of PFAS. Yet very little action has been taken to address this growing public health problem.

Deriving MRLs for PFNA and PFHxS is an important step towards developing health guidelines and regulations on PFASs other than PFOA and PFOS. As the profile documents there is sufficient evidence linking PFNA and PFHxS exposure to health hazards, including, but not limited to, developmental toxicity, hepatotoxicity, endocrine toxicity, and immunotoxicity.

However, there are some gaps in the information provided by ATSDR on the derivation of MRLs for these compounds that impede the process of stakeholder and expert review and input. For greater transparency, the revised protocol should clearly explain why a 6% increase in prothrombin time in males at 0.3 mg/kg/day\textsuperscript{8} was not considered the critical effect for PFHxS. Additionally, a clear rational for why the shorter half-life of 2.5 years for PFNA, which only applies to young women, was chosen for deriving PFNA’s MRL over the half-life of 4.3 years for all other groups (males of all ages and older women) should be provided.

3. **We support the decision to derive MRLs for PFOA and PFOS from more sensitive health endpoints than were used in ATSDR’s previous 2015 draft and EPA’s current health advisory levels.**

Current data suggest that developmental toxicity and immunotoxicity are among the most sensitive endpoints for PFASs. However, these endpoints have only recently been the focus of health and environmental agencies evaluating the potential health hazards associated with PFAS exposure.\textsuperscript{2} The acknowledgement of PFOA- and PFOS-associated immune and developmental effects more accurately reflects current data on PFOA and PFOS and results in critical doses/ risk thresholds considerably lower than before. ATSDR’s new draft MRL values for PFOA and PFOS are an order of magnitude lower than previous draft MRLs and are significantly more protective of human health. These new MRL values also suggest that current advisory and regulatory levels for PFOA and PFOS are much too permissive and do not protect human health.

4. **Immunotoxicity should be the critical endpoint for deriving a MRL for PFOS.**

Immunotoxicity is currently the most sensitive health endpoint for PFOS exposure. As documented in the profile, both animal and epidemiology studies provide strong evidence linking PFOS exposure to immunotoxic effects. The National Toxicology


Program reviewed the immunotoxicity data on PFOA and PFOS in 2016 and concluded that both are presumed to constitute immune hazards to humans.\textsuperscript{9}

The immunotoxic effects of PFOS could have significant detrimental impacts on public health. For example, PFOS is associated with reduced antibody titer rise in response to vaccines\textsuperscript{2,9}; resulting in increased risk of not attaining the antibody level needed to provide long-term protection from serious diseases such as measles, mumps, rubella, tetanus and diphtheria. PFASs can also be transferred to infants via breast milk\textsuperscript{10}, which presents a particular hazard to the adaptive immune system during this critical window of development.

One rationale given for not selecting an immunotoxicity study as the principle study to derive a MRL for PFOS from was that pharmacokinetic model parameters were not available for the mouse strains used in the immunotoxicity studies. However, this is inconsistent with the decision-making and rationales provided in the rest of the draft profile. Parameters for the Wambaugh model were not available for PFNA and PFHxS either. Instead, time weighted average (TWA) serum levels were predicted by using the trapezoid rule. This approach was also used to calculate a candidate MRL for Dong et al. 2011\textsuperscript{11} (pg. A-43). The lack of parameter data for one specific model should not be a barrier to ATSDR utilizing the best available data to derive a MRL that is protective of the most sensitive health endpoint for PFOS.

ATSDR states concern that immunotoxicity is a more sensitive endpoint than developmental toxicity; however, it stops short of deriving a MRL from this endpoint. Instead, ATSDR inaccurately claims that a modifying factor of 10 is sufficient to address the doses where immunotoxic effects have been observed. However, this value is only consistent with the immunotoxicity study with the highest LOAEL, Dong et al. 2011. The other immunotoxicity studies all result in MRLs approximately 2.5-100 times lower than currently calculated (Table 1). Critical doses based on benchmark dose calculations for immunotoxicity in children are also approximately an order of magnitude less than ATSDR’s current draft MRL. The final profile should be consistent with ATSDR’s practice of selecting the study with the lowest LOAEL when selecting the principle study for MRL derivation. Otherwise ATSDR should provide a thorough explanation justifying ATSDR’s rational for selecting a modifying factor that only aligns with the immunotoxicity study with the highest LOAEL.

\textsuperscript{9} National Toxicology Program. (2016) Immunotoxicity Associated with Exposure to Perfluorooctanoic Acid (PFOA) and Perfluorooctane Sulfonate (PFOS). https://ntp.niehs.nih.gov/ntp/ohat/pfoa_pfos/pfoa_pfosmonograph_508.pdf


\textsuperscript{11} Dong G.H., et al. (2011) Sub-chronic effect of perfluorooctanesulfonate (PFOS) on the balance of type 1 and type 2 cytokine in adult C57BL/6 mice. \textit{Arch Toxicol} 85(10):1235-1244.
Table 1: Comparison of critical endpoints, doses and risk thresholds for PFOS

<table>
<thead>
<tr>
<th>Source</th>
<th>Year</th>
<th>Critical Endpoint</th>
<th>Critical Dose (mg/kg/day)</th>
<th>Risk Threshold in Drinking Water (ng/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EPA</td>
<td>2016</td>
<td>Developmental toxicity (decreased pup body weight)</td>
<td>2 x 10^{-5} RfD</td>
<td>70</td>
</tr>
<tr>
<td>New Jersey</td>
<td>2017</td>
<td>Immunotoxicity (impaired response to sRBC)</td>
<td>1.8 x 10^{-6} RfD</td>
<td>13(^{d})</td>
</tr>
<tr>
<td>ASTDR</td>
<td>2018</td>
<td>Developmental toxicity (delayed eye opening, decreased pup weight) + MF</td>
<td>2 x 10^{-6} MRL</td>
<td>7(^{e})</td>
</tr>
<tr>
<td>Dong et al.</td>
<td>2011</td>
<td>Immunotoxicity (impaired response to sRBC)</td>
<td>2.7 x 10^{-6} Estimated MRL(^{b})</td>
<td>10(^{e})</td>
</tr>
<tr>
<td>Dong et al.</td>
<td>2009</td>
<td>Immunotoxicity (impaired response to sRBC)</td>
<td>7.8 x 10^{-7} Estimated MRL(^{b})</td>
<td>3(^{e})</td>
</tr>
<tr>
<td>Guruge et al.</td>
<td>2009</td>
<td>Immunotoxicity (decreased resistance to influenza virus)</td>
<td>2.2 x 10^{-7} Estimated MRL(^{b})</td>
<td>1(^{e})</td>
</tr>
<tr>
<td>Peden-Adams et al.</td>
<td>2008</td>
<td>Immunotoxicity (impaired response to sRBC)</td>
<td>2.1 x 10^{-8} Estimated MRL(^{b})</td>
<td>&lt; 1(^{e})</td>
</tr>
<tr>
<td>Grandjean et al.</td>
<td>2013</td>
<td>Immunotoxicity (reduced vaccine antibody response in children)</td>
<td>9 x 10^{-9} BMDL(^{c})</td>
<td>&lt; 1(^{e})</td>
</tr>
</tbody>
</table>

\(^{a}\) - Calculated from Dong et al. 2009; NJ did not calculate time weighted average serum, instead used the measured serum concentration directly; also used a slightly different clearance factor (8.1 x 10^{-5} for NJ versus 6.9 x 10^{-5} for ATSDR)

\(^{b}\) - Calculated using the derivation method described on pg. A43 of the profile

\(^{c}\) - External steady state critical dose calculated from internal BMDL\(_{5}\) dose of 1.3 ng/mL by using the model described in “MRL Approach” on pgs. A6-A10 of the profile, with an uncertainty factor of 10 applied for human variability

\(^{d}\) - NJ used different values to estimate total intake, NJ’s values are for average adults versus EPA’s values are for lactating women

\(^{e}\) - Estimated from total intake limits, assuming 20% exposure contribution from water (rounded values), as done by the EPA for its PFOA and PFOS health advisory calculation

Given the above information, immunotoxicity should be officially recognized as the critical endpoint for PFOS and the MRL for PFOS should be recalculated using the immunotoxicity study with the lowest NOAEL, not the highest, to be truly protective of the effects of PFOS on the immune system.

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5. Altered mammary gland development should be considered an adverse health effect and the critical endpoint for deriving a MRL for PFOA.

In a 2009 workshop of experts in mammary gland biology and risk assessment came to the consensus that changes in mammary gland growth and differentiation, including changes in developmental timing, are a health concern. Altered mammary gland development may lead to difficulty in breastfeeding and/or an increase in susceptibility to breast cancer later in life. Due to the numerous demonstrated benefits of breastfeeding, the American Association of Pediatrics recommends that all infants are exclusively fed breastmilk for the first six months. However, an estimated 3-6 million mothers each year are unable to produce milk or have difficulty breastfeeding. The cause of this remains unclear, however, exposure to toxic environmental chemicals are one candidate explanation for the inability to initiate and/or sustain breastfeeding.

Altered mammary gland development has been observed in conjunction with impaired lactation in one or more generations after gestational exposure to dioxin, atrazine, and BPA. Only one study, White et al. 2011, has assessed the effects of PFOA exposure on mammary gland growth and differentiation for multiple generations. The authors saw striking morphological abnormalities in the lactating glands of dams chronically exposed to environmentally relevant levels of PFOA; however, no effects on body weight of their pups were seen. It is possible that compensatory behavior, such as increased number of nursing events per day or longer nursing per event masked a decreased potential in milk production by the dams, however the authors did not evaluate these endpoints in the study. It is also possible that PFOA exposure could increase time to peak milk output through the reduction in number and density of alveoli available to produce milk. For human mothers, low-level functional effects on lactation that cause even a short delay in substantial milk output might result in cessation in breastfeeding before the recommended time-frame.

Early life exposures to factors that disrupt development may influence susceptibility to carcinogens later in life. For example, hormone disruption is an important determinate of breast cancer susceptibility in humans and rodents.\(^{27}\) Proliferating and undifferentiated structures, such as TEBs, display elevated DNA synthesis compared to other mammary gland structures; which is why TEBs are considered the most vulnerable mammary gland target structure of carcinogen exposure.\(^{28}\) Delays in mammary gland development would result in a prolonged window of increased vulnerability to carcinogens. In humans, earlier menarche is an established risk factor for breast cancer.\(^{29}\) This further raises the concern that changes in patterns of breast development in U.S. girls\(^ {30}\) could be contributing to an increased risk of breast cancer or other adult diseases later in life. However, an increase in susceptibility to breast cancer later in life was not explored in White et al. 2011.

Studies have shown a relationship between altered breast development, lactational deficits and breast cancer. Therefore, unless it can be shown that this relationship does not exist for PFOA, altered mammary gland growth and differentiation should be considered an adverse health effect of PFOA exposure and the critical endpoint for PFOA. The MRL for PFOA should be recalculated to be protective of the effects of PFOA on mammary gland development.

6. **As documented in this profile, data also suggest potential toxicity for perfluoroalkyls for which ATSDR did not derive a MRL for. ATSDR should take action on these perfluoroalkyls to protect human health.**

Not providing a health benchmark or guidance on a chemical suggests that there is no risk associated with the chemical. However, almost every perfluoroalkyl in this profile has data linking its exposure to health hazards, including PFDeA, PFBA, PFHxA, PFbSU, PFDoA, and PFUA. Existing data, with appropriate uncertainty factors, should be used to derive MRLs for chemicals that are linked to health hazards. This may require the use of alternative models and/ or approaches than ATSDR is currently using, or simply addressing data limitations with additional uncertainty factors.

For example, one rationale given by ATSDR for not calculating a MRL from acute exposure studies was that acute exposures could not be modeled for compounds with long half-lives. However, an intermediate exposure MRL was calculated for PFNA from a 17-day study and for PFOA from a 21-day study. An acute 14-day study is within the same range of exposure and therefore could be used, with an additional

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uncertainty factor if needed, to calculate an acute exposure MRL; especially when intermediate exposure studies are not available.

Another explanation provided by ATSDR for not calculating a MRL was when sensitive endpoints, such as immunotoxicity and developmental toxicity, have not yet been examined in animal studies; resulting in the database being considered inadequate. The lack of data on potential sensitive endpoints is not ideal. However, the absence of action by ATSDR deprives the public from important health protections that can be provided by setting health benchmarks. ATSDR could consider setting an MRL based on current toxicity data and use an uncertainty factor to account for database limitations, as was done with PFHxS and PFNA. A MRL can always be updated when further studies, including ones that examine potentially more sensitive endpoints, are performed. ATSDR should always strive to take the most health protective route by setting a MRL whenever possible. Otherwise ATSDR should provide a clear explanation for why the public is better protected by delaying action to fill specific data gaps.

For PFBA, studies have both examined PFBA’s effect on sensitive endpoints and measured serum levels, but the database was still considered insufficient due to an unreliable estimation of half-life in humans. Although the Chang et al. 2008 study did not have enough female subjects to get a reliable estimation of half-life for females, their estimation for males could be used with a small uncertainty factor to account for the differences between males and females.

One significant source of data that is not being utilized fully is epidemiologic data. To generate accurate and relevant health benchmarks, ATSDR should use all toxicological information available. In particular, occupational or environmental epidemiologic studies – cohort, case-control, ecological, and others – can provide very valuable information to inform risk evaluation because such studies capture real-world exposure conditions that do not exist in laboratory settings. Critical doses can and should be based on epidemiologic studies when they are the best source of toxicological data on a chemical. For example, epidemiologic data was used quantitatively in a EPA evaluation of risk for methylmercury, as recommended by the NAS. The EPA based the oral reference dose on lasting neurological effects in children exposed during early life. Other examples of the EPA using

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epidemiologic data to calculate risk estimates include tetrachlorethylene\textsuperscript{34}, 1,3-butadiene\textsuperscript{35}, benzene\textsuperscript{36} and arsenic\textsuperscript{37}.

7. **ATSDR should use a class-based approach to for PFASs that have insufficient data to calculate a MRL on their own.**

Although PFASs are a broad class of chemicals, they are related in their extreme persistence in the environment. Subgroups within the PFAS class, such as perfluoroalkyls, share even more chemical and toxicological properties. ATSDR should utilize toxicological information on chemicals with greater amounts of data, such as PFOA and PFOS, to estimate toxicity of perfluoroalkyls with data limitations. For example, in 2016, the Food and Drug Administration ruled that perfluoroalkyl ethyl containing food-contact substances (FCSs) were no longer authorized for food-contact use because the toxicity of structurally similar compounds, like PFOA, demonstrated there was no longer a reasonable certainty of no harm in their use.\textsuperscript{38}
The FDA determined that due to similar structure and biopersistence, long-chain perfluorinated compounds could be treated as a class of chemicals. Therefore, in the absence of contradictory data, the toxicology information on one or a subset of the chemicals in the class could be applied to the entire class.

“The in the absence of data specific to the three FCSs to address these endpoints, FDA utilized the available data demonstrating reproductive and developmental toxicity for long-chain perfluorocarboxylic acids to assess the safety of the approved food-contact use of the FCSs.”

By treating a group of related chemicals as a class, the FDA was able to make a health-protective regulatory decision on chemicals with limited data. In order to meet ATSDR’s public health goals, it should use a similar approach to derive MRLs for chemicals within a class that are linked to health hazards. Specifically, for the perfluoroalkyls examined in this profile, ATSDR should apply the most sensitive MRL to any perfluoroalkyl for which there is not enough data to calculate a chemical-specific MRL.

8. Exposures to PFASs do not occur in isolation. The current profile is incomplete without an examination of the threat from concurrent exposures.

We urge ATSDR to account for people’s concurrent exposure to multiple PFAS chemicals. Biomonitoring studies demonstrate that Americans have chronic exposure to multiple PFAS chemicals throughout their lifetimes. CDC’s NHANES studies reveal that nearly every American has PFOS, PFOA, PFHxS and PFNA detected in their blood stream, including young children. At least seven other compounds are detected by NHANES studies: MeFOSAA, PFDeA, PFUA, PFHpA, PFBS, FOSA, EtFOSAA and PFDoA. Most other PFAS chemicals are not routinely included in biomonitoring studies.

Multiple PFAS are found in drinking water, food, dust, personal care products and a variety of different environmental media. The EPA has monitored for PFAS contamination in water systems under the third Unregulated Contaminant Monitoring Rule (UCMR3). Six PFAS compounds were monitored for under UCMR3 (PFOA, PFOS, PFHxA, PFHpA, PFNA and PFBS). UCMR3 data shows that a single Public Water System can contain detectable levels above the overly high minimum reporting levels for up to four different PFAS compounds. Food contact materials and packaging in the United States has shown detectable levels of PFOA, PFHxS, PFDA, PFHpA, PFDoA, PFHxA, PFBA, PFPeA, PFUA, PFOS and 8:2 FTOH. A single consumer product such as carpet, clothing, outdoor gear, dental floss, etc. can contain up to nine different PFAS compounds. Samples of dust collected throughout homes and offices have shown high concentrations of 8:2 FTOH, PFDA, PFHpA, PFNA, 10:2 FTOH, PFDoA and PFTeDA with detection frequencies over 70%.

Therefore, ATSDR should not assume that exposures occur in isolation. A person is likely to be concurrently exposed to most of the PFASs analyzed in this profile, as well as dozens of additional PFAS chemicals throughout their lifetimes. We recommend that ATSDR work with leading scientists to develop health thresholds for combined PFAS exposures to provide more robust health protection. A class-based approach should be emphasized and ATSDR should consider the impacts of multiple PFAS chemicals that target the same body systems regardless of detailed knowledge of the underlying mechanism of action. Because perfluoroalkyls are chemically related, they likely have additive or synergistic effects on target systems. Additionally, the agency should explore all types of data available, including

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emerging and existing methods, and always use the most sensitive toxicological endpoint to derive health thresholds. This will allow ATSDR to develop MRLs for groups of chemicals, including those with sparse toxicological data.

9. **Greater transparency is required, especially with respect to the process of deriving MRLs.**

As noted from the above comments, there are many instances where the rationale behind certain choices and interpretations was not clearly explained in the profile. Decisions made while deriving MRLs must be explicitly stated for stakeholders and experts to properly review the profile and provide meaningful input in their comments. The final profile should include a more detailed rational on the selection of critical endpoints, the selection of studies to base MRLs on, and why MRLs can’t be calculated for specific chemicals.

10. **Decisions delayed are health protections denied.**

As the National Academy of Sciences (NAS) stated in its 2009 report *Science and Decisions*: “The design of a risk-assessment process should balance the pursuit of individual attributes of technical quality in the assessment and the competing attribute of timeliness of input into decision-making.”

The environmental and public health threat of PFAS contamination and exposure is growing. Unnecessary delays in the finalization of this profile will hinder the regulatory community from acting to adopt necessary safeguards to protect public health. We urge ATSDR to move quickly to consider and incorporate recommendations to improve the quality of this profile, so that this critical public health tool can be finalized and used in a timely manner.

Thank you again for the opportunity to provide comments and for your review and consideration of the science and public health implications of exposure to perfluoroalkyls. We urge ATSDR to carefully consider our comments and recommendations and finalize the profile in a timely manner. This will provide a critical tool that the public health community can use to better protect people from harmful exposures to PFASs.

We greatly appreciate your time and effort in considering this important issue. We look forward to working with you to protect the public from the health threats posed by PFAS compounds.

Respectfully,

Anna Reade, PhD
Staff Scientist
Natural Resources Defense Council

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