BEFORE THE ILLINOIS POLLUTION CONTROL BOARD

IN THE MATTER OF:	)	
	)	
PROPOSED AMENDMENTS TO	)	R2022-018
GROUNDWATER QUALITY	)	(Rulemaking – Public Water Supply)
(35 Ill Adm. Code 620)	)	

NOTICE

TO: SEE ATTACHED CERTIFATE OF SERVICE LIST

PLEASE TAKE NOTICE that I have today electronically filed with the Office of the Clerk of the Illinois Pollution Control Board the PRE-FILED TESTIMONY OF THE AMERICAN CHEMISTRY COUNCIL on the Illinois Environmental Protection Agency's proposed amendments to groundwater quality, a copy of which is herewith served upon you.

Dated: September 15, 2022

Respectfully Submitted,

AMERICAN CHEMISTRY COUNCIL

By: /s/ Stephen P. Risotto

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PRE-FILED TESTIMONY OF STEPHEN P. RISOTTO
OF THE AMERICAN CHEMISTRY COUNCIL

I) INTRODUCTION:

My name is Stephen Risotto. I received my undergraduate degree from Cornell University in 1978, and my Master of Sciences degree from Louisiana State University in 1983.

I joined the American Chemistry Council (ACC) in July 2009 where I am a Senior Director in the Chemical Products and Technology Division. In that position I manage regulatory and technical issues related to individual chemicals and chemical groups. Since 2018 I have managed regulatory and technical issues involving perfluorooctanoic acid (PFOA), perfluorooctane sulfonic acid (PFOS), and other per- and polyfluoroalkyl substances (PFAS). In that capacity I have reviewed and developed written comments on a multitude of federal and state initiatives affecting these substances, including the current proposal before the Pollution Control Board. As a result of these efforts, I have become familiar with the toxicological data base for PFOA, PFOS, and other PFAS.

II) BACKGROUND

As part of my ordinary course of responsibilities as a Senior Director, I have reviewed the proposed groundwater standards for the six PFAS proposed by the Illinois Environmental Protection Agency (IL EPA) and have submitted written comments on the proposal and participated in the hearing process before this Board.

The IL EPA proposal would establish standards for six PFAS in Class I and II groundwater in the state: hexafluoropropylene oxide dimer acid (HFPO-DA), perfluorobutane sulfonic acid (PFBS), perfluorohexane sulfonic acid (PFHxS), perfluorononanoic acid (PFNA),

PFOA, and PFOS. Federal standards do not currently exist for any of these substances, but the US Environmental Protection Agency (USEPA) has indicated that it will promulgate drinking water standards for PFOA and PFOS by the end of 2023. USEPA has developed lifetime health advisories for HFPO-DA, PFBS, PFOA, and PFOS under the Safe Drinking Water Act. The Agency has not developed advisories for PFHxS or PFNA, although these two substances are scheduled to be reviewed under USEPA's Integrated Risk Information System (IRIS) in the next year or so. USEPA has established regional screening levels (RSLs) for soil, air, and tap water for all six PFAS. For PFHxS and PFNA the RSLs are based on the analysis conducted by the Agency for Toxic Substances and Disease Registry (ATSDR) of the US Department of Health and Human Services.

Illinois has not previously established standards for these PFAS. Several states have established standards and/or guidelines for PFOA and PFOS in ground water and drinking water. Fewer have established standards for PFHxS and PFNA; some of which are in combination with other PFAS. Even fewer states have established values for HFPO-DA and PFBS. Standards and guidelines also have been established internationally. Among these, Health Canada has established maximum allowable concentrations (MACs) for PFOA and PFOS in drinking water.

USEPA conducted a national survey of drinking water concentrations between 2013 and 2015 for all but HFPO-DA under its Unregulated Contaminant Monitoring Rule (UCMR). It is scheduled to monitor for all six compounds under the UCMR beginning in 2023. The Center for Disease Control and Prevention (CDC) has conducted biomonitoring for PFHxS, PFNA, PFOA, and PFOS in the US population since 1999. CDC discontinued monitoring for PFBS in 2014 since the substance was rarely detected. The results of CDC monitoring for the four PFAS is summarized in Figure 1. As noted, blood PFOA levels have declined by more than 70 percent since 1999; blood PFOS levels have declined by more than 85 percent.

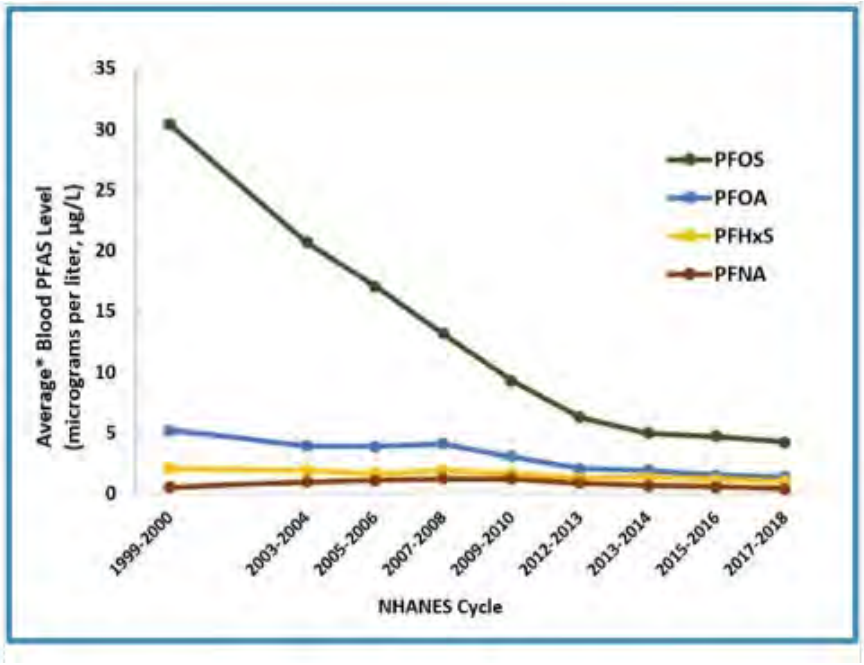

Figure 1. Geometric Mean of Blood Levels in People in the United States, 1999-2018.[1]

III) ANALYSIS

IL EPA has proposed to establish standards for Class I and II ground water for the six PFAS as follows:

Table 1. Proposed Groundwater Standards

Chemical	Proposed Class I/II Standard		Source
	Milligrams/Liter (mg/L)	Parts per trillion (ppt)	
HFPO-DA	0.000012	12	USEPA
PFBS	0.0012	1200	USEPA
PFHxS	0.000077	77	ATSDR
PFNA	0.000012	12	ATSDR
PFOA[2]	0.000002	2	CA EPA
PFOS	0.0000077	7.7	ATSDR

In addition, IL EPA has proposed guidelines for determining when to use dose addition of

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1 CDC. National Report on Human Exposure to Environmental Chemicals, Biomonitoring Data Tables for Environmental Chemicals. U.S. Department of Health and Human Service. Atlanta, GA. https://www.cdc.gov/exposurereport/data_tables.html

2 The proposed standard for PFOA is based on IL EPA's determination of the lower limit of quantification (LLOQ)/lowest concentration minimum reporting level (LCMRL). The others are based on IL EPA's calculation of the human threshold toxicant advisory concentration (HTTAC).

similar acting substances in Class I ground water.

Subpart D: Groundwater Quality Standards

The proposed standards for five of the PFAS (HFPO-DA, PFBS, PFHxS, PFNA, and PFOS) are based on the calculation of the human threshold toxicant advisory concentration (HTTAC) as outlined in Appendix A of the proposal; the proposed standard for PFOA, on the other hand, is based on a minimum reporting level as determined by IL EPA. To calculate the HTTAC for PFHxS, PFNA, and PFOS, IL EPA used the minimum risk level (MRL) determined by ATSDR. For HFPO-DA and PFBS, the reference dose (RfD) as determined by USEPA is used. For all five substances, IL EPA assumes the default relative source contribution (or RSC) of 0.2[3] and the average weight and daily water consumption of a child of 0 to 6 years of age. The selection of an RSC of 0.2 is inappropriate. For example, PFHxS, PFNA, and PFOS have not been manufactured in the US, Europe, and Japan for many years. Use of the default RSC also is inconsistent with the assumptions of other states.[4]

The calculation of an acceptable daily exposure (ADE) for a child between the ages of 0 and 6 years of age is similarly not appropriate for PFNA and PFOS for which the ATSDR MRL is based on developmental effects among laboratory animals exposed *in utero*. For HFPO-DA and PFBS, USEPA's RfD is based on chronic exposure to the substance. For these substances, the ADE for the applicable adult population is the more appropriate metric for calculating the HTTAC.

Section 620.410 – Groundwater Quality Standards for Class I; Potable Resource Groundwater

Although the proposed standards for the six PFAS are based on assessments conducted by other agencies, using USEPA's hierarchy for selecting toxicity values in Superfund risk assessments, it is important that IL EPA consider the underlying data. Such a review is necessary to ensure that the assessment is consistent with accepted risk assessment practices and

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[3] The RSC estimates the portion of the reference dose that is attributable to drinking water (directly or indirectly); the remainder is allocated to other potential exposure sources. USEPA recommends a default of 0.2 in the absence of chemical-specific data. https://www.nj.gov/drbc/library/documents/EPA_human-health-criteria2000.pdf

[4] The state of Michigan, for example, assumes an RSC of 50 percent.

considers the weight of the scientific evidence available for the substance, including data that have become available since the assessment was completed. This information available for each of the selected PFAS is provided below.

Hexafluoropropylene Oxide Dimer Acid (HFPO-DA)

The 2021 assessment by USEPA's Office of Water[5] forms the basis of the proposed standard for HFPO-DA. There are multiple and significant substantive technical and scientific issues with the assessment, however, that require further analysis prior to deciding to use it as a basis for regulation. Of principal concern is that the liver effects seen in animals from which USEPA's reference dose was derived are not relevant to humans. In addition, USEPA bases its analysis on a new and unprecedented toxicological endpoint and misapplies scientific criteria in determining whether the observed effects are adverse. Finally, the assessment uses improper and unwarranted uncertainty factors in calculating the RfD.

There is considerable evidence that the liver effects observed in mice that are the focus of the USEPA assessment occur via the peroxisome proliferation-activated receptor alpha (PPARα) mode of action (MOA). The overwhelming weight of evidence from multiple peer-reviewed studies previously published by USEPA and outside scientists indicates that liver effects occurring in rodents via PPARα have limited to no human relevance.[6] Although USEPA acknowledges that the PPAR-alpha mode of action contributes to the liver effects and "could be more relevant to rodents than humans," it suggests that other MOAs with potential human relevance could be responsible.[7] The available evidence, however, overwhelmingly supports the conclusion that the observed liver effects in animals exposed to HFPO-DA occur through the PPARα MOA. Many of the gaps in the evidence for the MOA identified by USEPA in its assessment are addressed in an analysis by Chappell *et al.* (2020)[8] which was not considered in the Agency's assessment. Moreover, the evidence for an alternate MOA of potential relevance to humans is weak or not supportive.

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5 USEPA. Human health toxicity values for hexafluoropropylene oxide (HFPO) dimer acid and its ammonium salt (CASRN 13252-13-6 and CASRN 62037-80-3). Office of Water. EPA/822/R-21/010 (2021).

6 See for example: Corton JC *et al.* The PPARα-dependent rodent liver tumor response is not relevant to humans: addressing misconceptions. *Arch Toxicol* 92(1):83–119 (2018).

7 USEPA HFPO-DA assessment, at 29.

8 Chappell GA et al. 2020. Assessment of the Mode of Action Underlying the Effects of GenX in Mouse Liver and Implications for Assessing Human Health Risks. *Toxicol Pathol* 48(3):494-508 (2020).

USEPA's analysis is based on combining four liver effects observed in the animal studies into a never-before-used toxicological endpoint – a so called "constellation of liver effects." Not only is this combination of effects a significant departure from standard risk assessment methods, it also is at odds with the available science. USEPA misapplies the criteria from Hall *et al.* (2012)[9] in determining whether the liver effects observed are adverse effects. Had USEPA properly applied these scientific criteria, the Agency would have instead correctly determined that dosing levels in treated mice did not generate effects relevant to humans.

USEPA compounds its mistake in selecting liver effects as a basis for its assessment by adding a total uncertainty factor of 3000 – the maximum uncertainty that the Agency could have used.[10] This total includes a 10-fold uncertainty for the use of a subchronic study and, despite the impressive amount of data available for HFPO-DA, a data base uncertainty (UF_D) of 10. Both are inappropriate. There is no indication of a progression in the rodent liver lesions with longer exposure duration to justify the need for subchronic-to-chronic adjustment. Moreover, the critical effects that are the basis of USEPA's assessment are from a maternal rodent toxicity study for which, according to its own guidance "an uncertainty factor is not applied to account for duration of exposure."[11]

While inconsistent with Agency guidance to assign a UF_D of 10 to a chemical with such a robust database,[12] USEPA suggests it is appropriate in light of concerns about reproductive and developmental effects. However, the RfDs derived from the available reproductive and developmental data are significantly higher than the RfD for liver effects. Consequently, notwithstanding its relevance to humans, an RfD based on liver effects would be protective of any potential reproductive and developmental effects.

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[9] Hall AP *et al.* Liver hypertrophy: a review of adaptive (adverse and non-adverse) changes—conclusions from the 3rd international ESTP expert workshop. *Toxicol Pathol* 40(7):971–994 (2012).

[10] USEPA. A Review of the Reference Dose and Reference Concentration Processes. Risk Assessment Forum. EPA/630/P-02/002F (2002). (The document recommends limiting the total UF applied for any particular chemical to no more than 3000.). https://www.epa.gov/sites/default/files/2014-12/documents/rfd-final.pdf

[11] USEPA, Guidelines for Developmental Toxicity Risk Assessment. Risk Assessment Forum. EPA/600/FR-91/001 (1991). https://ofmpub.epa.gov/eims/eimscomm.getfile?p_download_id=4560

[12] USEPA. Reference Dose/Reference Concentration Processes (2002).

Perfluorobutane Sulfonic Acid (PFBS)

In calculating the proposed standard for PFBS, IL EPA uses the chronic RfD developed by USEPA in its April 2021 assessment[13] based on a report of thyroid effects in newborn mice from a study by Feng *et al.* (2017).[14] In deriving the RfD, USEPA makes several key assumptions that are inconsistent with the available information and standard Agency practice - including the use of a dose adjustment factor (DAF) based on serum half-life and a benchmark response (BMR) of 0.5 standard deviation and the addition of a database uncertainty factor (UF_D) of 10.

USEPA's RfD is based on the result of benchmark modeling (BMD) to determine the dose level associated with a response rate of a standard deviation (SD) of 0.5. Although the use of standard deviation is consistent with Agency guidance for assessing a continuous data in the absence of a basis for establishing a cut-point for biological significance,[15] the selection of a value of 0.5, rather than the 1.0, is not justified by the available data. While USEPA guidance that a 0.5 SD may be appropriate for "more severe" effects, it notes that judgments about the biological and statistical characteristics of the data must be made as part of the BMR selection.[16] In the case of PFBS, the available animal data do not suggest a risk of developmental effects at such a low level of perturbation of thyroid levels. Moreover, the use of a BMR of 0.5 SD contrasts sharply with the recommendation of the Science Advisory Workgroup convened by Michigan's PFAS Action Response Team for a BMR of 20 percent.[17] While using the BMR of 20 may not be sufficiently protective for assessing developmental effects, the default of 1 SD is

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[13] USEPA. Human health toxicity values for perfluorobutane sulfonic acid (CASRN 375-73-5) and related compound potassium perfluorobutane sulfonate (CASRN 29420-49-3). Office of Research and Development. EPA/600/R-20/345F (2021).

[14] Feng X *et al*. Exposure of pregnant mice to perfluorobutanesulfonate causes hypothyroxinemia and developmental abnormalities in female offspring. *Toxicol Sci* 155: 409-419 (2017).

[15] USEPA. Benchmark Dose Technical Guidance. Risk Assessment Forum. EPA/100/R-12/001 (2012). https://www.epa.gov/risk/benchmark-dose-technical-guidance

[16] Ibid, at 23.

[17] USEPA guidance indicates that a BMR of 1 SD is equivalent to a 10 percent response level.

consistent with USEPA guidance and the available data.[18] It further would recognize the significant differences in thyroid function between rodents and humans.[19]

USEPA's analysis also includes a DAF based on the ratio of the biological half-life of PFBS in laboratory animals and humans,[20] rather than its default body weight method, to account for the potential for PFBS to accumulate in humans, despite the fact that PFBS was not detected in the CDC's biomonitoring survey and that the Agency had used body weight in an earlier version of the assessment.

In calculating the toxicity value for PFBS, USEPA includes a UF_D of 10 based on a lack of information on neurodevelopmental and immunotoxicity effects. For PFBS, however, robust data are available on reproductive and developmental effects, including both a prenatal toxicity study and a two-generation reproduction study. USEPA notes, moreover, that "changes reported in mice by Feng *et al.* (2017) were observed in parallel with effects on thyroid hormone levels."[21] Consequently, a toxicity value that protects against effects on thyroid hormones also will protect against developmental effects, particularly effects on neurodevelopment since USEPA's stated concern is that perturbations in thyroid hormones may trigger neurodevelopmental effects. After pointing out the connection between thyroid hormones and neurodevelopment, USEPA provides no rationale for why neurodevelopmental effects should then be considered separately.

The Agency's concern for the potential immunotoxicity of PFBS is based entirely on suggestions of immunotoxicity related to other PFAS. In explaining the addition of the UF_D, the Agency suggests that "immunotoxicity is an effect of increasing concern across several members of the larger PFAS family." The human data for immune effects, while limited, show no clear association with asthma, atopic dermatitis, and cytokine secretion.[22] I am not aware of other data that would suggest that immunotoxicity is a concern for PFBS, which – as clearly demonstrated

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[18] According to USEPA's analysis, the human equivalent dose used to calculate the RfD based on a BMR of 1 SD is 0.25 milligrams/kilogram per day (mg/kg-day), compared to the dose at 0.5 SD of 0.095 mg/kg-day. (USEPA PFBS assessment, at 79)

[19] Capen CC *et al.* Species differences in thyroid, kidney, and urinary bladder carcinogenesis. *IARC Scien Publ* 147:1-14 (1999).

[20] According to USEPA, the mean serum elimination half-life in humans is 1050 hours, compared to about 5 hours in rats and mice.

[21] USEPA. PFBS assessment (2021), at 57.

[22] Ibid, at 47.

by USEPA's analysis – exhibits dramatically different properties than other PFAS that it has evaluated.

Perfluorohexane Sulfonic Acid (PFHxS)

Very few studies exist that can be used as a basis for calculating a groundwater quality standard for PFHxS. The available information report liver and thyroid effects in laboratory animals. The increases in liver weight and hepatocellular hypertrophy that have been reported, however, appear related to PPARα activity which ATSDR notes is a mechanism that "cannot be reliably extrapolated to humans" in the absence of other degenerative lesions.[23] ATSDR derived its MRL, which is the basis for the proposed IL EPA standard, from thyroid follicular cell damage reported by Butenhoff *et al.* 2009, despite the fact that the authors noted that the observed changes in rats "are consistent with the known effects of inducers of microsomal enzymes where the hepatocellular hypertrophy results in a compensatory hypertrophy and hyperplasia of the thyroid."[24] While ATSDR acknowledged the questions regarding the relevance of the thyroid alterations reported by Butenhoff *et al.* to humans, including the significant differences in thyroid function between rodents and humans, [25] it nevertheless selected thyroid as the basis for the MRL in the absence of other data.

Since ATSDR completed its analysis, the National Toxicology Program (NTP) has released the results of a 28-day study in rats that adds additional uncertainty to the relevance of the thyroid effects.[26] Consistent with the earlier studies, NTP reported liver weight increases and decreases in thyroid hormones (T3, free and total T4) in rats exposed to PFHxS, along with a significant increase in PPARα activity.[27] Despite the decrease in hormone levels in a dose-response manner, the NTP study did not observe a consistent increase in thyroid stimulating

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[23] ATSDR. Toxicological Profile for Perfluoroalkyls. US Department of Health and Human Services. Atlanta, GA. (2021).

[24] Butenhoff JL *et al.* Evaluation of potential reproductive and developmental toxicity of potassium perfluorohexanesulfonate in Sprague Dawley rats. *Reprod Toxicol* 27:331-341 (2009).

[25] Capen *et al.* (1999).

[26] Although the ATSDR Toxicological Profile was released in May 2021, much of the data analysis was conducted in 2018.

[27] NTP. Technical report on the toxicity studies of perfluoroalkyl sulfonates (perfluorobutane sulfonic acid, perfluorohexane sulfonate potassium salt, and perfluorooctane sulfonic acid) administered by gavage to Sprague Dawley (HSD:Sprague Dawley SD) Rats. NTP Tox 96. US Department of Health and Human Services (2019). https://ntp.niehs.nih.gov/ntp/htdocs/st_rpts/tox096_508.pdf?utm_source=direct&utm_medium=prod&utm_campaign=ntpgolinks&utm_term=tox096

hormone (TSH), as would be expected, nor were any histopathological changes (hyperplasia/ hypertrophy) observed in the thyroid gland. In reviewing these findings, the NTP report explained that "[t]he reason for a lack of TSH response in the face of substantially low thyroid hormone concentrations in these sulfonate studies is not clear and not consistent with a disruption in the hypothalamic-pituitary-thyroid axis." NTP further hypothesizes that the observed decrease in total T4 and T3 may be "related to activation of PPARα and constitutive androstane receptor (CAR) resulting in an increase in thyroxine-UDP glucuronosyltransferase and accelerated degradation of thyroxine by the liver."

Given the likelihood that both the available hepatic and thyroid effects data from studies of laboratory animal exposed to PFHxS are associated with PPARα in the liver which, as noted by ATSDR, cannot be reliably extrapolated to humans, IL EPA should withdraw the proposed standard for PFHxS until more robust data are available. At the very least, IL EPA should update its analysis to reflect the information available from the NTP study.

Perfluorononanoic Acid (PFNA)

As is the case with other PFAS, the liver appears to be a major organ of toxicity for PFNA in laboratory animals. Consistent with the evidence for PFHxS, animals exposed to PFNA exhibited a significant increase in PPARα suggesting that the hepatic effects may be a rodent-specific phenomenon. Deceases in thyroid hormones also have been consistently reported in the animal studies, with no resulting increase in TSH, suggesting that the thyroid effects may be related to PPARα activity in the liver and of questionable relevance to humans.

The MRL developed by ATSDR, which is the basis for the proposed groundwater standard, is based on developmental effects reported by Das *et al.* 2015 who reported decreased body weight and developmental delays in the offspring of female mice exposed during gestation.[28] The doses at which these developmental effects were observed also resulted in maternal effects, however. More significantly Wolf *et al.* (2010) did not find alterations in body weight or postnatal development in the offspring of PPARα knockout mice dams exposed to 2 mg/kg-day.[29] This finding supports the conclusion that the developmental effects noted in rodents are dependent on PPARα and not relevant to humans.

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[28] Das KP *et al.* Developmental toxicity of perfluorononanoic acid in mice. *Reprod Toxicol* 51:133-144 (2015).

[29] Wolf CJ *et al.* Developmental effects of perfluorononanoic Acid in the mouse are dependent on peroxisome proliferator-activated receptor-alpha. *PPAR Res* 282896 (2010).

The 2019 NTP 28-day study included exposure to up to 2.5 mg/kg-day of PFNA in males (6.25 mg/kg-day in females) and measured the PFNA serum levels in the animals.[30] As with PFHxS, the hepatic and thyroid effects were accompanied by a significant increase in PPARα and CAR activity and suggest that these effects may not be relevant to humans. Among the other effects reported, NTP observed decreases in absolute and relative spleen and thymus weights in males exposed to 1.25 mg/kg-day and reduced testosterone levels and testis damage in male rats exposed to 2.5 mg/kg-day. No thymus weight or reproductive effects were reported in the female rats.

In its analysis ATSDR also applies a modifying uncertainty factor of 10 for PFNA based on the lack of a comprehensive study of reproductive effects and a general concern about sensitivity to immune function for other PFAS. While ATSDR provides no guidance on how to apply a modifying factor based on data base uncertainty, USEPA's guidance explains that a database uncertainty factor (UF_D) is applied when reproductive and developmental toxicity studies are missing since they have been found to provide useful information for establishing the lowest no adverse effect level.[31] The USEPA guidance notes that, for an RfD based on animal data, a factor of 3 is often applied if either a prenatal toxicity study or a two-generation reproduction study is missing, or a factor of 10 may be applied if both are missing.[32] Since the reproductive data base for PFNA is lacking, a UF_D of 3 may be appropriate. Although reports of reduced spleen and thymus weight may suggest effects on the immune system, the doses at which the effects have been observed are comparable to those for other effects and do not suggest a greater sensitivity of the immune system.

Notwithstanding the question about the relevance of the developmental effects reported by Das *et al.* to humans, it is important for IL EPA to critically review ATSDR's assumptions about RSC and target population. The inappropriate addition of a 10-fold modifying factor also warrants scrutiny.

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[30] The NTP study included a higher dose group for either sex – 5 mg/kg for males and 12.5 mg/kg for females – but serum levels for animal in these groups was not reported.

[31] Dourson ML *et al.* Evolution of science-based uncertainty factors in noncancer risk assessment. *Regul Toxicol Pharmacol* 24:108–120 (1996).

[32] USEPA Risk Assessment Forum. A review of the reference dose and reference concentration processes. EPA/630/P-02/002F (2002). https://www.epa.gov/sites/production/files/2014-12/documents/rfd-final.pdf

Perfluorooctane Sulfonic Acid (PFOS)

The proposed groundwater standard for PFOS is based on ATSDR's analysis of a two-generation study by Luebker *et al.* (2005) [33] reporting delayed eye opening and decreased pup weight in rats. In its analysis, however, ATSDR ignored the conclusions of the authors regarding the relevant dose resulting in the adverse effects and inappropriately applied an additional uncertainty factor.

In the case of pup weight, Luebker *et al.* noted the decreases observed in the second generation (F2) offspring at 0.4 mg/kg-day were transient, disappearing by the end of lactation. Reduced body weights were not reported in the F1 pups from the 0.4 mg/kg dose group. For both F1 and F2 offspring, body weight was reduced in the 1.6 mg/kg group. As a result, the authors identified 0.4 mg/kg as a no-observed-adverse-effect level (NOAEL) and 1.6 mg/kg as a lowest-observable-adverse-effect level (LOAEL). ATSDR, in contrast, inappropriately considered the LOAEL to be 0.4 mg/kg without explanation.

Similarly, Luebker *et al.* concluded that the slight delay in eye opening observed in the F1 pups from the 0.4 mg/kg dose group should not be considered an adverse effect and identified 0.4 mg/kg as the NOAEL. This finding is consistent with the results from the other studies in rats and mice referenced in the ATSDR Toxicological Profile which report NOAELs of 1.0 mg/kg or more. The decision to consider 0.4 mg/kg as a LOAEL, rather than NOAEL, has a significant impact on the ATSDR calculation and the proposed standards.

In its analysis ATSDR also applies a modifying uncertainty factor of 10 for PFOS based on a concern that "immunotoxicity may be a more sensitive endpoint of PFOS toxicity than developmental toxicity." As noted previously USEPA's guidance explains that a database uncertainty factor (UF_D) is applied when reproductive and developmental toxicity studies are missing since they have been found to provide useful information for establishing the lowest no adverse effect level.[34] The USEPA guidance notes that, for an RfD based on animal data, a factor of 3 is often applied if either a prenatal toxicity study or a two-generation reproduction study is missing, or a factor of 10 may be applied if both are missing.[35] In deciding whether to

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[33] Luebker DJ *et al.* Two-generation reproduction and cross-foster studies of perfluorooctanesulfonate (PFOS) in rats. *Toxicol* 215(1-2):126-148 (2005).

[34] Dourson ML *et al.* (1996)

[35] USEPA Risk Assessment Forum 2002.

apply an UF_D, USEPA advises that the assessor should consider both the data lacking and the data available for particular organ systems as well as life stages.

In the case of PFOS, the reproductive and development data base is robust and does not suggest the need to account for an incomplete characterization of toxicity. Similarly, the potential immunotoxic effects of PFOS have been studied in both laboratory animals and humans. The results of these studies are inconsistent and the relevance of immune system effects observed in mice and the small antibody variations seen in epidemiology studies to adverse health effects in humans has been questioned by the National Toxicology Program and others.[36] It is inappropriate, therefore, to conclude that immunotoxic effects represent a more sensitive health effect such that a modifying factor of 10 should be included.

Perfluorooctanoic Acid (PFOA)

The proposed groundwater quality standard for perfluorooctanoic acid (PFOA) is based on the assessment by California's Office of Environmental Health Hazard Assessment (OEHHA)[37] that the substance is carcinogenic and IL EPA's assessment of the lowest concentration at which PFOA can be reliably quantified. Both are incorrect. The OEHHA assessment is based on the results of a chronic animal bioassay conducted by NTP that reported increased incidence of hepatocellular and pancreatic tumors in male rats exposed to PFOA in their diet. Reports of unanticipated toxicity in the study and elevated preneoplastic lesions in the control group, however, raise concerns about the findings. The determination of a LLOQ/LCMRL of 0.000002 mg/L also is not consistent with the USEPA's minimum reporting level for PFOA.

In its study NTP reported an increased incidence of liver adenomas and pancreatic acinar cell (PAC) adenomas in male Sprague-Dawley rats exposed to PFOA in the diet.[38] In the study, male rats were exposed postweaning to 0, 20, 40, and 80 parts per million (ppm), equivalent to 0, 1.0, 2.2, and 4.6 milligrams per kilogram, or mg/kg, per day, while females were exposed to 0, 300, and 1000 ppm (0, 18.2, and 63.4 mg/kg per day).[39] The male rat portion of the study was

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[36] National Toxicology Program. Immunotoxicity Associated with Exposure to Perfluorooctanoic acid or Perfluorooctane Sulfonate. NTP Monograph. US Department of Health and Human Services. Research Triangle Park, NC (2016) https://ntp.niehs.nih.gov/ntp/ohat/pfoa_pfos/pfoa_pfosmonograph_508.pdf

[37] OEHHA. Notification Level recommendations – perfluorooctanoic acid and perfluorooctane sulfonate in drinking water. California Environmental Protection Agency (August 2019).

[38] NTP. Technical report on the toxicology and carcinogenesis studies of perfluorooctanoic acid administered in feed to Sprague-Dawley rats. Technical Report 598. Department of Health and Human Services. Research Triangle Park, NC (2019). https://ntp.niehs.nih.gov/ntp/htdocs/lt_rpts/tr598_508.pdf

[39] The study included groups of animals exposed to PFOA perinatally and postweaning to assess the potential

repeated using significantly lower exposures after "unanticipated toxicity" was observed in male rats exposed to 150 and 300 ppm after 16 weeks. In light of the fact that male SD rats tolerated doses as high as 300 ppm in a previous chronic studies (described below), the reports of unanticipated toxicity at comparable levels in the male rats in the NTP study raise concern about the overall confidence in the study.[40]

Statistically significant increases in hepatocellular adenomas were reported among the male rats exposed to the two highest doses (2.2 and 4.6 mg/kg per day). Hepatocellular carcinomas were increased at the highest dose (4.6 mg/kg per day), but the increase was not statistically significant. The study also reported significant increases in hepatocyte cytoplasmic alteration and hypertrophy in the males in all exposure groups. Significant increases were also observed in single cell hepatocyte death, necrosis, mixed cell foci, inflammation, cystic degeneration, and bile duct hyperplasia.

An increase in PAC adenomas was statistically significant in male rats in all exposure groups, but not in the female groups.[41] PAC adenocarcinomas were also increased in the males, but the increase was not statistically significant. The study also noted a significant increase in PAC hyperplasia - a potentially preneoplastic lesion - in all the male groups, including the control group in which hyperplasia was reported in 36 percent of the animals. The high background rate for preneoplastic lesions observed in this study is consistent with the historical sensitivity of the Sprague-Dawley rats compared to other rat stains – and more significantly - when compared to humans.

Epidemiology

Occupational studies examining cancer mortality have been conducted among workers occupationally exposed to PFOA in Minnesota and West Virginia focusing on kidney, bladder, liver, pancreatic, testicular, prostate, thyroid, and breast cancers. Two studies of communities exposed to PFOA in drinking water also are available. The results from these studies are

impact of gestational and lactational exposure but reported very few significant differences between the response in animals exposed postweaning only to those with both perinatal and postweaning exposure.

[40] In addition, survival rates among the female animals were quite low – ranging from 46 percent in the control group to between 46 and 64 percent in the exposure groups.

[41] A non-significant increase of combined PAC adenomas and carcinomas was observed in females at the highest dose. Unlike in the males, acinus hyperplasia was not reported in the females.

conflicting and interpretation is limited by the small number of observed deaths and incident cases.

Raleigh et al. (2014) updated a study of cancer mortality among 4,668 PFOA workers in Minnesota followed through 2008.[42] Exposure estimates for inhalation exposures were calculated from work history records and industrial hygiene monitoring data; notably serum levels were not reported. The analysis reported no association between PFOA exposure and mortality from any cancer type. A slight elevation of bladder and pancreatic cancer incidence was reported although the confidence intervals were quite large; no association with kidney cancer incidence and PFOA exposure was reported.[43] The mean age of the workers was 29 years at the start of employment and 63 years at the end of follow-up.

Steenland and Woskie (2012) updated a cohort mortality study of 5,791 workers in West Virginia who had worked in a manufacturing facility using PFOA for at least 1 year between 1948 and 2002.[44] Mean duration of employment was 19 years. Exposure quartiles were assessed by estimated cumulative annual serum levels based on blood samples taken from 1,308 workers and time spent in various job categories. Referent groups included both nonexposed workers in the same region and the U.S. population. Overall, the mean cumulative exposure among the workers was 7.8 ppm-years and the estimated average annual serum level was 0.35 milligrams per liter (mg/L).[45] The authors reported a significant positive trend for kidney cancer incidence among workers in the highest exposure quartile, while no association was reported between PFOA exposure and liver, pancreatic, testicular, or bladder cancer incidence.

Liver cancer mortality was elevated in a small observational study of 642 male employees who had worked at least 6 months before 2009 for a factory producing PFOA and other chemicals.[46] Confounding factors were not well controlled. Serum levels in 120 workers

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[42] Raleigh KK *et al.* Mortality and cancer incidence in ammonium perfluorooctanoate production workers. *Occup Environ Med* 71(7):500-506 (2014).

[43] The authors report that the study had limited power to evaluate exposure response for testicular, bladder, liver, and pancreatic cancers.

[44] Steenland K and Woskie S. Cohort mortality study of workers exposed to perfluorooctanoic acid. *Am J Epidemiol* 176(10):909–917 (2012).

[45] For comparison, the mean serum level of PFOA in the 2016 biomonitoring survey conducted by the Center for Disease Control and Prevention was 0.0016 mg/L.

[46] Girardi P and Merler E. A mortality study on male subjects exposed to polyfluoroalkyl acids with high internal dose of perfluorooctanoic acid. *Env Research 179(Part A)*:108743 (2019).

were used to predict PFOA concentrations of each individual; serum concentrations ranged from 19 to 91,900 nanograms per milliliter (ng/mL). A statistically significant increase for mortality of liver cancer and liver cirrhosis was reported in the highest cumulative internal dose group when compared to the regional populations and workers of a nearby factory.

Two studies involving communities in West Virginia and Ohio affected by contaminated drinking water (the C8 Health Project) reported a positive association between blood levels of PFOA and kidney and testicular cancers. Vieira *et al.* (2013) investigated incidences of 18 cancer types among residents supplied by six public water districts in Ohio and West Virginia contaminated with PFOA.[47] The analysis included over 25,000 cancer cases. Exposure levels and serum PFOA concentrations were estimated based on residence at time of diagnosis. Exposures were categorized as very high, high, medium, low, or unexposed based on PFOA serum concentrations.

Among all cancer endpoints, the odds ratio for testicular cancer was elevated in one of the two areas with the highest concentration of PFOA in drinking water. There was no statistically significant increase in the odds ratio for testicular cancer in the total exposed population, however, or in the other districts, or in the other estimated dose-level categories. Kidney cancer incidence was increased significantly in one district with the two highest levels of individual exposure. Despite the large overall sample size, the authors noted that their analysis was limited by small numbers of individual cancers in the high-exposure groups. Moreover, there was little consistency across exposure categories, with no evidence of a dose response.

Barry *et al.* (2012) conducted an analysis of cancer incidence among 32,254 individuals in the same geographic area as Vieira *et al.*, including 3,713 workers with occupational exposure to PFOA.[48] Cumulative PFOA serum concentrations were estimated based on historical regional monitoring data and individual residential histories. Based on measurements taken in 2005-2006, mean serum concentrations were 0.024 mg/L for community residents and 0.113 mg/L for workers. A total of 2,500 cancers were validated through a cancer registry or medical records. The authors reported that PFOA exposure was positively associated with kidney and testicular

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[47] Vieira VM *et al.* Perfluorooctanoic acid exposure and cancer outcomes in a contaminated community: a geographic analysis. *Environ Health Persp* 121(3):318-323 (2013).

[48] Barry V *et al.* Perfluorooctanoic acid (PFOA) exposures and incident cancers among adults living near a chemical plant. *Environ Health Persp* 121(11-12): 1313-1318 (2013).

cancer across the exposure quartiles within the population, although the incidence of either tumor type was not elevated when compared to the US population.

Two additional population studies did not report an association of liver or pancreatic cancer and PFOA exposure. A study of 57,000 individuals with no previous cancer diagnosis enrolled in a prospective cohort during 1993-97 reported no association between liver and pancreatic cancer and elevated levels of PFOA; kidney and testicular cancer information was not presented.[49] PFOA concentrations were based on a single measure of plasma level taken at recruitment. A study of residents exposed to contaminated drinking water near a PFAS manufacturing facility in the Veneto Region of Italy with exposure to multiple PFAS, reported no overall increase in mortality caused by kidney, pancreatic, liver, or testicular cancer.[50] Some Kidney cancer mortality was slightly elevated among women.

A review of the epidemiological evidence for cancer from 18 studies of occupational and general population exposure to PFOA reported a lack of concordance between community exposures and occupational exposures one or two magnitudes higher than those for the general population.[51] The authors evaluated the studies based on the study design, subjects, exposure assessment, outcome assessment, control for confounding, and sources of bias using Bradford Hill guidelines and concluded that the discrepant findings across the study populations were likely due to chance, confounding, and/or bias. A more recent review of the evidence by the epidemiologists involved in the C8 study concluded that there was little evidence for an association with liver or pancreatic cancer.[52]

The relevance of the liver tumor data from the NTP study is further called into question by recent clinical data reported by Convertino *et al.* (2018).[53] In a study of a sensitive subpopulation of cancer patients with normal liver function exposed to weekly PFOA doses as

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[49] Eriksen KT *et al.* Perfluorooctanoate and perfluorooctanesulfonate plasma levels and risk of cancer in the general Danish population. *J Natl Cancer Inst* 101:605–609 (2009).

[50] Mastrantonio M *et al.* Drinking water contamination from perfluoroalkyl substances (PFAS): an ecological mortality study in the Veneto Region. Italy. *Eur J Public Health* 28(1):180–185 (2018).

[51] Chang ET *al.* A critical review of perfluorooctanoate and prefluorooctanesulfonate exposure and cancer risk in humans. *Crit Rev in Toxicol* 44(51):1–81 (2014).

[52] Steenland K *et al.* Review: evolution of evidence on PFOA and heath following the assessments of the C8 Science Panel. *Environ Intl* 145: 106125 (2020).

[53] Convertino M *et al.* Stochastic pharmacokinetic-pharmacodynamic modeling for assessing the systematic health risk of perfluorooctanoate (PFOA). *Toxicol Sci* 163(1) 293-306 (2018).

high as 1,200 mgs (about 16 mg/kg per day), Convertino *et al.* reported no differences in clinical hepatic measures.[54] Similarly a study of PFOA production workers reported no abnormal liver function, hypolipidemia, or cholestasis.[55]

Animal Bioassays

In addition to the NTP study, two chronic bioassays have been conducted in rats exposed to PFOA through diet. Although the results are not consistent, one or both studies have reported liver, Leydig cell (LC), or PAC tumors.[56]

Butenhoff *et al.* (2012), reporting on a previously conducted study of male and female Sprague- Dawley (SD) rats exposed to dietary levels of 30 and 300 ppm of PFOA (approximately 1.5 and 15 mg/kg per day), observed a dose-dependent increase in LC adenomas that was statistically significant at the highest dose.[57] Elevated incidence of hepatic and PAC lesions were also reported in males at 300 ppm, but the authors did not report increases in hepatic or PAC tumors despite exposures that were three times higher than those used in the NTP study.

A subsequent single-dose, dietary study with male Crl:CD BR (CD) rats reported LC adenomas, as well as liver and PAC adenomas and combined pancreatic adenomas and carcinomas at 300 ppm (13.6 mg/kg per day).[58] Increased incidences of LC and PAC hyperplasia were also observed. Hepatic ß-oxidation activity was significantly elevated, but cell proliferation in the liver was not.

Relevance of the Animal Data

A significant amount of genotoxicity and mechanistic data are available to assist in evaluating the results of the epidemiology and animal bioassay results described above. Multiple *in vivo* and *in vitro* assays provide clear evidence that PFOA is not mutagenic and may only

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54 Clinical measurements included triglycerides, urea, glucose, AST, GGT, alkaline phosphatase, total bilirubin, fibrinogen, PTT and aPTT.

55 Olsen GW *et al.* Plasma cholecystokinin and hepatic enzymes, cholesterol and lipoproteins in ammonium perfluorooctanoate production workers. *Drug Chem Toxicol* 23(4):603–20 (2000).

56 The incidence of testicular (Leydig cell, or LC) adenomas was not reported in the NTP bioassay.

57 Butenhoff JL *et al.* Chronic dietary toxicity and carcinogenicity study with ammonium perfluorooctanoate in Sprague-Dawley rats. *Toxicol* 298(1–3): 1–13 (2012). Target doses for the study were 0, 1.3, and 14.2 mg/kg body weight per day in males and 0, 1.6, and 16.1 mg/kg per day in females.

58 Biegel LB *et al.* Mechanisms of extrahepatic tumor induction by peroxisome proliferators in male CD rats. *Toxicol Sci* 60(1): 44–45 (2001).

cause genotoxicity at toxic concentrations. Consequently, it is generally agreed that PFOA causes tumors in laboratory animals via a non-genotoxic or epigenetic mechanism.[59]

The tumor types that have been reported consistently in rats exposed to PFOA – liver, LC, and PAC – have been observed with other substances that are PPARα agonists. Because of key toxicodynamic and biological differences in responses between rodents and humans, PPARα activators are considered unlikely to induce tumors in humans. For liver tumors, this conclusion is based on minimal or no effects observed on growth pathways, hepatocellular proliferation and liver tumors in humans and/or species (*e.g.*, hamsters, guinea pigs and *Cynomolgus* monkeys) where PPARα expression is more similar to humans.

Several key studies provide support for the key events in the proposed PPARα-activated MOA for rat liver tumors (Table 1) and confirm that the MOA has little relevance to humans. These data are summarized by Klaunig *et al.* (2012) –

> Analysis of gene expression changes elicited following short-term administration of PFOA demonstrated the up regulation of genes characteristic of PPARα activation, including genes involved in fatty acid homeostasis/peroxisomal proliferation as well as those related to cell cycle. In addition, PFOA has been shown to induce peroxisome proliferation in mouse and rat liver and causes hepatomegaly in mice and rats. While the liver growth caused by PFOA was predominantly attributed to a hypertrophic response, an increase in DNA synthesis following PFOA exposure was observed and predominated in the periportal regions of the liver lobule. Thus, the effect of PFOA on induction of cell cycle gene expression and the increase in DNA synthesis provide evidence in support of both key events 2 and 3 in the proposed MOA for liver tumor induction by PFOA. Empirical evidence also exists in support of the clonal expansion of preneoplastic hepatic lesions by PPARα activators (Step 4). Using an initiation-promotion protocol for induction of liver tumors in Wistar rats, PFOA was shown to increase the incidence of hepatocellular carcinomas in rat liver (33% in PFOA exposed rats vs. 0% in controls).[60]

Klaunig *et al.* also note that the key events in Table 1 appear in a temporal sequence and demonstrate dose-related effects further strengthening the evidence for the PPARα-agonist

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[59] USEPA. Health Effects Support Document for Perfluorooctanoic Acid (PFOA). EPA 822-R-16-003. Office of Water (2016).

[60] Klaunig JE *et al.* Mode of action analysis of perfluorooctanoic acid (PFOA) tumorigenicity and human relevance. *Reprod Toxicol* 33:410-418 (2012). 2012). https://doi.org/10.1016/j.reprotox.2011.10.014

MOA. Although there are indications that PFOA may also act through PPARα-independent mechanisms in rodents,[61] differences in binding affinity between the rodent and human receptors suggest that it is also unlikely that PFOA induces cancers in humans through the other mechanisms that have been suggested.[62] In evaluating their results, Convertino *et al.* concluded that the disparity between animal and human liver endpoint studies, emphasizing a lack of risk of hepatomegaly, fatty liver, or cirrhosis, are likely due to MOA differences. Increased liver weight due to hepatocellular hypertrophy can often be an adaptive (protective) response in animals due to up-regulation of detoxification enzymes, leading toxicologists to revisit the relevance key liver endpoint studies in animals.[63]

Table 2. PPARα Mode of Action for PFOA-Induced Liver Tumors in Rats (from Klaunig *et al.* 2012)

	Key Event	Support	Key Reference[64]
1	Activation of the PPARα receptor	√	Maloney *et al.* 1999; Vanden Heuvel *et al.* 2006
2	Induction of cell growth gene expression in the liver	√	Martin *et al.* 2007; Kennedy *et al.* 2004
3	Cell proliferation	√	Biegel *et al.* 2001; Martin *et al.* 2007; Thottassery *et al.* 1992
4	Selective clonal expansion of preneoplastic hepatic foci	√	Abdellatif *et al.* 1990
5	Liver neoplasms	√	Biegel *et al.* 2001

For the induction of rat PAC tumors by PFOA, the available mechanistic data are less robust, but also point to the importance of PPARα activation in the liver. Several factors may contribute to the development of PAC hypertrophy, hyperplasia, and adenomas in the rat, such as testosterone and estradiol levels, growth factor expression (cholecystokinin, or CCK), growth

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61 Activation of the constitutive activated receptor (CAR) and pregnane X receptor (PXR) by PFOA have been suggested in animal studies.

62 Hall AP *et al.* Liver Hypertrophy: A Review of Adaptive (Adverse and Non-Adverse) Changes-Conclusions from the 3rd International ESTP Expert Workshop. *Toxicol Pathol* 40:971-994 (2012).

63 See for example: Bjork JA *et al.* Multiplicity of nuclear receptor activation by PFOA and PFOS in primary human and rodent hepatocytes. *Toxicol* 288: 8-17 (2011).

64 Complete citations are provided in Klaunig *et al.* 2012.

factor receptor overexpression (CCKA receptor),and high fat diet (Klaunig *et al.*).[65] Studies with the compound Wyeth 14,643, a well-studied and potent peroxisome proliferator in rodents, suggest that peroxisome proliferation induces PAC tumors by an indirect mechanism. In this study PPARα activation in the liver caused by exposure to Wyeth triggered reduced bile flow and/or changes in bile composition that produced an increase in CCK levels secondary to hepatic cholestasis.[66] As CCK has been shown to act as a growth factor for PACs in rats, a sustained increase in CCK levels would explain the increase in PAC proliferation observed following PFOA exposure and is likely therefore a preneoplastic lesion.

As with PPARα, expression of CCK receptors in humans is much lower as compared to rodents, and the available non-human primate and human data suggest that the CCK pathway is not relevant to human cancer risk. A study with Cynomolgus monkeys exposed to PFOA did not demonstrate an effect on CCK levels or evidence of hepatic cholestasis.[67] Olsen et al reported a statistically significant negative (inverse) association between mean CCK levels and serum PFOA levels among PFOA production workers, even after adjusting for potential confounders.[68]

Minimum Reporting Level

In its submission to the Board, IL EPA indicates that the LLOQ/LCMRL for all six PFAS using USEPA Method 537.1 is 0.000002 mg/L (2 parts per trillion). In the information provided in preparation of the next nationwide drinking water monitoring program under the Unregulated Contaminant Monitoring Rule (UCMR), USEPA indicates that the minimum reporting level for the six PFAS are as follows:

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[65] Differences in the diets used in the Butenhoff *et al.* and Biegel *et al*. studies have been suggested as the likely reason for the quantitative difference in the PAC lesions observed in the two studies (USEPA 2016).

[66] Obourn JD *et al*. Mechanisms for the pancreatic oncogenic effects of the peroxisome proliferator Wyeth-14,643. *Toxicol Appl Pharmacol* 145:425–36 (1997).

[67] Butenhoff JL *et al*. Toxicity of ammonium perfluorooctanoate in male cynomolgus monkeys after oral dosing for 6 months. *Toxicol Sci* 69(1):244–57 (2002).

[68] Olsen GW *et al*. Plasma cholecystokinin and hepatic enzymes, cholesterol and lipoproteins in ammonium perfluorooctanoate production workers. *Drug Chem Toxicol* 23(4):603–20 (2000).

Table 3. Minimum Reporting Levels for USEPA's Fifth Unregulated Contaminant Monitoring Rule[69]

	Minimum Reporting Level	
	Micrograms/Liter (µg/L)	**Parts per trillion (ppt)**
HFPO-DA	0.005	5
PFBS	0.003	3
PFHxS	0.003	3
PFNA	0.004	4
PFOA	0.004	4
PFOS	0.004	4

Consequently, the proposed groundwater standard for PFOA is below USEPA's reporting level - suggesting that such a low level cannot be reliably measured and raising significant uncertainty about the ability of entities to comply with the standard.[70] It is not clear why IL EPA would propose a standard that is below the reporting level specified by USEPA. Should IL EPA continue to rely on the OEHHA analysis of carcinogenicity, it must revise its proposed standard to align with USEPA's conclusion on the reporting level.

Section 620.420 – Groundwater Quality Standards for Class II: General Resource Groundwater

IL EPA has proposed that the standards for the six PFAS in Class II groundwater be the same as those for Class I, based on the criteria it has established for physical and chemical properties of the substance. As noted in the submission to the Board, the substances do not meet the criteria for organic carbon partition coefficient (Koc).[71] Yet, available data indicate that the substances can be readily removed by treatment with granular activated carbon,[72] an "efficient and cost-effective treatment technology for removing various organic contaminants from water."[73] Since a primary factor in establishing Class II standards is "the capabilit[y] of

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69 USEPA. The Fifth Unregulated Contaminant Monitoring Rule (UCMR 5) – Program Overview Fact Sheet. Office of Water. EPA 815-f-21-009 (2021). The Fact Sheet suggest the use of USEPA Method 533, rather than Method 527.1. https://nepis.epa.gov/Exe/ZyPURL.cgi?Dockey=P1014715.txt

70 Such uncertainty also could impact reporting of PFOS, per the provisions of Section 620.310(c).

71 Koc is the ratio of a chemical's concentration absorbed per unit mass of soil to its concentration in the aqueous phase. It is used to estimate the mobility of an organic compound in soil.

72 According to USEPA's Drinking Water Treatability Database, activated carbon can remove up to >99 percent of the six PFAS. https://www.epa.gov/water-research/drinking-water-treatability-database-tdb

73 35 Ill. Adm. Code 611, Subpart F.

treatment technologies to bring Class II waters to qualities suitable for potable use," [74] it is not clear why IL EPA would depend on arbitrary cutoffs in lieu of empirical data in determining applicable Class II standards. Based on these data, a treatment factor of 5 or greater should be applied to all six PFAS.

Section 620. Appendix C – Guidelines for Determining when Dose Addition of Similar-Acting Substances in Class I: Potable Resource Groundwater is Appropriate

The Appendix C of the proposal lists numerous substances that IL EPA indicates should be considered similar acting in various organ systems and, for which it assumes additivity of health effects and for which the dose-addition model described in Appendix B would be applied. However, while the proposed Appendix provides information on the target organ/system, it fails to identify a "common mode of toxic action" by which the substances cause an effect in the organ - as required in Appendix C. In fact, IL EPA has not identified the MOA for any of the substances included in Appendix E much less established a common MOA for multiple substances. The additivity of potential health effects of these substances should not be considered unless and until a common MOA can be established through an established framework. Such frameworks exist for both cancer[75] and non-cancer[76] MOAs.

The proposal for identifying similar acting substances also inappropriately seeks to apply the advisory concentration (threshold or non-threshold) to organs/systems for which the reference dose of slope factor do not apply. Since the advisory concentrations are based on the most sensitive effect that has been observed, applying that same level of toxicity to organs for which effects occur at higher does or that are clearly established for a substance significantly overstates the toxicity of the mixture. For example, as proposed Appendix E would include PFHxS in estimates of mixture toxicity for five organs or systems – circulatory, immune, developmental, liver, and thyroid - despite the fact that the advisory concentration for the substance is based on effects in only one (thyroid). IL EPA has provided no data to support an association between circulatory, developmental, and immune effects and PFHxS exposure.

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[74] 35 Ill. Adm. Code 620.

[75] Boobis AR *et al.* IPCS Framework for analyzing the relevance of a cancer mode of action for humans. *Crit Rev Toxicol* 36(10):781-92 (2006)

[76] Boobis AR *et al.* IPCS Framework for analyzing the relevance of a noncancer mode of action for humans. *Crit Rev Toxicol* 38(2):87-96 (2008).

Moreover, ATSDR, the source for the proposed HTTAC, has concluded that the liver effects observed in animals are not relevant to humans.

IV) CONCLUSION

The above concludes my pre-filed testimony on behalf of the American Chemistry Council relating to the above captioned rulemaking. The Council will supplement the testimony herein, as needed or requested, during hearing.

By: /s/ Stephen P. Risotto
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DATED: September 15, 2022

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CERTIFICATE OF SERVICE

I, the undersigned, certify that I have today filed the attached NOTICE OF FILING and PRE-FILED TESTIMONY in PCB R2022-18 upon the below service list by electronic mail.

Dated: September 15, 2022

Respectfully Submitted,

AMERICAN CHEMISTRY COUNCIL

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