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BEFORE THE ILLINOIS POLLUTION CONTROL BOARD

IN THE MATTER OF:	)	
PROPOSED AMENDMENTS TO GROUNDWATER QUALITY (35 ILL. ADM. CODE 620)	)	**R 2022-018 (Rulemaking - Public Water Supply)**

NOTICE OF FILING

To: ALL PARTIES ON THE ATTACHED SERVICE LIST

PLEASE TAKE NOTICE that I have today electronically filed with the Office of the Clerk of the Illinois Pollution Control Board the attached **Pre-filed Testimony of Robyn Prueitt**, and a **Certificate of Services**, copies of which are hereby served upon you.

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Dated: September 15, 2022

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CERTIFICATE OF SERVICE

I, the undersigned, certify that on this 15th day of September, 2022, I have electronically served the attached **Pre-filed Testimony of Robyn Prueitt** upon the individuals on the attached service list. I further certify that my email address is Sarah.Lode@afslaw.com; the number of pages in the email transmission is 40; and the email transmission took place before 5:00 p.m.

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Pre-Filed Testimony of Robyn Prueitt, Ph.D., DABT Regarding the Illinois Environmental Protection Agency's Proposed Amendments to Illinois Administrative Code Title 35, Part 620: Groundwater Quality Standards

Docket Number R22-18

Prepared by

Robyn Prueitt, Ph.D., DABT

September 15, 2022

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Abbreviations

ACC	American Chemistry Council
ATSDR	Agency for Toxic Substances and Disease Registry
Board	Pollution Control Board
CalOEHHA	California Environmental Protection Agency's Office of Environmental Health Hazard
CCK	Cholecystokinin
HEAST	Health Effects Assessment Summary Table
HFPO-DA	Hexafluoropropylene Oxide Dimer Acid
IARC	International Agency for Research on Cancer
IEPA	Illinois Environmental Protection Agency
IGPA	Illinois Groundwater Protection Act
IRIS	Integrated Risk Information System
LLOQ	Lower Limit of Quantification
LOAEL	Lowest Observed Adverse Effect Level
MDH	Minnesota Department of Health
MDHHS	Michigan Department of Health and Human Services
MRL	Minimal Risk Level
NOAEL	No Observed Adverse Effect Level
NTP	National Toxicology Program
PFAS	Per- and Polyfluoroalkyl Substances
PFBS	Perfluorobutanesulfonic Acid
PFHxS	Perfluorohexanesulfonic Acid
PFNA	Perfluorononanoic Acid
PFOA	Perfluorooctanoic Acid
PFOS	Perfluorooctanesulfonic Acid
PPARα	Peroxisome Proliferator-Activated Receptor Alpha
PPRTV	Provisional Peer-Reviewed Toxicity Value
RfD	Reference Dose
RSC	Relative Source Contribution
RSL	Regional Screening Level
T4	Thyroxine
TSCA	Toxic Substances Control Act
TSH	Thyroid Stimulating Hormone
UF	Uncertainty Factor

1 Introduction

1.1 Overview of Proposed Amendments

In 2021, the Illinois Environmental Protection Agency (IEPA) proposed amendments to its groundwater quality standards, which include the addition of new standards for several per- and polyfluoroalkyl substances (PFAS) (the Proposed PFAS Standards) and updates to some of its procedures for developing standards, such as the selection of toxicity values (IEPA, 2021). The Proposed PFAS Standards were filed with the Pollution Control Board (the Board) under Docket Number R22-18 and state an intent to uphold the policy of the Illinois Groundwater Protection Act (IGPA) by "keeping groundwater quality standards current as scientific data and methods supporting the development of groundwater quality standards have evolved" (IEPA, 2021, p. 1). However, IEPA's process for developing the Proposed PFAS Standards is problematic. In these comments, I outline the many issues I have identified with the agency's process.

The Proposed PFAS Standards consist of Class I (potable resource) and Class II (general resource) groundwater quality standards for six PFAS: perfluorooctanoic acid (PFOA), perfluorooctanesulfonic acid (PFOS), perfluorohexanesulfonic acid (PFHxS), perfluorononanoic acid (PFNA), perfluorobutanesulfonic acid (PFBS), and hexafluoropropylene oxide dimer acid (HFPO-DA), which is also sometimes referred to as "GenX." IEPA inappropriately derived the proposed groundwater quality standards for these PFAS without independent analysis or reasonable scientific scrutiny of the underlying toxicity data. Instead, IEPA developed its Proposed PFAS Standards in a formulaic manner based on third-party evaluations developed for inapposite situations.

IEPA's process for developing the Proposed PFAS Standards is not scientifically sound and consisted of two simple steps. First, IEPA selected a toxicity value for each of the six PFAS based on a single third-party evaluation for each substance. To do this, IEPA rigidly applied a toxicity value hierarchy framework established by the United States Environmental Protection Agency (US EPA) to guide its work in developing regional screening levels (RSLs) for initial investigations of chemicals at contaminated sites (*i.e.*, the US EPA Screening Level Hierarchy). As I will explain below, there is no sound scientific basis for using the US EPA Screening Level Hierarchy to select a toxicity value for developing enforceable groundwater quality standards. Indeed, none of the US EPA guidance provided within IEPA's Statement of Reasons (IEPA, 2021) suggests that the US EPA Screening Level Hierarchy should be used by states to establish enforceable standards.

The US EPA Screening Level Hierarchy used by IEPA is outlined as follows:

- **Tier 1:** US EPA Integrated Risk Information System (IRIS).
- **Tier 2:** US EPA Provisional Peer-Reviewed Toxicity Values (PPRTVs).
- **Tier 3:** Agency for Toxic Substances and Disease Registry (ATSDR) minimal risk levels (MRLs), the California Environmental Protection Agency's Office of Environmental Health Hazard Assessment (CalOEHHA) toxicity values, PPRTV "Appendix" values, and US EPA Health Effects Assessment Summary Table (HEAST).

IEPA compared the available PFAS toxicity values from third-party evaluations against the US EPA Screening Level Hierarchy to identify the single toxicity value for each PFAS preferred by IEPA. The hierarchy represents a highly limited set of evaluations with potential toxicity values, and does not represent the full extent to which PFAS have been evaluated in the context of risk assessment by other state, federal, and international agencies.

IEPA then used the selected toxicity value for each PFAS to calculate the Proposed PFAS Standards according to specific equations based on either noncancer or cancer effects (IEPA, 2021, Attachment 1G1). Standards based on noncancer effects incorporated a default relative source contribution (RSC) from drinking water (*i.e.*, the percentage of a person's exposure to a particular chemical that comes from drinking water) of 20% for the PFAS noted above (IEPA, 2021), despite available data on PFAS exposure that supports a higher RSC (as explained further below).

The Proposed PFAS Standards and the toxicity values used in their calculation are summarized in Table 1.1 below. The proposed standard for PFOA is based on cancer effects, and the proposed standards for the remaining PFAS are based on noncancer effects. As described further below, IEPA's chosen toxicity values for the Proposed PFAS Standards are problematic because IEPA deviated from standard risk assessment practice, failed to independently evaluate the scientific rigor and appropriateness of the toxicity values, and failed to investigate any criticisms of the underlying studies or the methods for their derivation.

Table 1.1 Proposed Groundwater Quality Standards for Per- and Polyfluoroalkyl Substances

Chemical	Proposed Groundwater Standard (ng/L)	IEPA Toxicity Value		
		Source	Type	Value
PFOA	2	CalOEHHA	CSF	143 per mg/kg-day
PFOS	7.7	ATSDR	MRL	2×10^{-6} mg/kg-day
PFHxS	77	ATSDR	MRL	2×10^{-5} mg/kg-day
PFNA	12	ATSDR	MRL	3×10^{-6} mg/kg-day
PFBS	1,200	PPRTV	RfD	3×10^{-4} mg/kg-day
HFPO-DA	12	US EPA Office of Water	RfD	3×10^{-6} mg/kg-day

Notes:
ATSDR = Agency for Toxic Substances and Disease Registry; CalOEHHA = California Environmental Protection Agency's Office of Environmental Health Hazard Assessment; CSF = Cancer Slope Factor; HFPO-DA = Hexafluoropropylene Oxide Dimer Acid; IEPA = Illinois Environmental Protection Agency; MRL = Minimal Risk Level; PFBS = Perfluorobutanesulfonic Acid; PFHxS = Perfluorohexanesulfonic Acid; PFNA = Perfluorononanoic Acid; PFOA = Perfluorooctanoic Acid; PFOS = Perfluorooctanesulfonic Acid; PPRTV = Provisional Peer-Reviewed Toxicity Values; RfD = Reference Dose; US EPA = United States Environmental Protection Agency.

1.2 Qualifications

I am a board-certified toxicologist with expertise in toxicology, carcinogenesis, and human health risk assessment. I received a B.S. degree in biology from Pacific Lutheran University and a Ph.D. in cell and molecular biology/human genetics from the University of Texas Southwestern Medical Center at Dallas. I was a postdoctoral fellow at the National Cancer Institute, where I managed multiple projects related to breast and prostate carcinogenesis. I was also a staff scientist at Fred Hutchinson Cancer Research Center, where I studied prostate tumor biology and biomarkers. I joined Gradient in 2007, and my work has focused on evaluating human, experimental animal, and *in vitro* toxicology studies for health risk assessments of cancer and noncancer endpoints, with special emphasis on mechanistic and weight-of-evidence evaluations of health risk and causation for chemical exposures. I have been active in the Society of Toxicology since 2008. I have published multiple articles on toxicology, carcinogenicity, and risk assessment in peer-

reviewed journals, books, and meeting proceedings, and I have been a peer reviewer for multiple toxicology journals.

My *curriculum vitae* is attached to these comments as Appendix A.

2 IEPA's Process of Selecting Toxicity Values Is Not Scientifically Appropriate and Results in Proposed Standards That Are Not Scientifically Sound

In developing toxicity values for use in the derivation of regulatory standards, state and federal agencies traditionally follow established human health risk assessment practices. These practices include reviewing all available evidence to assess the weight of the evidence for a substance to cause health effects, evaluating the exposure levels at which those health effects are observed, and choosing the most sensitive adverse health effect (*i.e.*, the adverse health effect observed at the lowest tested exposure level) from reliable studies as a point of departure for deriving the toxicity value.

IEPA failed to follow this standard and universally accepted risk assessment practice in its development of the Proposed PFAS Standards. Instead, IEPA followed its own process of choosing toxicity values by relying on values developed by other agencies to use in its calculations of the Proposed PFAS Standards, using a rigid hierarchy and failing to critically evaluate the toxicity evidence underlying those other agencies' selected toxicity values. This flawed approach resulted in Proposed PFAS Standards that are overly conservative, unreliable, and inappropriate as enforceable groundwater standards.

The toxicity values for six different PFAS were rigidly selected by IEPA according to the US EPA Screening Level Hierarchy, without any independent evaluation of the scientific rigor and appropriateness of the toxicity values and their derivation. The US EPA Screening Level Hierarchy is intended for use in the selection of toxicity values for the derivation of RSLs, which are screening levels for the initial evaluation of a contaminated site that are used to determine which substances detected at the site warrant further investigation (US EPA, 2022). RSLs are not intended to be legally enforceable standards, but instead are guidance values used for screening purposes. The US EPA Screening Level Hierarchy is not intended to be used for choosing a toxicity value upon which to base an enforceable groundwater standard, and it is not appropriate to use it for this purpose without a careful evaluation of the available toxicity values to ensure that standard practices were used in deriving those values and that the values represent appropriate health endpoints. In fact, US EPA specifically states in its RSL "User's Guide" that "[w]hen using toxicity values other than tier 1, users are encouraged to carefully review the basis for the value…" (US EPA, 2022). The toxicity values at issue are not Tier 1 values.

IEPA's process for selecting toxicity values blindly follows what other agencies have done and ignores any issues related to the underlying studies and the methods used to derive the toxicity values (as discussed further in Section 3, below), or the appropriateness of their use in the development of legally binding groundwater standards. In answering questions about the toxicity values from which IEPA chose to derive its proposed groundwater standards, IEPA simply directed the public commenters to the specific agencies that derived the toxicity values (IEPA, 2022a). For example, IEPA stated that concerns brought up by the American Chemistry Council (ACC) regarding ATSDR's interpretation of the data from the study used as the basis for its PFOS MRL (which was chosen as the PFOS toxicity value by IEPA) should be directed to ATSDR (IEPA, 2022a, Agency Answer 7). IEPA should have evaluated this issue to see if it agreed with ATSDR's interpretation of the underlying data, but instead, it chose to ignore the issue altogether. In short, IEPA has assumed no responsibility for ensuring that the toxicity values it chooses are based on sound science and appropriate methodologies, and indeed, IEPA has failed to investigate any criticisms of the various toxicity values it chose.

It is unclear why IEPA believes it cannot deviate from the US EPA Screening Level Hierarchy in selecting toxicity values, as there are no Illinois statutes that require IEPA to adhere to the hierarchy so strictly. In fact, IEPA seemed to concede that it can deviate from the hierarchy when it stated that it prefers toxicity values to be based on the most recent data and effects at the lowest doses (IEPA, 2021, p. 3, 2022b, Agency Answer 5). With regard to recent data, IEPA acknowledges in its Proposed PFAS Standards that it is necessary to account for new scientific data (IEPA, 2021, p. 3). IEPA (2022a,b) stated that it chose the ATSDR MRL for PFOS because ATSDR relies on more recent toxicity studies than the US EPA Office of Water's evaluation and derivation of a PFOS toxicity value in 2016 (US EPA, 2016). Just because a study is published more recently, however, does not necessarily mean it is more scientifically sound or a better choice for an endpoint on which to derive a toxicity value for use in developing a regulatory standard. In addition, the interpretation of the study data must be scientifically sound, regardless of when the study was published. For example, ATSDR's interpretation of the underlying study used for its PFOS MRL results in a toxicity value that is overly conservative; ATSDR chose a nonadverse effect as the critical effect for the MRL, as described further in Section 3.2, below.

IEPA failed to critically evaluate the options within the US EPA Screening Level Hierarchy to determine whether there could be more appropriate toxicity values for a specific substance lower in the hierarchy. US EPA (2022) recently updated its Screening Level Hierarchy to include US EPA Office of Water toxicity values, and these values come immediately after the ATSDR MRLs and before the CalOEHHA toxicity values in Tier 3 of the updated hierarchy for RSLs (US EPA, 2022). By choosing an ATSDR MRL solely because it is one or two places higher in the hierarchy than other available toxicity values, without evaluating the science behind it and comparing it to other toxicity values, IEPA has not undertaken the scientific diligence required to select the most appropriate value. In addition, ATSDR's MRLs for PFAS are limited because, in deriving them, ATSDR only considered studies with animal strains that had pharmacokinetic model parameters available for predicting serum concentrations of PFAS in the animals from the administered PFAS doses (ATSDR, 2021), which precluded the use of many studies of various endpoints. For example, ATSDR reviewed, but did not consider, several studies of immunological, neurological, and developmental effects in mice and a study of neurodevelopmental effects in rats as a potential basis for its MRL for PFOS because of the lack of pharmacokinetic model parameters for the specific rodent strains used in those studies (ATSDR, 2021). IEPA did not take this limitation of the ATSDR MRLs into account when using the US EPA Screening Level Hierarchy to choose which toxicity values to use.

IEPA's calculations for PFAS groundwater standards based on noncancer effects incorporate a default RSC of 20%, as IEPA (2021) stated that the data on PFAS exposure are insufficient to deviate from this default value. The default 20% RSC value is not scientifically supported, however, and is more stringent than necessary. The default RSC of 20% is the most conservative RSC value used by regulatory agencies, but a higher (and less stringent) RSC value can be determined if information regarding exposure to the specific chemical of interest is known. The methodology for this is described by US EPA (2000) in its "Exposure Decision Tree" for selecting an RSC. Several other states have used this methodology, combined with publicly available data on background concentrations of PFAS in the serum of the general US population, to estimate higher RSC values for several PFAS. For example, the Michigan Department of Health and Human Services (MDHHS, 2019) assumed an RSC value of 50% for PFOA, PFOS, PFHxS, and PFNA in its derivation of public health drinking water screening levels for these PFAS, and the Minnesota Department of Health (MDH) also assumed an RSC value of 50% for deriving its health-based guidance for drinking water for PFOA (MDH, 2018), PFOS (MDH, 2019a), and PFHxS (MDH, 2019b).

Finally, IEPA's process for choosing toxicity values and developing groundwater standards has resulted in Proposed PFAS Standards that are so low that it is unlikely that some of them could be reliably measured, as they are below or almost identical to the method detection limits. For example, IEPA refers to US EPA

SW-846 Method 8327 as a validated test method for PFAS in groundwater (IEPA, 2022b, Agency Answer 2). The lower limits of quantification (LLOQs)[1] for PFOA, PFOS, PFBS, and PFNA for this method are 10 ng/L, and the LLOQ for PFHxS for this method is 40 ng/L (US EPA, 2019); concentrations of these PFAS lower than their corresponding LLOQs cannot be reliably measured by this method. However, IEPA's Proposed PFAS Standards for PFOA and PFOS (2 and 7.7 ng/L, respectively) are below their LLOQ, and the Proposed PFAS Standard for PFNA (12 ng/L) is almost identical to its LLOQ. Unreliable measurements of PFAS concentrations in groundwater samples cannot be used with any certainty to evaluate compliance with health-based groundwater standards. In fact, US EPA SW-846 Method 832 specifically advises that "optimally, the LLOQ should be less than the desired decision level or regulatory action level" for the intended application and the data quality objectives established for the method (US EPA, 2019).

[1] The LLOQ is defined as "the lowest concentration at which the laboratory has demonstrated target analytes can be reliably measured and reported with a certain degree of confidence" (US EPA, 2019).

3 There Are Multiple Issues with the Toxicity Values Selected by IEPA for the Proposed PFAS Standards

3.1 The PFOA Toxicity Value Is Inappropriately Based on Cancer Effects

The toxicity value for PFOA selected by IEPA (2021) is not an appropriate basis for a PFOA groundwater standard. This toxicity value is based on the incorrect assumption that PFOA is mutagenic, when PFOA is neither mutagenic nor genotoxic. It is also based on studies of tumor production in animals *via* a mechanism of action with limited or no relevance to humans. IEPA's assumption of PFOA's carcinogenicity in animals is based on weak and insufficient evidence of malignant tumors. Furthermore, the evidence in human studies does not support a conclusion that PFOA is carcinogenic to humans. Finally, other agencies have not classified PFOA as a known human carcinogen.

In its Proposed PFAS Standards, IEPA (2021) stated that PFOA meets the definition of a carcinogen, based on the International Agency for Research on Cancer (IARC) classification of PFOA as "possibly carcinogenic to humans." IEPA based its proposed groundwater standard for PFOA on an oral cancer slope factor of 143 per mg/kg-day, derived by CalOEHHA (2019) in its "Notification Level Recommendations" for PFOA and PFOS in drinking water. This value is based on the observation of hepatocellular adenomas/carcinomas and pancreatic acinar cell adenomas/carcinomas (mostly adenomas) in male rats in a study conducted by the National Toxicology Program (NTP, 2020). The tumors occurred in rats that received PFOA doses of 2.2 and 4.6 mg/kg-day in the diet. NTP (2020) concluded that there was "clear evidence of carcinogenic activity of PFOA in male Sprague Dawley rats…."

CalOEHHA (2019) derived its cancer slope factor using a linear multistage dose-response model. The use of a linear dose-response model and the derivation of a cancer slope factor are appropriate only for chemicals or substances that act as carcinogens *via* a mutagenic mode of action (US EPA, 2005), meaning that CalOEHHA's use of this model necessarily assumes that PFOA is a mutagen. However, it is well-documented in the literature that PFOA is not genotoxic or mutagenic (Crebelli *et al*., 2019; Kennedy and Symons, 2015; EFSA CONTAM, 2018; ATSDR, 2021). The derivation of a cancer slope factor with a linear dose-response model is therefore not appropriate for PFOA. IEPA failed to consider this in choosing its toxicity value for PFOA.

The scientific literature indicates that hepatocellular and pancreatic acinar tumors purportedly associated with PFOA in rats are likely mediated by modes of action that are not relevant to humans. The liver tumor response in rats is likely mediated by peroxisome proliferator-activated receptor alpha (PPARα) receptors (Corton *et al*., 2018; Kennedy and Symons, 2015; Biegel *et al*., 2001), the activity of which was elevated in the rats in the underlying NTP (2020) study. PPARα receptor-mediated processes occur much more readily in rats than in humans (Klaunig *et al*., 2003, 2012); therefore, a mode of action for PFOA involving PPARα is likely not relevant to humans (Corton *et al*., 2018). Similarly, pancreatic tumors in rodents may occur by a mode of action that is mediated by downstream events following activation of PPARα receptors, and thus not relevant to humans, and/or by a process involving sustained increases in cholecystokinin (CCK), a mode of action that is also not relevant to humans (Klaunig *et al*., 2012). In the very same ATSDR toxicological profile for PFOA that IEPA relied on for a toxicity value for a noncancer groundwater

standard for PFOA,[2] ATSDR (2021) agreed that liver effects in animals cannot reliably be extrapolated to humans. Yet, IEPA (2022a) disregarded ATSDR's finding and stated that liver effects caused by PFOA can occur through other mechanisms besides PPARα, and that the relevance to humans should not be dismissed. These statements were excerpted directly from CalOEHHA (2019), however, and IEPA did not independently evaluate the evidence and reach its own conclusions regarding the potential human relevance of a PPARα mode of action for liver tumors in rats. In fact, CalOEHHA (2019) did not present any evidence that liver tumors could arise from PFOA treatment in the absence of PPARα.

A groundwater standard for PFOA based on cancer effects is not appropriate, because neither animal nor human data support the conclusion that PFOA is a human carcinogen. Several agencies have guidelines that require findings of an increased incidence of malignant tumors or a combination of malignant and benign tumors in animal studies before they are able to conclude that there is sufficient evidence of a chemicals' carcinogenicity (see for example, US EPA [2003], NTP [2015], and IARC [2016a]). Apart from the NTP (2020) study, rat carcinogenicity studies of PFOA have reported increases only in benign tumors, and no tumors have been reported in mouse carcinogenicity studies of PFOA (Butenhoff *et al*., 2012; Biegel *et al*., 2001). Furthermore, the NTP (2020) study upon which CalOEHHA based its cancer slope factor reported small increases in malignant carcinomas that were not dose-dependent or statistically significant, and this does not meet NTP's or other agencies' guidelines for sufficient evidence of carcinogenicity. Overall, the findings in animal studies do not provide sufficient evidence of PFOA's carcinogenicity.

Human data also do not support the conclusion that PFOA is a human carcinogen (see, for example, Raleigh *et al*. [2014], Steenland *et al*. [2015], and Steenland and Winquist [2021). Because both animal and human data do not support PFOA being a human carcinogen, a groundwater standard for PFOA based on cancer effects is not appropriate.

In defining PFOA as a carcinogen, IEPA failed to consider that other agencies, such as IARC and NTP, have not classified PFOA as a *known* human carcinogen. For example, NTP (2021) does not include PFOA on its list of substances that are known or reasonably anticipated to cause cancer in humans. In addition, as noted above, IARC (2016b) only classified PFOA as a "possible" human carcinogen, stating that the evidence in humans and experimental animals supporting carcinogenicity was only "limited," and that it could not rule out chance, bias, or confounding in human studies with reasonable confidence. There is simply no certainty as to whether a causal relationship exists between PFOA and cancer in humans. This uncertainty is underscored by the fact that the rat tumor findings used by CalOEHHA to derive a cancer slope factor have not been replicated in other rodent studies (as noted above) and that PFOA likely exerts its effects *via* the activation of PPARα (a mode of action for tumor development that is likely not relevant to humans). Overall, IEPA did not independently evaluate the evidence for the potential human carcinogenicity of PFOA and did not consider these important uncertainties.

3.2 The PFOS Toxicity Value Is Based on Nonadverse Effects and Is Overly Conservative

IEPA's (2021) chosen toxicity value for PFOS is overly conservative. It is based on effects that are not adverse (*i.e*., they do not represent toxicity), ignores the conclusions of the authors of the study upon which it is based, includes an unnecessary modifying factor, and was derived using a half-life for PFOS that is not well supported.

[2] IEPA ultimately chose a standard based on cancer effects because it was more stringent.

In its Proposed PFAS Standards, IEPA (2021) based its groundwater standard for PFOS on the ATSDR (2021) intermediate MRL for PFOS of 0.000002 mg/kg-day. This value is based on a study by Luebker *et al*. (2005) that reported delayed eye opening and transient decreased body weight in rat pups that were exposed to PFOS at 0.4 mg/kg-day. ATSDR considered 0.4 mg/kg-day to be the lowest observed adverse effect level (LOAEL) and 0.1 mg/kg-day to be the no observed adverse effect level (NOAEL) in this study. In contrast, Luebker *et al*. (2005) considered 0.4 mg/kg-day to be the NOAEL, based on reduced pup survival and reduced weight gain observed at a dose of 1.6 mg/kg-day. The study's authors did not consider the slight delay in eye opening to be an adverse outcome and did not consider the transient decrease in body weight to be toxicologically significant. Thus, IEPA based its groundwater standard for PFOS on a toxicity value that ignores the conclusions of the authors of the underlying study and is based on nonadverse effects, which goes against established practice for developing toxicity factors for use in determining regulatory standards (see, for example, US EPA [1989]).

IEPA's reliance on ATSDR's PFOS MRL also is misplaced, because ATSDR used an unnecessary extra modifying factor of 10 to reduce the MRL 10-fold based on the concern that immunotoxicity may be a more sensitive endpoint than developmental toxicity. This modifying factor is inappropriate and results in an overly conservative MRL, as the occurrence of immunological effects at such low doses of PFOS is not supported by the science. For example, ATSDR (2021) cited a study by Peden-Adams *et al*. (2008) as evidence for immunological effects occurring at low doses of PFOS. However, the findings from this study have not been replicated in other studies (see, for example, Qazi *et al*. [2010]), and a dose-response relationship was not observed for the most sensitive endpoint cited by ATSDR (2021).

Furthermore, in deriving its MRL, ATSDR (2021) chose a half-life for PFOS of 5.4 years, which is not supported by the science. This half-life is based on an occupational study of fluorochemical workers by Olsen *et al*. (2007). However, two other studies that were based on community populations, which are more relevant to the general population (*i.e*., the population that the Proposed PFAS Standards are intended to protect), derived shorter half-lives of 3.4 years (Li *et al*., 2018) and 3.3 years (Worley *et al*., 2017) for PFOS. Had ATSDR chosen one of these half-lives to incorporate into its derivation of a PFOS MRL, the MRL would have been higher.

IEPA failed to evaluate whether it was appropriate for ATSDR to ignore the conclusions of Luebker *et al*. (2005) regarding the choice of a NOAEL, and did not consider ATSDR's inclusion of an extra modifying factor without scientific support for immunological effects occurring at low PFOS doses and selection of a high PFOS half-life that is unsupported by the prevailing science, all of which resulted in a MRL that is overly conservative.

3.3 The PFHxS Toxicity Value Is Based on Effects with Uncertain Clinical Significance That Were Not Observed in Other Studies

The toxicity value for PFHxS selected by IEPA (2021) is not appropriate, as it is based on effects with unclear clinical significance that were not observed in other studies, and was derived using a half-life for PFHxS that is not scientifically supported.

In its Proposed PFAS Standards, IEPA (2021) based its groundwater standard for PFHxS on the ATSDR (2021) intermediate MRL for PFHxS of 0.00002 mg/kg-day without considering other prevailing studies of PFHxS toxicity. ATSDR based this MRL on a study by Butenhoff *et al*. (2009) that reported thyroid follicular cell hyperplasia in adult male rats after exposure to PFHxS at 3 mg/kg-day. Butenhoff *et al*. (2009) noted that this effect was consistent with an increase in liver hypertrophy and induction of liver enzymes (observed in this study) that in turn induce the metabolism of thyroid hormones. The authors did not measure thyroid hormones in this study, however, so the clinical significance of the thyroid cell

hyperplasia is unknown. ATSDR (2021) concluded that the liver effects observed in the only other candidate study it selected for deriving an MRL for PFHxS (a mouse study reporting liver effects) were *not* considered to be adverse. Moreover, another study (Chang *et al*., 2018) did not find any changes in either thyroid stimulating hormone (TSH) levels in response to PFHxS exposure or thyroid histopathology at doses up to 3 mg/kg-day. The Chang *et al*. (2018) study is a more appropriate principal study from which to derive a PFHxS toxicity value, but IEPA did not consider this study or any other studies of PFHxS toxicity and instead chose the ATSDR MRL without conducting its own evaluation.

In its derivation of the PFHxS MRL, ATSDR (2021) chose an overly conservative half-life for PFHxS of 8.5 years, based on a study of retired fluorochemical workers by Olsen *et al*. (2007). In contrast, another study reported a PFHxS half-life of 5.3 years in an exposed community (Li *et al*., 2018). Because the community population in this study is more relevant to the general population (*i.e*., the population that the Proposed PFAS Standards are intended to protect), the half-life of 5.3 years derived in this study is more relevant to the general population as well. Had ATSDR chosen this half-life to incorporate into its derivation of a PFHxS MRL, the MRL would have been higher. IEPA did not consider the appropriateness of the half-life that ATSDR (2021) chose in deriving the MRL for PFHxS.

3.4 The PFNA Toxicity Value Is Based on an Effect with Limited or No Relevance to Humans

IEPA's (2021) reliance on the ATSDR (2021) intermediate MRL for PFNA of 0.00002 mg/kg-day is overly conservative, because the study underlying the MRL has little relevance to humans. The ATSDR MRL is based on a study by Das *et al*. (2015) that reported decreased body weight and developmental delays in mouse pups exposed to PFNA at 3 mg/kg-day.

PFNA activates PPARα (Wolf *et al*., 2008; Vanden Heuvel *et al*., 2006) and induces PPARα-dependent gene expression (Rosen *et al*., 2017). There is direct evidence that PPARα mediates many of the reported effects of PFNA in experimental animals, including developmental effects (Rosen *et al*., 2017; Wolf *et al*., 2010). Delayed eye opening and reduced pup body weight in PFNA-exposed mice have been shown to be dependent on PPARα activity (Wolf *et al*., 2010), which calls into question the relevance of these endpoints to humans. As noted above, PPARα-mediated events are less relevant to humans than to rodents, and therefore, the uncertainty factor (UF) of 3 for interspecies differences that ATSDR (2021) included in its derivation of an MRL for PFNA, which decreased the MRL value by 3-fold, is overly conservative. An interspecies UF is generally applied when a toxicity value is based on an animal experiment, as an added protection in case humans are more sensitive than the test animals to the adverse effect. Because PPARα-mediated processes are less active in humans than in mice, it is likely that humans are *less* sensitive than mice to the effects of PFNA, making the interspecies UF unnecessary. Thus, the MRL could be higher and still be protective of human health. IEPA did not consider these issues and did not independently evaluate whether ATSDR's derivation of the MRL for PFNA was appropriate.

3.5 The PFBS Toxicity Value Is Based on an Effect of Uncertain Adversity and Human Relevance

IEPA's (2021) reliance on the PPRTV/reference dose (RfD) of 0.0003 mg/kg-day for chronic exposure to PFBS derived by US EPA (2021a) is misplaced, because US EPA's RfD for PFBS is based on an effect with uncertain adversity and human relevance. The RfD is based on decreased serum thyroid hormone (thyroxine [T4]) levels in mouse pups exposed to PFBS at doses above 50 mg/kg-day in a study by Feng *et al*. (2017).

However, observations in the study by Feng *et al*. (2017) indicate that the decrease in serum T4 levels after PFBS exposure was not a specific developmental effect, and there is uncertainty as to whether the decrease in T4 levels was a toxicologically relevant, adverse effect in this study. For example, there was no increasing dose-response for the T4 effects or other reported effects (Feng *et al*., 2017). In addition, Feng *et al*. (2017) did not compare the T4 values to the range of normal values, did not indicate if the T4 values were low enough to constitute hypothyroidism, and did not indicate whether there were any changes in thyroid histology.

Furthermore, US EPA's (2021a) choice of thyroid hormone changes in mice as a critical effect is overly conservative, because rodents are highly susceptible to thyroid hormone perturbations when compared to humans (NRC, 2005; Bartsch *et al*., 2018; Parker and York, 2014; Brown-Grant, 1963), due to their smaller reserve capacity of thyroid hormones (NRC, 2005; Lewandowski *et al*., 2004; Hayes, 2014). This suggests that the UF of 3 for interspecies differences that US EPA (2021a) included in its derivation of the RfD for PFBS is unnecessary, and that the RfD could be higher and still protective of human health.

The US EPA's RfD for PFBS is clearly based on uncertain science, but IEPA did not consider these issues in selecting a toxicity value for PFBS.

3.6 The HFPO-DA Toxicity Value Is Based on Uncertain Science

IEPA's selection of US EPA's chronic RfD for HFPO-DA of 0.000003 mg/kg-day (US EPA, 2021b) as the toxicity value for deriving the proposed groundwater standard for HFPO-DA is inappropriate, as there is much uncertainty in the underlying science associated with this RfD, and IEPA did not evaluate the scientific appropriateness of this toxicity value.

US EPA's RfD for HFPO-DA is based on an unpublished reproductive and developmental study in mice that was submitted to US EPA by DuPont under a Toxic Substances Control Act (TSCA) Consent Order. US EPA (2021b) stated that the study had a NOAEL of 0.1 mg/kg-day and a LOAEL of 0.5 mg/kg-day, based on single-cell necrosis in the livers of male mice. However, the critical effect chosen for derivation of the RfD was actually a "constellation of liver lesions" (US EPA, 2021b), rather than a single liver effect, in both male and female mice. These different effects were not consistently observed for each animal evaluated, but US EPA (2021b) determined that taken together, they constituted a critical effect. In addition, there is uncertainty as to the adversity of some of these effects. Some of the observed liver effects, such as single-cell and focal necrosis, are adverse, but other effects are either adaptive changes (*i.e*., hepatocellular hypertrophy, or enlargement of liver cells) or of unclear adversity (alterations in the cytoplasm of liver cells). It is only when the incidence of all of these effects were combined together that the 0.5 mg/kg-day dose group showed a clear increase in incidence compared to the unexposed control group.

The pathological slides from the critical study were re-evaluated by other investigators, using more current diagnostic criteria (Thompson *et al*., 2019). Thompson *et al*. (2019) determined that the liver effect observed in mice that was described as single-cell necrosis in the original study was actually apoptosis (an effect not considered to be adverse), and this effect was likely mediated by PPARα, a pathway of limited relevance in humans (Klaunig *et al*., 2012). In response to this re-evaluation, US EPA requested another re-evaluation of the liver slides from an NTP Pathology Working Group, which generally supported the original study findings of single-cell necrosis but also observed liver cell apoptosis in some animals (US EPA, 2021b). The Pathology Working Group concluded that the constellation of liver lesions, rather than one lesion by itself, represents an adverse effect, and US EPA (2021b) stated that the re-evaluation confirms that the NOAEL for this constellation of lesions was 0.1 mg/kg-day. US EPA (2021b) accepted the

Pathology Working Group's conclusion and set the HFPO-DA RfD based on US EPA's summation of the individual lesion incidence data reported by the Pathology Working Group for each animal in the study.

Several other mouse and rat studies did not observe the same constellation of effects in the liver at such a low dose. For example, in another unpublished study by DuPont in which mice were exposed to HFPO-DA for 90 days at the same doses as in the reproductive and developmental study, the NOAEL for liver effects was 0.5 mg/kg-day, rather than 0.1 mg/kg-day (US EPA, 2021b). In addition, there was no observed dose-response for these liver effects in the female mice (US EPA, 2021b). Similarly, an unpublished chronic rat study of HFPO-DA by DuPont did not report liver effects at comparable doses to those used in the mouse reproductive and developmental study used as the basis for the HFPO-DA RfD. The differences among studies in NOAELs and dose-response, the choice of a "constellation" of effects rather than one critical effect, and the possible involvement of PPARα in mediating those effects all represent uncertainties in US EPA's derivation of an RfD for HFPO-DA. These uncertainties were not taken into consideration by IEPA in its decision to select US EPA's RfD as its toxicity value for HFPO-DA.

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Appendix A

***Curriculum Vitae* of Robyn Prueitt, Ph.D., DABT**

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Principal Scientist

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Areas of Expertise

Toxicology, carcinogenesis, human genetics, toxicogenomics, molecular biology, molecular epidemiology, weight-of-evidence analysis, mode-of-action analysis, systematic review, human health risk assessment, risk communication.

Education and Certifications

Ph.D., Cell and Molecular Biology/Human Genetics, University of Texas Southwestern Medical Center at Dallas, 2001

B.S., Biology, Pacific Lutheran University, 1994

Diplomate of the American Board of Toxicology (DABT), 2013; recertified 2018

Professional Experience

2007 – Present GRADIENT, Seattle, WA
Provides toxicology and related expertise in support of human health risk assessment, regulatory comment, and toxic tort litigation. Reviews and evaluates toxicology and health-related data.

2006 – 2007 FRED HUTCHINSON CANCER RESEARCH CENTER, Seattle, WA
Staff Scientist. Managed studies of prostate cancer biomarker detection and glycoprotein mass spectrometry analysis. Designed and managed multiple large-scale prostate tumor xenograft studies.

2001 – 2006 NATIONAL CANCER INSTITUTE, Bethesda, MD
Post-doctoral Research Fellow. Investigated genetic susceptibility of cancer risk through molecular epidemiology studies. Managed multiple studies related to breast and prostate carcinogenesis. Performed genome-wide expression analysis of genes and microRNAs associated with prostate carcinogenesis. Developed animal models of leukemias associated with chromosome translocations.

Professional Activities

- Mentor: Society of Toxicology Mentor Match Program, 2015.
- Peer Reviewer: Toxicological Profile for Toluene Diisocyanates and Methylenediphenyl Diisocyanates, Agency for Toxic Substances and Disease Registry Draft Document, 2014.
- Reviewer: *Archives of Oral Biology; Biomedicine Hub; Biomedicines; Cancers; Critical Reviews in Toxicology; Dose-Response; Ecotoxicology and Environmental Safety; Environmental Pollution; Environmental Research; Human and Experimental Toxicology; Inhalation Toxicology; International Journal of Hygiene and Environmental Health; Science of the Total Environment; Toxicology; Toxicology and Applied Pharmacology*; *Toxicology In Vitro; Toxicology and Industrial Health; Toxics.*

Professional Affiliations

Society of Toxicology; Pacific Northwest Association of Toxicologists

Continuing Education Courses and Other Training

- An Introduction to New Approach Methodologies (NAMs) and Understanding Their Potential to Support Regulatory Decisions, Society of Toxicology 58th Annual Meeting, Virtual Course, 2020.
- Uncertainty Characterization in 21st Century Toxicology: Current Practice and Practical Methods Supporting Regulatory Risk Assessment, Society of Toxicology 57th Annual Meeting, San Antonio, TX, 2018.
- Current Principles for Nonclinical Chronic Toxicity/Carcinogenicity Testing of Environmental Chemicals, Society of Toxicology 56th Annual Meeting, Baltimore, MD, 2017.
- Genetics and Population Variability in Chemical Toxicity: The What, the How, and So What? Society of Toxicology 55th Annual Meeting, New Orleans, LA, 2016.
- Toxicogenomics Meets Regulatory Decision-Making: How to Get Past Heat Maps, Network/Pathway Diagrams, and "Favorite" Genes, Society of Toxicology 54th Annual Meeting, San Diego, CA, 2015.
- Effective Risk Communication: Theory, Tools, and Practical Skills for Communicating About Risk, Harvard School of Public Health, Boston, MA, 2014.
- Methodologies in Human Health Risk Assessment, Society of Toxicology 53rd Annual Meeting, Phoenix, AZ, 2014.
- Mid-America Toxicology Course, Kansas City, MO, 2013.
- Epidemiology for Toxicologists, Society of Toxicology 47th Annual Meeting, Seattle, WA, 2008.
- Public Health Toxicology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, 2007.
- Principles of Clinical Pharmacology, National Institutes of Health, Bethesda, MD, 2004-2005.

Honors and Awards

- Best Overall Abstract, Risk Assessment Specialty Section, Society of Toxicology, 2013.
- Top Ten Best Published Papers of 2012, Risk Assessment Specialty Section, Society of Toxicology, for the article "Hypothesis-Based Weight-of-Evidence Evaluation of Methanol as a Human Carcinogen."
- NIH/NHGRI Institutional Training Grant Award in Genomic Science, 1997-2001.

Selected Projects

Confidential Client: Assessed the toxicological significance and human health risks of exposure to per- and polyfluoroalkyl substances (PFAS) in drinking water and ambient air. Reviewed the literature regarding animal toxicology, human health effects, and chemical and environmental characteristics of PFAS, as well as the historical state of knowledge of these topics.

Industrial Client: Evaluated the potential for cancer and noncancer health effects from exposures to ethylene oxide in ambient air for individuals living near an industrial facility that used ethylene oxide.

Health Care Company: Evaluated the potential cytotoxicity of a medical device by critically reviewing the experimental data and human clinical studies for the device and its components.

Law Firm: Evaluated potential associations between exposures to formaldehyde and methylenediphenyl diisocyanate emissions from application of spray foam insulation and respiratory health effects and multiple chemical sensitivity.

Manufacturing Companies: Reviewed the state of knowledge regarding asbestos exposures and health effects from the manufacture, installation, and repair of automotive friction products.

Manufacturing Company: Evaluated potential cancer risks from exposures to dioxins in ambient air for individuals residing near a copper recycling facility.

Industrial Client: Assessed toxicity and risks of methyl tert-butyl ether (MTBE) from tap water exposure, including evaluation of whether its metabolite, formaldehyde, can cause leukemia or other cancers by inhalation or oral exposure.

Waste Management Company: Evaluated exposures to hydrogen sulfide, dimethyl sulfide, and methyl mercaptan and potential health effects from these exposures in individuals residing near a municipal solid waste landfill. Evaluated potential odor impacts and the differences between odor perception and adverse health effects.

Railroad Company: Critically reviewed global gene expression profiling data for a population exposed to benzene and determined whether the expression profile could be used as a biomarker of benzene toxicity in a broader population, particularly without proof of benzene exposure from a specific source.

Energy Company: Evaluated potential toxicity and odor impacts of mercaptan compounds by comparing odor thresholds to health-based exposure limits.

Public Transportation Agency: Evaluated the potential for respiratory health effects from occupational use of a cleaning solution containing sulfuric and phosphoric acid.

Trade Organization: Summarized the literature regarding the potential reproductive, neurological, immunological, and carcinogenic effects of bisphenol A.

Health Care Company: Evaluated claims of associations between metals and fragrances in talc products and ovarian cancer, considering toxicological principles and best practices for evaluating causation.

Manufacturing Company: Evaluated the epidemiology and toxicology literature and conducted an exposure and risk assessment for cancer and non-cancer health effects of benzene, dioxin, and pentachlorophenol. Conducted a cluster analysis to determine whether individuals residing in an area with alleged exposures had increased rates of several cancers and non-cancer health effects.

Industrial Client: Evaluated the scientific basis for class certification in the context of property damage and medical monitoring for residents near a former zinc smelter site.

Industrial Client: Conducted weight-of-evidence evaluations of the potential carcinogenicity of inhalation exposure to trichloroethylene.

Law Firm: Developed a presentation on toxicology principles as part of a communication effort, using formaldehyde as an example chemical.

Trade Organization: Evaluated the basis for the American Conference of Governmental Industrial Hygienists (ACGIH) lowering the Threshold Limit Value for toluene diisocyanate.

Transportation Company: Evaluated whether occupational exposure to toluene diisocyanate *via* inhalation and dermal contact is a causal factor in acute myeloid leukemia.

Confidential Client: Compiled and reviewed studies regarding chemical-induced chromosome abnormalities to assess their potential association with acute myeloid leukemia.

Trade Organization: Critically reviewed the methodology and underlying toxicity data used as a basis for non-health-based occupational exposure limits (OELs) for bisphenol A and di- and triisocyanates and recommended health-based OELs in written comments to a European health agency.

Trade Association: Critiqued draft templates for tabulating epidemiology and experimental animal study data for hazard identification proposed by the Developmental and Reproductive Toxicant Identification Committee (DARTIC) of California's Office of Environmental Health Hazard Assessment (CalOEHHA). Proposed an alternative set of tables to systematically present data for consideration in a full evidence integration process.

Industrial Client: Evaluated the state of the science as to the ability of asbestos in electrical products to cause mesothelioma and lung cancer.

Confidential Client: Conducted an analysis to evaluate the potential causality of various health symptoms from exposures to metals and odorous chemicals, including hydrogen sulfide, benzene, methane, and tert-butyl mercaptan.

Trade Organization: Evaluated best practices for evidence integration in National Ambient Air Quality Standards (NAAQS) Integrated Science Assessments (ISAs).

Trade Organization: Assessed whether a post-market skin patch epidemiology study should be used for risk assessment.

Trade Organization: Evaluated whether nickel should be classified as a reproductive or developmental toxicant under California EPA's Proposition 65.

Pharmaceutical Company: Evaluated the potential side effects and dose-response relationships for cosmetic botulinum toxin injections from reviews of clinical trials and FDA warning labels. Assessed whether claimed health effects in an individual were indicative of systemic toxicity.

State Environmental Agency: Conducted weight-of-evidence evaluations of the association between short-term and long-term ozone exposure and cardiovascular effects.

State Environmental Agency: Reviewed epidemiology, controlled human exposure, experimental animal, and mechanistic studies of ozone and markers of inflammation and oxidative stress.

Industrial Client: Evaluated the potential lung cancer risk from exposure to asbestos during vehicle brake repair and considered the association between cigarette smoking and lung cancer in comparison to that expected from asbestos exposure.

Trade Organization: Evaluated whether the weight of the evidence from epidemiology, controlled human exposure, and experimental animal studies supports ozone exposure as a causal factor in cardiovascular disease morbidity and mortality. This analysis used a causal framework developed at Gradient and was published in a peer reviewed journal.

Insurance Company: Evaluated whether exposure to asbestos can exacerbate chronic obstructive pulmonary disease (COPD) and examined the literature on the effects of smoking on COPD and its potential interaction with asbestos exposure.

Industrial Client: Reviewed the scientific literature spanning several decades to assess the state of knowledge regarding toxicity and exposure of asbestos in various industries, including knowledge of asbestos hazards on merchant ships.

Trade Organization: Conducted a critical review of the potential association between talc exposure and ovarian cancer.

Trade Organization: Reviewed and commented on the International Agency for Research on Cancer (IARC) Preamble, which summarizes the underlying scientific principles of the IARC Monographs, which evaluate the carcinogenic hazards of chemicals and other substances.

Chemical Company: Evaluated whether neural reflex activation is a plausible mode of action for respiratory toxicity caused by ozone exposure.

Trade Association: Evaluated whether atherosclerosis development is a plausible mode of action for particulate matter-induced cardiovascular disease and whether this is supported by epidemiology evidence.

Trade Organization: Conducted a survey of nearly 50 weight-of-evidence frameworks to evaluate best practices for determining causation. Defined the key concepts of weight-of-evidence analyses and their application to particular problems, and articulated the best practices from among the spectrum of approaches.

Trade Organization: Evaluated whether the weight of epidemiology, animal toxicity, mechanistic, and pharmacokinetic evidence indicates that toluene diisocyanate is a human carcinogen. This analysis used Gradient's hypothesis-based weight-of-evidence approach and was published in a peer-reviewed journal.

Chemical Company: Assessed the potential toxicological and ecological effects of bisphenol A using a modification of the Green Screen method that was designed to advance the development of green chemistry. Modified the method to be risk-based, rather than hazard-based, by considering exposure information. For many endpoints, a weight-of-evidence approach was taken to integrate all the available data and to resolve conflicting information.

Trade Organization: Evaluated whether the weight of the evidence supports the plausibility of methanol as a causal factor in human lymphoma. This analysis used Gradient's hypothesis-based weight-of-evidence approach and was published in a peer-reviewed journal.

Trade Organization: Evaluated epidemiology and animal toxicity studies of styrene and their bearing on a weight-of-evidence analysis of whether styrene should be considered a human carcinogen. This work was submitted as written and oral testimony to the US National Toxicology Program and its Board of Scientific Councilors.

Trade Organization: Conducted a quantitative analysis of controlled human exposure studies to address whether there is a subset of individuals who are susceptible to health effects of ozone at particular exposure levels but whose response is obscured by analyzing data at the group level.

Chemical Company: Used Gradient's hypothesis-based weight-of-evidence approach to assess whether the epidemiology, toxicology, and mechanistic evidence supports chlorpyrifos being a neurobehavioral toxicant in humans at relatively low exposure levels.

Trade Organization: Conducted a weight-of-evidence review of epidemiology studies examining exposures to dioxins and dioxin-like compounds and thyroid hormone levels during early development.

Trade Organization: Assessed whether animal, mechanistic, and epidemiological data are consistent with the nickel ion bioavailability model, which asserts that the carcinogenicity of nickel-containing substances is based on the bioavailability of the nickel ion at nuclear sites of target respiratory epithelial cells.

Trade Organization: Classified, summarized, and entered relevant studies of lead into IUCLID (International Uniform Chemical Information Database) 5.2, a database for the intrinsic and hazard properties of chemical substances that companies can use to submit data under the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) legislation in Europe.

Trade Organization: Provided written and oral comments on several occasions to US EPA on clinical and epidemiology studies and their bearing on US EPA's National Ambient Air Quality Standards (NAAQS) for ozone.

Trade Organization: Conducted a critical review and a weight-of-evidence assessment of causality based on animal carcinogenicity studies, mode-of-action studies, and occupational epidemiological studies of soluble nickel compounds and respiratory cancer risk.

Law Firm: Critically reviewed potential health effects associated with exposure to heating oil from a basement spill.

Trade Organization: Classified, summarized, and entered all relevant studies of bisphenol A into the toxicity section of IUCLID (International Uniform Chemical Information Database) 5, an electronic repository for the intrinsic and hazard properties of chemical substances that companies can use to submit data under the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) legislation in Europe.

Consumer Product Company: Examined the underlying biological mechanisms for ionizing radiation-induced cancers, including those involving radiation in cigarettes.

Chemical Manufacturing Plant: Evaluated the toxicology and epidemiology literature regarding mercury and determined whether levels in residential soil were above background and likely attributable to a nearby manufacturing plant.

Industrial Client: Provided litigation support regarding health effects associated with lead for a case involving exposures in the vicinity of a smelter facility.

Industrial Client: Provided technical support in the evaluation of cost allocation issues at an industrial site. Reviewed information regarding the nature and extent of contamination within the site and assessed factors that could be evaluated to apportion costs among potentially responsible parties.

Industrial Company: Summarized literature on toxicity studies of perfluorinated alkane acids.

Confidential Client: Reviewed current data on background levels of trichloroethylene in the environment.

Confidential Client: Performed literature review of chemical associations and alternative causes of claimed health effects in individuals exposed to PCBs.

Publications – *Articles and Book Chapters*

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Publications – *Abstracts*

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Prueitt, RL; Li, A; Chang, RY; Goodman, JE. 2020. "Systematic review of the potential respiratory carcinogenicity of metallic nickel in humans." Prepared for Society of Toxicology (SOT) 59th Annual Meeting, Anaheim, CA, March 15-19 (Conference cancelled).

Goodman, JE; Johnson, G; Prueitt, RL; Zu, K. 2019. "Systematically evaluating and integrating evidence in National Ambient Air Quality Standards (NAAQS) reviews." National Academies of Sciences, Engineering, and Medicine (NASEM) Evidence Integration Workshop, Washington, DC, June 3-4.

Zu, K; Goodman, JE; Prueitt, RL. 2019. "Strengthening the evaluation of mechanistic evidence categorized by the IARC 10 key characteristics of carcinogens." National Academies of Sciences, Engineering, and Medicine (NASEM) Evidence Integration Workshop, Washington, DC, June 3-4.

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Prueitt, RL; Goodman, JE. 2017. "Mode-of-action Evaluation for Ozone-induced Respiratory Effects Through Activation of Neural Reflexes." Society of Toxicology (SOT) 56th Annual Meeting, Baltimore, MD, March 12-16.

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Prueitt, RL; Cohen, JM; Goodman, JE. 2016. "Evaluation of Atherosclerosis as a Mode of Action for the Cardiovascular Effects of Particulate Matter." Society of Toxicology (SOT) 55th Annual Meeting, New Orleans, LA, March 13-17.

Sax, SN; Pizzurro, DM; Zu, K; Lynch, HN; Prueitt, RL; Goodman, JE. 2015. "Ozone Exposure and Systemic Biomarkers: Evaluation of Evidence of Adverse Cardiovascular Health Impacts." Society of Toxicology (SOT) 54th Annual Meeting, San Diego, CA, March 22-26.

Prueitt, RL; Lynch, HN; Tabony, JA; Beck, NB; Goodman, JE; Rhomberg, LR 2015. "Evaluation of Study Quality Criteria Frameworks." Society of Toxicology (SOT) 54th Annual Meeting, San Diego, CA, March 22-26.

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Presentations and Oral Testimony

Prueitt, RL. 2022. "What's Next for Groundwater Claims: Emerging Contaminants and Related Litigation." Panelist for presentation at the Defense Research Institute (DRI) Toxic Torts and Environmental Law Seminar, Atlanta, GA, March 14-16.

Prueitt, RL. 2021. "Regulating PFAS as a Class." Panelist for presentation at the Chemical Watch PFAS Updates 2021 Virtual Conference, June 23.

Prueitt, RL. 2021. "PFAS 360: Risk Assessment Update." Panelist for presentation at the Association for Environmental Health Sciences (AEHS) Foundation 30th Annual International Conference on Soil, Water, Energy, and Air (virtual conference), March 24.

Prueitt, RL. 2021. "PFAS Updates." Presented at the North Atlantic Chapter of the Society of Environmental Toxicology and Chemistry (NAC-SETAC) Webinar Series, February 10.

Prueitt, RL. 2019. "Diagnosis and Pathogenesis of Mesothelioma: Genomics of Asbestos-related Cancer." Panelist for presentation at the Perrin Conferences National Asbestos Litigation Conference, San Francisco, CA, September 9.

Prueitt, RL. 2018. Oral testimony on the proposed listing of nickel and nickel compounds as reproductive toxicants under Proposition 65. Presented to the Developmental and Reproductive Toxicant Identification Committee (DARTIC) of the California EPA Office of Environmental Health Hazard Assessment (OEHHA), Sacramento, CA, October 11.

Prueitt RL. 2016. "Genetic Susceptibility in Toxic Tort Litigation." Panelist for presentation at the American Bar Association (ABA) 25th Annual Spring CLE Meeting: Trends in Toxic Torts and Environmental Law, Phoenix, AZ, April 7-9.

Prueitt, RL; Gold, SC. 2016. "The Holy Grail? The Potential of Genomics to Shape Toxic Tort Litigation." Presented at the DRI Toxic Torts and Environmental Law Seminar, New Orleans, LA, March 17-18.

Prueitt, RL. 2012. Oral testimony on the proposed rule for the National Ambient Air Quality Standards (NAAQS) for particulate matter. Presented to US EPA, Sacramento, CA, July 19.

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