DEPARTMENT OF HEALTH

February 21, 2025

Mr. Robert J. Simon
Vice President
Chemical Products and Technology
American Chemistry Council

Re: Proposed Amendments to Rules Governing Health Risk Limits for Groundwater, Minnesota Rules, Chapter 4717, Part 7500 and Part 7860; Revisor's ID Number R-4803 OAH Docket No. 22-9000-40331

Dear Mr. Simon,

We thank the American Chemistry Council (ACC) for their comments regarding the Minnesota Department of Health's (MDH) Proposed Amendments to Rules Governing Health Risk Limits (HRLs) for Groundwater, Minnesota Rules, Chapter 4717, Parts 7500 and 7860; Revisor's ID Number R-4803, OAH Docket No. 22-9000-40331, submitted on December 4, 2024.

HRLs play a critical role in protecting public health in Minnesota. They represent the amount of a groundwater contaminant that can be consumed with little or no risk to health and which has been promulgated under rule. When MDH derives their proposed HRLs, it does so with the intention and the mandate of protecting Minnesota's most vulnerable and most highly exposed populations. The guiding legislation for MDH in deriving HRLs, the Groundwater Protection Act, Minn. Stat. § 103H.201, and Health Standards Statute, Minn. Stat. § 144.0751, direct MDH to solely consider human health without consideration for technical feasibility or cost of implementation. Accordingly, HRLs are nonregulatory, yet they remain a powerful tool for MDH, other Minnesota state agencies, and public water systems to protect public health.

Please see MDH's responses to ACC's comments below.

ACC Section I. Overview

Comments regarding selection of critical studies for PFOA and PFOS nHRLs

ACC notes that MDH follows similar recent practice as several regulatory agencies, such as the US Environmental Protection Agency (US EPA), the California Environmental Protection Agency (CalEPA), and the European Food Safety Authority (EFSA), by using human epidemiology studies rather than animal experimental data for the purpose of risk assessment for PFOA and PFOS.

This is correct; there has been a worldwide shift in PFAS risk assessment away from animal experimental data towards human epidemiology studies. Over the past several years, sufficient epidemiological data have become available to perform risk assessments and derive human health guidance values.

When deriving these types of values, it is always better if the studies used are done in humans. This is especially true for PFAS, because humans and rodents respond very differently to PFAS. Unlike many chemicals, humans are more sensitive to PFOA and PFOS than laboratory animals, particularly rats. This sensitivity is well-known and well-documented in the scientific community; it is largely due to differences in how long PFOA and PFOS are retained inside the body after an exposure. Rats excrete PFOA and PFOS after days or weeks. Humans retain PFOA and PFOS for years after exposure, leading to an ongoing internal exposure that endures much longer than in rats. This longer exposure results in humans experiencing health impacts at much lower PFOS or PFOA water concentrations than observed in rats.

The chosen studies fulfill MDH's requirement under the Groundwater Protection Act, Minn. Stat. § 103H.201, and Health Standards Statute, Minn. Stat. § 144.0751(a)(1)-(2), to be "based on scientifically acceptable, peer-reviewed information" and to "adequately protect the health of infants, children, and adults by taking into consideration risks to…immunologic suppression or hypersensitization…[and]…general infant and child development." The studies selected by MDH were critically evaluated by MDH toxicologists as well as by federal and state regulatory agencies and represent the best available science. The critical study for the PFOS nHRL (decreased birthweight in Wikstrom *et al.* 2020) formed part of the basis of US EPA's 2024 PFOS Maximum Contaminant Level Goal (MCLG) reference dose (US EPA, 2024a), while the critical study and effect for the PFOA nHRL (anti-Hib antibody level from Abraham *et al.* 2020) was included in the CalEPA 2024 Public Health Goal (PHG) analysis where it was noted "the impacts of these small [antibody] decreases could be much more important in children who already have compromised or borderline-compromised immune systems for other reasons. As such, these small effects could have important implications for the population as a whole, especially given the very widespread nature of PFOA exposure" (page 176) (CalEPA Office of Environmental Health Hazard Assessment, 2024). MCLGs and PHGs are both comparable values to HRLs in that they are strictly human health based. Therefore, these studies and selected endpoints are in accordance with MDH's promulgated methodology directing us to protect the most sensitive and most highly exposed populations (Minnesota Department of Health, 2008).

Comments regarding MDH's breastmilk model

The breastmilk model used by MDH in derivation of the proposed 2025 PFOA and PFOS HRLs has been validated and has undergone multiple rounds of internal and external review. The

MDH breastmilk model was first created to support derivation of the 2018 PFOA nHRL (Minnesota Department of Health, 2020); during development, the model was validated using available relevant empirical data (Fromme, 2010). Model development and validation was documented in a 2019 peer-reviewed journal (Goeden et al., 2019). The model was subsequently used in derivation of the 2019 perfluorohexane sulfonate (PFHxS) noncancer health-based value that was promulgated into rule as an nHRL in 2023 (Minnesota Department of Health, 2023). The 2019 MDH model also has been requested by and shared freely with other states and federal agencies. CalEPA evaluated the 2019 MDH model while developing their PHGs, noting "[t]his model demonstrated good fit of predicted to observed plasma data" (page 48) (CalEPA Office of Environmental Health Hazard Assessment, 2024). The 2019 MDH model was also referenced heavily by the Agency of Toxic Substances and Disease Registry (ATSDR), a division of the Centers for Disease Control and Prevention (CDC), in their development of a web-based PFAS serum modeling tool (Lynch et al., 2023).

For the proposed 2025 PFOA and PFOS nHRLs, MDH developed an updated and refined breastmilk model. The updated model was similarly validated with empirical data and development was documented in a 2024 peer-reviewed publication (Greene et al., 2024).

Comments regarding LaKind et al. 2022 commentary

ACC mischaracterizes the purpose of the LaKind *et al.* 2022 commentary as a critique of the MDH breastmilk model (LaKind et al., 2022). This is incorrect. As stated in the abstract, the commentary has three aims:

- Document published PFAS breast milk concentrations in the United States and Canada;
- Estimate breast milk PFAS levels from maternal serum concentrations in national surveys and communities impacted by PFAS, and;
- Compare measured or estimated milk PFAS concentrations to screening values

The LaKind *et al.* 2022 commentary is not an analysis of various PFAS breastmilk models, which are only mentioned in passing. Rather, the vast majority of the commentary discussed the lack of available data for PFAS concentrations in breastmilk, specifically in the United States and Canada when compared to other countries; indeed, the dataset used to validate the MDH breastmilk model is from Germany. Standard methods for developing water guidance values often underestimate exposures to infants, and understanding chemical exposures through breastmilk are increasingly important to human health risk assessment, especially in the public health setting where there is not an acceptable risk level to infants from chemicals. This commentary was a call for more of these important data to be collected.

Comments regarding PFOA and PFOS cHRLs

The Groundwater Protection Act directs MDH to derive cancer HRLs (cHRLs) for known or probable carcinogens "from a quantitative estimate of the chemical's carcinogenic potency published by the United States Environmental Protection Agency or determined by the commissioner to have undergone thorough scientific review." (Minn. Stat. § 103H.201, subd. 1(d)).

The proposed 2025 cHRLs for PFOA and PFOS were derived using information from US EPA's PFOA and PFOS MCLGs (US EPA, 2024a, 2024b) and CalEPA's PHGs (CalEPA Office of Environmental Health Hazard Assessment, 2024). In addition to intense internal scrutiny by CalEPA and EPA scientists, the MCLGs and PHGs went through multiple rounds of public drafts and public comment periods before final adoption. Additionally, scientific review occurred as part of MDH's standard risk assessment process when MDH's team of toxicologists performed their own review of the information prior to incorporating it into the analysis for cHRL derivation. MDH's review supported use of the calculated cancer slope factors, and all publicly available peer review documents used to derive the CalEPA PHGs and EPA MCLGs. All of this information meets the statutory requirement of thorough scientific review.

ACC Section II. Supporting Technical Comments

Comments regarding Analytical Considerations and Implications

It is inappropriate for ACC to compare HRLs to maximum contaminant levels (MCLs) for several reasons. ACC correctly notes that several proposed 2025 PFOA and PFOS HRLs are below the 2024 US EPA MCLs and states that the "guidance values proposed by MDH will be difficult to achieve." However, HRLs are strictly health-based values and do not consider technical feasibility and cost, as directed in statute under the Groundwater Protection Act and the Health Standards Statute. HRLs are nonregulatory risk-based values that are derived as part of a larger MDH effort to protect public health from contaminants in drinking water, whereas MCLs are meant to represent a maximum level of a contaminant allowable in a public water drinking system. MCLs can be higher than HRLs, as HRLs prioritize the impact of the contaminant on human health and do not take into account the technical feasibility of achieving a certain level of contaminant in water.

Remaining technical comments submitted by ACC

The remaining technical comments submitted by ACC are expansions of issues covered above. In addition to thorough consideration by MDH scientists during the review process, these issues were also included in the analyses by other regulatory agencies consulted during derivation of

the proposed 2025 PFOA and PFOS HRLs. As noted above, these include (but were not limited to) the US EPA PFOA and PFOS MCLGs and CalEPA PHGs, each going through multiyear and multi-round public draft and public comment periods (CalEPA Office of Environmental Health Hazard Assessment, 2024; US EPA, 2024a, 2024b). Accordingly, MDH considers its evaluations supporting the proposed 2025 PFOA and PFOS HRLs as based on the best available science and satisfying all obligations under the Groundwater Protection Act and Health Standards Statute.

We thank ACC for providing additional detail and data and address their comments further below.

PFOA nHRL study selection

Abraham *et al.* 2020 was used by CalEPA to derive its 2024 PFOA PHG (CalEPA Office of Environmental Health Hazard Assessment, 2024) and by EFSA to derive a PFOA tolerable weekly intake (European Food Safety Authority: Panel on Contaminants in the Food Chain, 2020). The US EPA also selected decreased serum antibodies in humans as their critical endpoint for the 2024 PFOA MCL, although they chose this endpoint from a different study (US EPA, 2024b). While the particular study or antibody may vary, decrease of serum antibodies in humans have consistently been deemed relevant to human health outcomes by state, federal, and international public health agencies and is appropriate for use in nHRL derivation.

PFOS nHRL study selection

Decreased birthweight described in Wikstrom *et al.* 2020 was used by the US EPA, in part, as the basis of the 2024 PFOS MCL (US EPA, 2024a). As noted in the US EPA and CalEPA review documents, Wikstrom *et al.* 2020 is not the only study demonstrating associations between PFOS exposure and decreased birthweight; many studies, including epidemiological and controlled laboratory animal, demonstrate an association between PFOS/PFOA exposure and decreased birthweight (CalEPA Office of Environmental Health Hazard Assessment, 2024; US EPA, 2024a, 2024b; USEPA, 2016a, 2016b).

ACC ends their comment stating that Wikstrom *et al.* 2020 showed a sex-specific difference in the association (i.e., there was no association observed in male infants). This finding does not weaken the low birthweight association observed in female infants, and it is ultimately irrelevant to the development of HRLs and to MDH's mission. We protect, maintain, and improve the health of all Minnesotans.

Breastmilk model

Validation of MDH's breastmilk model was thoroughly addressed above. Regarding the issue of water intake rates, ACC is correct that many state and federal agencies rely on the US EPA's

Exposure Factors Handbook for parameters like intake rates (US EPA, 2019). MDH did the same, as noted in our two scientific manuscripts describing model development and validation (Goeden et al., 2019; Greene et al., 2024). Without seeing their calculations, we cannot comment why ACC's analysis resulted in an overestimation.

Regarding LaKind *et al.* 2022, the purpose of the commentary was thoroughly discussed above.

PFOA cHRL

As noted above, Shearer *et al.* 2021 was used by the US EPA and CalEPA as their critical cancer study for PFOA with renal cell carcinoma as the tumor type (CalEPA Office of Environmental Health Hazard Assessment, 2024; US EPA, 2024b). These assessments went through rigorous internal and external peer review and public drafts. MDH performed a thorough review of these assessments and based its own PFOA cancer analysis on them.

PFOS cHRL

ACC questions how MDH and the US EPA can update their PFOS cancer classification to "likely to be carcinogenic to humans" based on a reanalysis of data. Significantly, CalEPA also recognizes PFOS cancer risk based on the same dataset, classifying PFOS as presenting "a carcinogenic hazard" (CalEPA Office of Environmental Health Hazard Assessment, 2024).

First, ACC notes that PFOS treatment did not affect survival of rats in Butenhoff *et al.* 2012. However, the rats in this study still developed hepatocellular tumors, and the PFOS cHRL is a guidance value based on cancer, not mortality.

ACC next implies combining adenomas and carcinomas into total tumor incidence, as EPA did in their calculations, is atypical. That is a standard risk assessment practice, one that the authors of Butenoff *et al.* 2012 themselves did in the study table. Regarding quantifying tumor incidence starting from time-to-first-tumor, EPA states "[e]xpressing incidence in this way quantitatively eliminates animals that died prior to the PFOS treatment duration plausibly required to result in tumor formation in the critical study" (US EPA, 2024a). It is an accepted method of clarifying a chemical's carcinogenic potential by grouping similar outcomes together in an experimental system.

Finally, ACC presents a discussion on the PFOS mode of action (MOA). MDH's default assumption is that a carcinogen's MOA is relevant to humans. Without evidence to the contrary, MDH assumes that a chemical which causes cancer in laboratory animals can also do so in humans. This is the public health-protective position. While there have been several proposed MOAs for PFOS-mediated carcinogenesis in rodents with varying degrees of evidence, there is no consensus on the exact MOA by which PFOS causes liver tumors. This is not

uncommon when studying chemical carcinogenesis and ultimately is irrelevant when creating cHRLs; MOA is not required, only high-quality science establishing a chemical's carcinogenic characteristics, allowing for a quantitative analysis and calculation of a cHRL.

Conclusion

We again thank the ACC for their comments on the 2025 PFOA and PFOS HRLs. As a public health agency, MDH's stated mission is to protect, maintain, and improve the health of all Minnesotans. The proposed 2025 PFOA and PFOS HRLs fulfill this mission.

Sincerely,

Kristine S. Klos Digitally signed by Kristine S. Klos Date: 2025.02.21 17:05:50 -06'00'

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