38941 Minnesota Department of Health Notice of Hearing (Initial Comment Period)

Closed Mar 08, 2023 · Discussion · 5 Participants · 1 Topics · 6 Answers · 0 Replies · 1 Votes

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“Other programs within MDH or other agencies may independently adopt these health-based values and incorporate them within enforceable requirements related to permitting or remediation activities.” SONAR p. 81-82.

MHD argues that no law tells it how to enforce HRL rules so it has no enforcement responsibility. But the law tells the commissioner to enforce standards. In this case, the standards the commissioner must enforce are HRLs that have been adopted into rule and new proposed HRLs once they have been adopted in this rulemaking. Minn. Stat. 144.0751 Health Standards does not provide for any exceptions that would give the commissioner discretion. Nor does the law give the commissioner the authority to tell other state agencies and others responsible for safe drinking water that they don’t have to follow rules that have the force and effect of law.

The OAH must determine, whether, given MDH’s stated intention to not enforce rules, this rulemaking should proceed.

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(1). https://www.ewg.org/interactive-maps/2020_nitrate_in_minnesota_drinking_water_from_groundwater_sources/
(2) https://minnesotareformer.com/2023/01/17/agriculture-pollutes-underground-drinking-water-in-minnesota-well-owners-pay-the-price/
(3) https://www.pca.state.mn.us/sites/default/files/wq-rule4-24c3.pdf

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Jean Wagenius · Citizen · (Postal Code: unknown) · Mar 06, 2023 7:35 pm
0 Votes

The comments that I submitted on March 4 need a correction. With the obvious exception of MDH, state agencies and others referred to in the SONAR that are not providing drinking water are not required to use or enforce HRLs. Other state agencies may adopt HRLs by reference but are not required to.

Steve Risotto · Citizen · (Postal Code: unknown) · Mar 08, 2023 2:22 pm
0 Votes

The comments of the American Chemistry Council on the proposed amendments to the rules governing health risk limits for groundwater are attached.

Barbara Losey · Citizen · (Postal Code: unknown) · Mar 08, 2023 2:25 pm
0 Votes

The Alkylphenols & Ethoxylates Research Council opposes the subchronic and chronic noncancer Health Risk Limits (HRL) for p-Nonylphenol (pNP) currently proposed under Ch. 4717.7860 Subpart 13a for the reasons explained in the attached comments.

March 8, 2023

Brooke Cunningham, MD
Commissioner
Minnesota Department of Health
625 Robert Street North
St. Paul, MN 55155

Re: Proposed Amendments to Rules Governing Health Risk Limits for Groundwater, Minnesota Rules, Chapter 4717, Part 7500, Part 7850, and Part 7860; Revisor's ID Number 4587, OAH Docket No. 5-9000-38941

Dear Commissioner Cunningham:

The American Chemistry Council (ACC) appreciates the opportunity to submit comments on the proposed amendments to the Health Risk Limits (HRLs) Rules announced on February 6, 2023. As discussed below, ACC opposes the proposed health risk limits (HRLs) for perfluorobutane sulfonate (PFBS), perfluorohexane sulfonate (PFHxS) and salts, and perfluorohexanoate (PFHxA) and salts. For all three substances, the Department inappropriately uses the results of a short-term study as the basis for its proposed subchronic and chronic HRLs, despite the fact that data from longer-term studies are available. For all three substances, MDH also inappropriately applies a database uncertainty factor (UF_D) – 3 in the case of PFBS and 10 in the case of PFHxS and PFHxA.

Perfluorobutane Sulfonate

The database for PFBS includes multiple sub chronic-duration toxicity studies of laboratory animals, multiple developmental toxicity studies with mice and rats, and a two-generation reproductive toxicity study with rats. MDH selected the results of a short-term study, however, despite the fact that the biological significance of the Department's critical effect from that study (*i.e.*, decreased T4 in adult euthyroid animals) is unclear in the absence of additional signs of overt thyroid toxicity (*e.g.*, reflex increase in thyroid stimulating hormone and/or alterations in tissue weight or histology).[1]

[1] USEPA. Human health toxicity values for perfluorobutane sulfonic acid (CASRN 375-73-5) and related compound potassium perfluorobutane sulfonate (CASRN 29420-49-3). EPA/600/R-20/345F. Office of Research and Development. Washington, DC (2021), at 82.

The developmental study by Feng *et al.* (2017)[2] also reported thyroid effects and is the more appropriate study to use as a basis for the proposed HRL. Feng *et al.* reported decreased serum total thyroxine (T4) in newborn mice which is considered to be important for normal growth of developing offspring across animal species.

For short-chain PFAS like PFBS, use of the default approach of body-weight scaling to estimate the human equivalent dose is consistent with USEPA guidance[3] and the state of the science.[4] Although the data may not be sufficient to model external dose and clearance in humans, the information available for the substance suggests that it is eliminated relatively rapidly and thus will not accumulate.[5] As a result, body-weight scaling is the most appropriate approach to estimating the human equivalent dose – rather than the serum elimination, half-life adjusted approach used by the Department.

In calculating the toxicity value for PFBS, MDH includes a UF_D of 3 based on concerns about developmental 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. Moreover, the developmental effects appear to be "less sensitive than thyroid hormone perturbations in developing mice."[6] Consequently, a toxicity value that protects against effects on thyroid hormones also will protect against developmental effects. The Department provides no explanation for its concern for the potential immunotoxicity of PFBS, moreover. ACC is not aware of available data that would suggest that immunotoxicity is a concern for PFBS, which -- as clearly demonstrated by MDH's analysis -- exhibits dramatically different properties from the PFAS previously evaluated.

Perfluorohexane Sulfonate and Salts

The data selected by the Health Department to derive the proposed HRL for PFHxS come from the results of a 28-day toxicity study conducted by the federal National Toxicology Program (NTP). The Department's analysis provides no discussion of the available chronic

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2 Feng X *et al.* Exposure of Pregnant Mice to Perfluorobutanesulfonate Causes Hypothyroxinemia and Developmental Abnormalities in Female Offspring. *Toxicol Sci* 155(2): 409-419 (2017).

3 USEPA. Recommended Use of Body Weight ¾ as the Default Method in Derivation of the Oral Reference Dose. Office of the Science Advisor. Risk Assessment Forum. Washington, DC. EPA/100.R11/001 (2011). https://www.epa.gov/risk/recommended-use-body-weight-34-default-method-derivation-oral-reference-dose

4 Sharma V and McNeill JH. To scale or not to scale: the principles of dose extrapolation. *Brit J of Pharma* 157(6):907-921 (2009). https://doi.org/10.1111/j.1476-5381.2009.00267.x

5 Xu Y *et al.* Serum half-lives for short- and long-chain perfluoroalkyl acids after ceasing exposure from drinking water contaminated by firefighting foam. *Environ Health Persp* 128:7 (2020). https://doi.org/10.1289/EHP6785

6 USEPA. PFBS Assessment, at 60.

studies conducted by Butenhoff et al (2009)[7] and Chang et el. (2018).[8] While the effects reported by Chang *et al.* (2018) do not represent a significant health effect,[9] the study by Butenhoff *et al.* (2009) has been used by a number of other states to assess the health effects of PFHxS. The Department's analysis also does not address the suggestion by Butenhoff *et al.* that thyroid effects (such as those reported in the NTP study) may be related to hepatocellular hypertrophy caused by activation of the peroxisome proliferator-activated receptor alpha (PPARα) leading to hyperplasia of the thyroid that is likely not relevant to human health risk.[10]

Before committing to an onerous HRL based on thyroid effects, the Department should carefully review interspecies differences and human study data on the relevance of thyroid effects and the variability of thyroid hormones across life. A recent French study reports that PFAS levels at birth were not associated with thyroid stimulating hormone (TSH) levels later in life,[11] and similar studies are underway to continue to add to evaluate the potential significance of TSH variance. Previous study data show a lack of strong evidence to suggest that per- and polyfluoroalkyl substances (PFAS) are associated with overall TSH and free T4, and even at the highest levels, any statistical variance in TSH-PFAS concentration correlations does not persist in humans beyond gestational week 10.[12] This would suggest that, even if a potential mechanism of action included possible competition with T4 for binding to transthyretin (a main carrier protein of thyroid hormone in mammals), observational (community epidemiology) studies do not suggest this effect occurs at relevant human exposures, either in the mother or infant.

The decision to focus on a short-term study for deriving the proposed MCL reflects the limited amount of toxicity data available for PFHxS. This paucity of data is further amplified by the application of a UF_D of 10 based on unspecified concerns about early life sensitivity and the lack of two-generation and immunotoxicity studies. The lack of a two-generation study would

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7 Butenhoff JL *et al.* 2009. Evaluation of potential reproductive and developmental toxicity of potassium perfluorohexanesulfonate in Sprague Dawley rats. *Reprod Toxicol* 27(3-4):331-341 (2009).

8 Chang S *et al.* Reproductive and developmental toxicity of potassium perfluorohexanesulfonate in CD-1 mice. *Reprod Toxicol* 78:150-168 (2018).

9 Michigan Science Advisory Workgroup. Health-Based Drinking Water Value Recommendations for PFAS in Michigan. Report developed for the Michigan PFAS Action Response Team. Lansing, Michigan (2019). https://www.michigan.gov/pfasresponse/about/advisory-groups/science-advisory-workgroup

10 Wu KM Farrelly JG. Preclinical development of new drugs that enhance thyroid hormone metabolism and clearance: inadequacy of using rats as an animal model for predicting human risks in an IND and NDA. *Am J Ther* 13(2):141-44 (2006). https://www.doi.org/10.1097/01.mjt.0000209673.01885.b0

11 Dufour P *et al.* Association between exposure to persistent organic pollutants during pregnancy and thyroid function during childhood: a pilot longitudinal study and literature review. *Rev Med Liege* 75:37-42 (2020). https://www.rmlg.ulg.ac.be/

12 Inoue K *et al.* Perfluoroalkyl substances and maternal thyroid hormones in early pregnancy: Findings in the Danish National Birth Cohort. *Environ Health Persp* 127(11):117002 (2019). https://doi.org/10.1289/EHP5482

justify the use of a 3-fold uncertainty factor, based on USEPA guidance. Concern about early-life sensitivity is addressed by Chang *et al.* who reported no treatment-related effects on postnatal survival of development in offspring exposed in utero through PND 36. Although limited, Butenhoff *et al.* did not find evidence of immunotoxicity in rats exposed to up to 10 mg/kg per day by gavage for up to 56 days.

ACC's concerns about using the NTP study results, notwithstanding, the calculation on which the Department rely inappropriately uses a benchmark response (BMR) of 20 percent rather than a BMR of one standard deviation directly observed from study results as advised by USEPA's benchmark dose (BMD) modeling guidance.[13] Although the Department indicates that use of a BMR of 20% provides a more reliable result, that analysis has not been made available for review by external scientists and other stakeholders.

If MDH does not feel that published reports on PFHxS provide a sufficient basis for developing an MCL, the Department should defer establishing standards until more data on chronic effects are available. An assessment of the health effects of PFHxS is scheduled to be available from USEPA within the next year.[14]

Perfluorohexanoate and Salts

The animal evidence for PFHxA consists of short-term, subchronic, and chronic studies in adult male and female Sprague-Dawley rats with exposure durations spanning 28 days to 2 years. In addition, two developmental, gestational exposure, studies and a one-generation reproductive study are available. Despite the potential for a greater risk of bias and exposure extrapolation error, the Department chose the short-term study instead of one of the available subchronic, chronic, or developmental studies. Of these, the chronic study by Klaunig *et al.* (2015)[15] evaluated the standard full suite of organs, clinical observations, clinical pathology, reproduction and developmental effects and cancer following PFHxA exposure and is the logical choice for deriving the proposed HRL.

While the short-term study reported a decrease in thyroid hormones (*i.e.*, total T4), the inconsistency in findings for thyroid endpoints reported across several study designs reduces

[13] USEPA. Benchmark Dose Technical Guidance. Risk Assessment Forum. Washington, DC. EPA/100/R-12/001 (2012). https://www.epa.gov/sites/production/files/2015-01/documents/benchmark_dose_guidance.pdf

[14] https://www.epa.gov/iris/iris-program-outlook

[15] Klaunig JE *et al.* Evaluation of the chronic toxicity and carcinogenicity of perfluorohexanoic acid (PFHxA) in Sprague-Dawley rats. *Toxicol Pathol* 43(2), 209-220 (2015).

the strength of the available evidence.[16] Moreover, the developmental effects (*i.e.*, decreased pup body weight) reported by Loveless *et al.* (2009) coincided with evidence of maternal toxicity and generally disappeared after weaning. [17] As a result, the authors noted that "NaPFHx [the sodium salt of PFHxA] is therefore concluded not to present a reproductive or developmental hazard." Similarly, Iwai and Hoberman (2014) also reported pup body weight loss only at does resulting in significant maternal toxicity.[18] The decreases in pup weight were not statistically significant at postpartum day 20, moreover, and the authors reported no differences in terminal body weights among the dosage groups.

As with PFHxS, the Department inappropriately applies a UF_D of 10. In the case of PFHxA, MDH points to concerns about developmental, thyroid, and immunotoxicity. As noted however, the available evidence does not provide support for developmental effects and, while limited, the evidence for thyroid effects is inconsistent. With the exception of changes in thymus weights, the available animal evidence does not show a clear pattern of immune effects across studies.

Based on the information provided above, ACC recommends that the Department reevaluate the available evidence for PFBS, PFHxS, and PFHxA to ensure that the proposed HRLs reflect the best available science.

Sincerely,

Steve Risotto

Stephen P. Risotto
Senior Director

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16 USEPA. Toxicological Review of Perfluorohexanoic Acid (CASRN 307-24-4) and Related Salts. External Review Draft. EPA/635/R-21/312a. Office of Research and Development. Washington, DC (2022). https://cfpub.epa.gov/ncea/iris_drafts/recordisplay.cfm?deid=352767

17 Loveless SE *et al.*Toxicological evaluation of sodium perfluorohexanoate. *Toxicol* 264(1-2), 32-44 (2009)

18 Iwai H and Hoberman AM (2014). Oral (gavage) combined developmental and perinatal/postnatal reproduction toxicity study of ammonium salt of perfluorinated hexanoic acid in mice. *Int J Toxicol* 33(3):219-237 (2014).