Pew

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Submitted via: tox@tceq.texas.gov

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RE: TCEQ Systematic Review and Evidence Integration for 16 PFAS and the Draft Development Support Document for Perfluorooctanoic Acid (PFOA) and Perfluorooctane Sulfonic Acid (PFOS) and Salts

Dear Dr. Lange:

Thank you for soliciting feedback on the Texas Commission on Environmental Quality (TCEQ) Systematic Review and Evidence Integration for 16 Perfluoroalkyl and Polyfluoroalkyl Substances[1] (TCEQ PFAS SR) and the Draft Perfluorooctanoic Acid (PFOA) and Perfluorooctane Sulfonic Acid (PFOS) and Salts Development Support Document[2] (Draft PFOA/PFOS DSD). We appreciate TCEQ's efforts to advance science supporting public policy to improve the health of Texas residents.

The Pew Charitable Trusts is a non-profit, nonpartisan research and policy organization dedicated to informing the public, improving public policy, and invigorating civic life with several initiatives focused on the health and well-being of American communities. Pew's newest initiative, the Safer Chemicals project, is working to reduce Americans' exposures to endocrine-disrupting chemicals by engaging collaboratively with the private sector and the regulatory process at state and local levels and bringing new and existing evidence to inform policymaking.

[1] Texas Commission on Environmental Quality. (2025). Draft Systematic Review and Evidence Integration for 16 Perfluoroalkyl and Polyfluoroalkyl Substances (PFAS). Austin, TX: Texas Commission on Environmental Quality.
[2] Texas Commission on Environmental Quality. (2025). Draft Perfluorooctanoic Acid (PFOA) and Perfluorooctane Sulfonic Acid (PFOS) and Salts Development Support Document. Austin, TX: Texas Commission on Environmental Quality.

Overview

As TCEQ itself explains in the TCEQ PFAS SR, the previous update to PFAS toxicity factors occurring in February 2023[3] was an interim update and not based on a systematic review of the available evidence. We commend TCEQ for pursuing a systematic review approach in updating the 2023 interim toxicity factors as represented in the TCEQ PFAS SR—the assessment underpinning the Draft PFOA/PFOS DSD. As a general matter, we encourage TCEQ to continue to apply comprehensive systematic review approaches in its assessment of chemicals hazards and risks. In carrying out these assessments, however, we would urge TCEQ to update its approach to address shortcomings identified in these comments to strengthen the scientific basis of associated chemicals policies and regulations. Application of comprehensive systematic review approaches aligns with Texas statutory and regulatory obligations addressing toxics.[4,5]

The TCEQ PFAS SR represents a multi-year effort to apply systematic review principles to the assessment of 16 PFAS in support of deriving PFAS-specific toxicity factors. Of note, TCEQ previously derived toxicity factors for these same 16 PFAS over the years spanning 2011-2023. The current effort employs TCEQ's 2017 systematic review guidance[6] and heavily leverages the TCEQ 2021 Systematic Evidence Map (SEM) for PFAS (TCEQ PFAS SEM).[17] Specifically, TCEQ uses the literature identified as part of the TCEQ PFAS SEM as its starting point for literature identification in the TCEQ PFAS SR. TCEQ's Draft PFOA/PFOS DSD is an outgrowth of the TCEQ PFAS SR, and proposes updated toxicity factors for PFOA and PFOS and their salts. Together, these documents reflect TCEQ's effort to conduct broad

[3] Texas Commission on Environmental Quality. (2023). Per- and Poly-fluoroalkyl Substances (PFAS). Austin, Texas. Texas Commission on Environmental Quality.
[4] Texas Clean Air Act. 71st Leg., ch. 678, Sec. 1, Ch. 382 (1989).
The Texas Clean Air Act states that "(t)he policy of this state […] are to safeguard the state's air resources from pollution by controlling or abating air pollution and emissions of air contaminants, consistent with the protection of public health, general welfare, and physical property, including the esthetic enjoyment of air resources by the public and the maintenance of adequate visibility."
[5] Texas Commission on Environmental Quality, Texas Risk Reduction Program (1999). https://www.law.cornell.edu/regulations/texas/title-30/part-1/chapter-350.
The Texas Risk Reduction Program states that "[i]n all cases, the toxicity factors used must be protective of human health and the environment."
[6] Texas Commission on Environmental Quality. (2017). TCEQ Guidelines for Systematic Review and Evidence Integration. Austin, TX: Texas Commission on Environmental Quality.
[7] Texas Commission on Environmental Quality. (2021). Systematic Evidence Map for 16 PFAS Chemicals. Austin, Texas: Texas Commission on Environmental Quality.

evidence mapping to inform focused evidence evaluation and quantitative risk assessment for PFOA and PFOS.

Strengths

The TCEQ PFAS SR demonstrates positive elements that generally align with systematic review best practices.[8,9,10,11,12] For example,

- TCEQ defined key aspects of its systematic review protocols beforehand, including literature identification, inclusion/exclusion criteria, data extraction, study evaluation considerations, and piloting and calibration; and provided clear documentation of its process with changes noted and justified.
- TCEQ applied a structured Population, Exposure, Comparator, Outcome (PECO) framework to its systematic review and utilized a structured tool (DistillerSR) for review management.
- TCEQ used two independent reviewers to perform title/abstract screening and employed a third party to resolve any conflicts.
- TCEQ validated the TCEQ PFAS SEM literature search syntax and results by cross-checking references against ~50 primary publications used in the U.S. Environmental Protection Agency's (EPA) PFAS assessments.[13,14] TCEQ also cross-referenced the final set of studies advanced to the TCEQ PFAS SR

[8] National Academies of Science, Engineering, and Medicine. (2021). Review of U.S. EPA's Integrated Risk Information System (IRIS) Handbook. Washington, DC: National Academies Press.
[9] U.S. Environmental Protection Agency. (2022). ORD Staff Handbook for Developing IRIS Assessments. Washington, DC: U.S. Environmental Protection Agency.
[10] National Toxicology Program, Office of Health Assessment and Translation. (2019). Handbook for Conducting a Literature-Based Health Assessment Using OHAT Approach for Systematic Review and Evidence Integration. Research Triangle Park, NC: National Institute of Environmental Health Sciences.
[11] Woodruff, TJ, and Sutton, P. (2014). The Navigation Guide systematic review methodology: a rigorous and transparent method for translating environmental health science into better health outcomes. Environmental Health Perspectives, 122(10), 1007.
[12] Vandenberg, LN, Ågerstrand, M, Beronius, A, Beausoleil, C, Bergman, Å, Bero, LA, Bornehag, CG, Boyer, CS, Cooper, GS, Cotgreave, I, Gee, D, Grandjean, P, Guyton, KZ, Hass, U, Heindel, JJ, Jobling, S, Kidd, KA, Kortenkamp, A, Macleod, MR, Martin, OV, Nordiner, U, Scheringer, M, Thayer, KA, Toppari, J, Whaley, P, Woodruff, TJ, Rudén, C. (2016). A proposed framework for the systematic review and integrated assessment (SYRINA) of endocrine disrupting chemicals. *Environmental Health* 15:74. doi: 10.1186/s12940-016-0156-6.
[13] United States Environmental Protection Agency. (2016). Health effects support document for perfluorooctanoic acid (PFOA). Office of Water, Health and Ecological Criteria Division. EPA 822-R-16-003.
[14] United States Environmental Protection Agency. 2021. 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, D.C.

against publications identified in EPA reports and other systematic reviews of PFAS literature.[14,15,16,17,18,19]

- TCEQ implemented a structured process to identify, follow up, and link related publications that relied on overlapping or identical datasets, ensuring that such interrelated studies were evaluated together rather than treated as independent lines of evidence. This approach helps prevent double-counting of data, reduces the risk of overstating the weight or consistency of evidence, and supports more accurate interpretation of findings.

Collectively, these features reflect an intention to introduce consistency, rigor, and transparency into the evidence review process.

Key Limitations and Concerns

While TCEQ has taken steps toward a structured evidence review process, critical departures from established best practices in systematic evidence mapping and systematic review raise concerns about the completeness, transparency, and reliability of the conclusions drawn. These methodological limitations have direct implications for future and currently proposed toxicity factors (i.e., those proposed in the Draft PFOA/PFOS DSD). Overall, these limitations risk underestimating potential public health harms and therefore fall short of ensuring public health protection.

We respectfully urge TCEQ to revise the TCEQ PFAS SR to address the issues outlined below and reconsider the Draft PFOA/PFOS DSD following these revisions. Aligning TCEQ's approach to systematic review with established scientific best practices, such as those used by EPA's Integrated Risk Information System (IRIS) program and the European Food Safety Authority (EFSA), would strengthen

[15] United States Environmental Protection Agency. (2016). Health effects support document for perfluorooctane sulfonate (PFOS). Office of Water, Health and Ecological Criteria Division. EPA 822-R-16-002.
[16] United States Environmental Protection Agency. (2021). Proposed Approaches to the Derivation of a Draft Maximum Contaminant Level Goal for Perfluorooctane Sulfonic Acid (PFOS) (CASRN 1763-23-1) in Drinking Water. External Peer Review Draft. EPA Document No. 822-D-21-002 Office of Water, Washington D.C.
[17] United States Environmental Protection Agency. (2021). Proposed Approaches to the Derivation of a Draft Maximum Contaminant Level Goal for Perfluorooctanoic Acid (PFOA) (CASRN 335-67-1) in Drinking Water. External Peer Review Draft. EPA Document No. 822-D-21-001. Office of Water, Washington, D.C.
[18] Agency for Toxic Substances and Disease Registry (ATSDR). (2021). Toxicological profile for perfluoroalkyls. Available at: https://www.atsdr.cdc.gov/ToxProfiles/tp200.pdf
[19] Pelch K, A Reade, T Wolffe, C Kwiatkowski. (2019). PFAS health effects database: protocol for a systematic evidence map. Environ Int. doi: 10.1016/j.envint.2019.05.045

scientific credibility, public trust, and the protectiveness of resulting regulatory decisions.[9,20] The issues outlined below are approximately organized to parallel the TCEQ's described systematic review process.

- **Limited literature search scope**: The TCEQ PFAS SEM used to support the TCEQ PFAS SR relied exclusively on a search syntax developed to query only the PubMed database. As a result, references that are unpublished or not indexed by PubMed were not included. Unpublished studies should be considered during the systematic review, even if weighed differently from other studies during evidence integration. Excluding unpublished studies or data at this early stage of the systematic review process limits TCEQ's opportunities for accounting for crucial health-protective data that could lend additional robustness to the toxicity factors that are developed. Restricting searches primarily to a single database, while excluding unpublished and non-indexed studies, risks incomplete evidence capture and publication bias.[21,22,23] Newly published studies may not yet be completely indexed by PubMed, so exclusive reliance on this database also risks the exclusion of recent scientific evidence.[24,25]
- **Limiting studies to English-only**: Explicitly excluding studies published in languages other than English increases the risk of excluding key scientific information. This is particularly concerning for PFOA and PFOS, which have been extensively studied in international settings such as Europe and Asia. Limiting articles to English-only can lead to systematically underrepresenting certain findings, skew geographic representation of the evidence base, and

[20] European Food Safety Authority. (2015). Principles and process for dealing with data and evidence in scientific assessments. EFSA Journal Scientific Report. doi:10.2903/j.efsa.2015.4121

[21] Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, et al, (2024). Cochrane Handbook for Systematic Reviews of Interventions version 6.5. Cochrane. Available from www.cochrane.org/handbook.

[22] Page, MJ, McKenzie, JE, Bossuyt, PM, Boutron, I, Hoffmann, TC, Mulrow, CD, Shamseer, L, Tetzlaff, JM, Akl, EA, Brennan, SE and Chou, R. (2021). The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ, 372.

[23] Song, F, Parekh, S, Hooper, L, Loke, YK, Ryder, J, Sutton, AJ, Hing, C, Kwok, CS, Pang, C and Harvey, I. (2010). Dissemination and publication of research findings: an updated review of related biases. Health technology assessment, 14(8), pp.1-220.

[24] Falagas, ME, Pitsouni, EI, Malietzis, GA and Pappas, G. (2008). Comparison of PubMed, Scopus, web of science, and Google scholar: strengths and weaknesses. The FASEB Journal, 22(2), pp.338-342.

[25] Bramer, WM, Rethlefsen, ML, Kleijnen, J and Franco, OH, (2017). Optimal database combinations for literature searches in systematic reviews: a prospective exploratory study. Systematic Reviews, 6(1), p.245.

reduce completeness of the review.[26,27] Best practices for systematic review generally recommend either including non-English studies or, at a minimum, assessing and transparently discussing the potential impact of language restrictions on conclusions. Several online tools are available to assist with language translation, and at a minimum these could be used to readily translate and assess study abstracts for study inclusion.

- **Insufficient human review of AI-assisted screening of literature search results**: TCEQ's approach for applying AI capabilities in its systematic review involved limited human auditing of exclusion results, which could lead to critical gaps in quality control. After training, AI-embedded capabilities within DistillerSR were used to exclude studies predicted to be irrelevant once a threshold of expected included studies was met, with 10% of AI-excluded references reviewed for QC. The flow chart notes that 1,187 of the 6,931 (17%) titles and abstracts were excluded by AI with no second reviewer, with only 10% (118) of the AI-excluded studies reviewed for QC. This means that over 1,000 titles and abstracts were excluded without any human reviewer providing input. Excluding large numbers of studies based solely on AI predictions, with only limited quality control, increases the risk of missing eligible PFOS/PFOA studies and is in contradiction to recent reviews of the utility of AI in systematic reviews.[28,29] This is particularly concerning in a highly policy-sensitive context. Incorporating more stringent QC approaches to minimize the risk of missing relevant evidence or providing documentation regarding the validation and audit of these AI screening approaches would be appropriate to avoid the systematic omission of studies. An alternative approach would be to continue screening with a single human reviewer after the threshold of expected included studies (i.e., 99%) is reached, while using AI as a secondary reviewer. Studies for which the human reviewer and AI reach concordant inclusion or exclusion decisions could proceed accordingly, whereas records with discordant decisions would be adjudicated by a second

[26] Walpole, SC. (2019). Including papers in languages other than English in systematic reviews: important, feasible, yet often omitted. Journal of Clinical Epidemiology, 111, pp.127-134.
[27] Stern, C. and Kleijnen, J. (2020). Language bias in systematic reviews: you only get out what you put in. *JBI Evidence Synthesis*, *18*(9), pp.1818-1819.
[28] Clark, J, Barton, B, Albarqouni, L, Byambasuren, O, Jowsey, T, Keogh, J, Liang, T, Moro, C, O'Neill, H, Jones, M. (2025). Generative artificial intelligence use in evidence synthesis: A systematic review. Research Synthesis Methods, 16 (4) 601-619. doi:10.1017/rsm.2025.16.
[29] Thomas J, Flemyng E, Noel-Storr, A. et al. Responsible AI in Evidence Synthesis (RAISE): guidance and recommendations (version 2; updated 3 June 2025). In: Open Science Framework [https://osf.io/], Washington DC: Center for Open Science. DOI 10.17605/OSF.IO/FWAUD (accessed January 21, 2026).

human reviewer to ensure accuracy and consistency. At a minimum, TCEQ should provide detailed results from the quality control review of the 10% of studies excluded solely by the AI screening process, including a summary of whether any study relied upon in EPA assessments used for calibration were among those excluded by AI.

- **Selective data extraction**: TCEQ's data extraction rules state that "(s)tudies with no statistically significant findings were not captured in the data extraction table," with limited and vague exceptions. TCEQ reported that 15 references (human and animal studies) had no statistically significant findings and were thus not extracted. The exclusion of non-statistically significant findings from data extraction represents a major departure from systematic review norms and may bias effect estimates.[21,23] This could result in directional bias by structurally under-representing null findings, which are essential for balanced consideration of the totality of evidence and for evaluation consistency and heterogeneity in outcomes.[30] At a minimum, a sensitivity analysis should be conducted in order to calculate effect estimates with and without inclusion of non-statistically significant findings and to assess the impact of excluding these studies from the overall analysis.[10]
- **Limited capture of mechanistic evidence in extraction**: TCEQ did not extract mechanistic experimental endpoints during the systematic review. Instead, mechanistic information was limited to reviewer notes and was not systematically evaluated alongside human and animal evidence. However, mechanistic evidence (e.g., data or studies that elucidate mechanisms related to immunotoxicity, endocrine activity, or lipid metabolism) can be highly decision-relevant for integrating human and animal evidence findings and assessing biological plausibility. This limited-capture approach impacts the transparency and reproducibility of how mechanistic evidence informs the overall integration of evidence. Established frameworks for environmental health assessments emphasize the structured consideration of mechanistic evidence to support biological plausibility, coherence across evidence streams, and interpretation of both epidemiology and animal findings.[9,10] While mechanistic data are not always used directly for dose-response derivation, its systematic evaluation is considered important for evidence integration.[12]

[30] Ioannidis, J.P., 2005. Why most published research findings are false. PLoS Medicine, 2(8), p.e124.

- **Discounting of epidemiological evidence as insufficient for derivation of toxicity factors:** TCEQ discounted key epidemiological evidence in its systematic review. Notably, TCEQ excluded evidence that supports immunotoxicity as the most sensitive endpoint for PFOA and PFOS, resulting in the derivation of toxicity factors that do not adequately protect public health from exposure to these chemicals. TCEQ's provided rationale for discounting key epidemiological evidence, specifically studies evaluating decreased immune/vaccine antibody response following PFAS exposure,[31] refers to inconsistent results across studies, incomplete confounding control, small sample sizes, and potential reverse causation.[32] There are several concerns with this approach.
    - TCEQ cites broader conclusions by the Australian Government National Health and Medical Research Council (NHMRC)[33] as justification to exclude studies that link PFAS exposure to decreased vaccine antibody responses. This decision by TCEQ contradicts several EPA assessments of the same studies.[32] However, TCEQ's own guidelines for developing toxicity factors cites EPA as a credible source for guidance in methodologies pertaining to systematic review and risk assessments.[34]

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[31] Based on the inclusion review of the TCEQ PFAS SR, the following vaccine studies were excluded during the systematic review:
Abraham, K.,Mielke, H.,Fromme, H.,Volkel, W.,Menzel, J.,Peiser, M.,Zepp, F.,Willich, S. N.,Weikert, C.. (2020). Internal exposure to perfluoroalkyl substances (PFASs) and biological markers in 101 healthy 1-year-old children: associations between levels of perfluorooctanoic acid (PFOA) and vaccine response. Arch Toxicol 94(6).
Grandjean, P.,Andersen, E. W.,Budtz-Jorgensen, E.,Nielsen, F.,Molbak, K.,Weihe, P.,Heilmann, C.. (2012). Serum vaccine antibody concentrations in children exposed to perfluorinated compounds. JAMA 307(4).
Grandjean, P.,Budtz-Jorgensen, E.. (2013). Immunotoxicity of perfluorinated alkylates: calculation of benchmark doses based on serum concentrations in children. Environ Health 12(1).
Grandjean, P.,Heilmann, C.,Weihe, P.,Nielsen, F.,Mogensen, U. B.,Budtz-Jorgensen, E.. (2017). Serum Vaccine Antibody Concentrations in Adolescents Exposed to Perfluorinated Compounds. Environ Health Perspect 125(7).
Granum, B.,Haug, L. S.,Namork, E.,Stolevik, S. B.,Thomsen, C.,Aaberge, I. S.,van Loveren, H.,Lovik, M.,Nygaard, U. C.. (2013). Pre-natal exposure to perfluoroalkyl substances may be associated with altered vaccine antibody levels and immune-related health outcomes in early childhood. J Immunotoxicol 10(4).
Looker, C.,Luster, M. I.,Calafat, A. M.,Johnson, V. J.,Burleson, G. R.,Burleson, F. G.,Fletcher, T.. (2014). Influenza vaccine response in adults exposed to perfluorooctanoate and perfluorooctanesulfonate. Toxicol Sci 138(1).
Pilkerton, C. S.,Hobbs, G. R.,Lilly, C.,Knox, S. S.. (2018). Rubella immunity and serum perfluoroalkyl substances: Sex and analytic strategy. PLoS One 13(9).
Stein, C. R.,Ge, Y.,Wolff, M. S.,Ye, X.,Calafat, A. M.,Kraus, T.,Moran, T. M.. (2016). Perfluoroalkyl substance serum concentrations and immune response to FluMist vaccination among healthy adults. Environ Res 149.
Timmermann, C. A. G.,Jensen, K. J.,Nielsen, F.,Budtz-Jorgensen, E.,van der Klis, F.,Benn, C. S.,Grandjean, P.,Fisker, A. B.. (2020). Serum Perfluoroalkyl Substances, Vaccine Responses, and Morbidity in a Cohort of Guinea-Bissau Children. Environ Health Perspect 128(8).
[32] Page 88 in the Draft PFOA/PFOS DSD.
[33] Australian Government, National Health and Medical Research Council. (2025). Guideline development for review of PFAS in drinking water.
[34] Texas Commission on Environmental Quality. (2015). TCEQ Guidelines to Develop Toxicity Factors. Austin, TX: Texas Commission on Environmental Quality.

Furthermore, in accordance with the Texas Risk Reduction Program, TCEQ is supposed to prioritize evidence of chronic toxicity originating from EPA ahead of other sources based on their determined hierarchy of sources.[5]

- TCEQ's assertion that much of the epidemiological evidence included in the TCEQ PFAS SEM is inadequate for quantitative dose response is an evidentiary standard that does not appear to be applied symmetrically, specifically to animal studies. Animal studies can also face well-known translational uncertainties (e.g., species differences in kinetics/dynamics, endpoint comparability, relevance of dosing regiments, etc.), but these do not appear to be considered or assessed as thoroughly by TCEQ. Furthermore, residual uncertainties in animal-to-human extrapolations are not directly assessed or evaluated for appropriateness in targeting outcomes directly relevant to population health. In particular, because the immune/vaccine antibody response endpoint is not routinely tested in animal studies, the importance of the epidemiological evidence is even greater when assessing this outcome.
- TCEQ argues that attributing effects to a single PFAS within a correlated mixture is "not scientifically defensible" and criticized EPA for not controlling for co-exposures. However, extensive methodological literature demonstrates that correlated environmental exposures can be addressed using multi-pollutant models, mixture-based methods, and sensitivity analyses – approaches that are routinely applied in environmental epidemiology and regulatory risk assessment.[35,36,37] A more balanced approach would transparently evaluate how much confounding remains under different model specifications rather than making an overly broad conclusion that the evidence base is unusable for dose-response assessment. One example of this possible solution is in the EPA's 2025 IRIS assessment of perfluorohexanesulfonic acid (PFHxS),[38] in

[35] Dominici, F, Peng, RD, Barr, CD and Bell, ML. (2010). Protecting human health from air pollution: shifting from a single-pollutant to a multipollutant approach. Epidemiology, 21(2), pp.187-194.
[36] Braun, JM, Gennings, C, Hauser, R and Webster, TF. (2016). What can epidemiological studies tell us about the impact of chemical mixtures on human health?. Environmental Health Perspectives, 124(1), p.A6.
[37] Taylor, KW, Joubert, BR, Braun, JM, Dilworth, C, Gennings, C, Hauser, R, Heindel, JJ, Rider, CV, Webster, TF and Carlin, DJ. (2016). Statistical approaches for assessing health effects of environmental chemical mixtures in epidemiology: lessons from an innovative workshop. Environmental Health Perspectives, 124(12), p.A227.
[38] U.S. Environmental Protection Agency (EPA). (2025). IRIS Toxicological Review of Perfluorohexanesulfonic Acid (PFHxS) and Related Salts (EPA/635/R-25/012). U.S. EPA Integrated Risk Information System (IRIS).

which EPA explicitly treats PFAS co-exposure as a source of uncertainty and uses statistical approaches to address these co-exposures. The epidemiological dose-response data is modeled using single PFAS models as well as multi-PFAS models that adjust for the correlation between different types of PFAS. Another approach would be to draw on numerous comprehensive existing systematic evidence maps[39,40,41] of relevant epidemiological evidence that documents study-level limitations in internal and external validity, rather than simply categorically excluding the evidence from dose-response consideration. This approach would allow TCEQ to appropriately assess limitations at the individual study level and incorporate structured data extraction and sensitivity analyses, consistent with methodological frameworks proposed in the peer-reviewed literature, including recent work by Lange and colleagues[42,43] that outlines how improved extraction and evaluation of epidemiological data can better inform chemical risk assessment and support examination of how specific studies influence points of departure, toxicity factors, and key parameters.

- TCEQ argues that low U.S. incidence of diphtheria/tetanus undermines the finding that PFOS/PFOA exposure meaningfully suppresses vaccine response. But population disease incidence is driven by many factors (e.g., high vaccination coverage, herd immunity, surveillance, exposure heterogeneity) and may not be sensitive enough to detect modest immune impacts—particularly if the biomarker effect relates to antibody titers rather than outright vaccine failure. TCEQ's line of reasoning sets an unusually high bar (observable increases in rare diseases) that is not required for identifying immunotoxicity risk. TCEQ repeatedly states that the epidemiological evidence does not show "clear adverse effect" and

[39] Carlson, LM, Angrish, M, Shirke, AV, Radke, EG, Schulz, B, Kraft, A, Judson, R, Patlewicz, G, Blain, R, Lin, C, Vetter, N. (2022). Systematic evidence map for over one hundred and fifty per-and polyfluoroalkyl substances (PFAS). Environmental Health Perspectives, 130(5), p.056001.
[40] Shirke, AV, Radke, EG, Lin, C, Blain, R, Vetter, N, Lemeris, C, Hartman, P, Hubbard, H, Angrish, M, Arzuaga, X, Congleton, J. (2024). Expanded systematic evidence map for hundreds of per-and polyfluoroalkyl substances (PFAS) and comprehensive PFAS human health dashboard. Environmental Health Perspectives, 132(2), p.026001.
[41] Shirke, AV, Radke, EG, Jones, R, Allen, BD, Lin, CJ, Ross, A, Vetter, N, Lemeris, C, Hartman, P, Eftim, S, Varghese, A. (2025). Systematic Evidence Map for the Per-and Polyfluoroalkyl Substances (PFAS) Universe. Environmental Health Perspectives. DOI: 10.1289/ehp16952.
[42] LaKind, JS, Burns, CJ, Johnson, GT and Lange, SS. (2023). Epidemiology for risk assessment: the US Environmental Protection Agency quality considerations and the Matrix. Hygiene and Environmental Health Advances, 6, p.100059.
[43] Schaefer, HR, Vincent, MJ, Burns, CJ and Lange, SS. (2025). Increasing the utility of epidemiologic studies as key evidence in chemical risk assessment. Toxicological Sciences, 203(2), pp.166-170.

that clinical implications are uncertain. However, TCEQ's systematic review protocol does not present a clear, prespecified framework for translating biomarker changes (e.g., antibody titers, cholesterol) into adversity determinations for risk assessment. Without a clear, pre-specified adversity framework, this argument is subjective and outcome-dependent.

  - TCEQ states that EPA's RfDs are "not scientifically defensible" due to "flawed epidemiological data." While epidemiological studies may present certain limitations (e.g., confounding, reverse causation, narrow exposure range), systematic review best practice generally calls for downgrading confidence, characterizing the uncertainty, and/or increasing uncertainty bounds - not broadly declaring the entire epidemiologic basis invalid, particularly when multiple endpoints converge and there is supporting toxicological plausibility. This aligns with established guidance from other government agencies.[9,10] A recent National Academies committee review of TCEQ's assessment of ethylene oxide, where TCEQ excluded epidemiological evidence, similarly recommended that TCEQ should not treat standard limitations in epidemiological data as categorically disqualifying.[44]

- **Absence of a transparent evidence integration framework**: The protocol in the TCEQ PFAS SR explicitly excludes the step of evidence synthesis and integration, leaving unclear how disparate evidence streams are assessed and integrated to support regulatory conclusions. As a result, the majority of the Draft PFOA/PFOS DSD is structured like a narrative review, rather than a structured systematic review following a transparent process for evidence evaluation and integration. Lacking structured evidence integration and steps for its application in a pre-published protocol reduces the transparency and replicability of this review. This is inconsistent with systematic review best practices demonstrated in EPA's IRIS program and recommendations from the National Academy of Sciences.[8,9]

[44] National Academies of Sciences, Engineering, and Medicine. (2025). Review of Texas Commission on Environmental Quality's Ethylene Oxide Development Support Document. Washington, DC: The National Academies Press. https://doi.org/10.17226/180.

Systematic Review Recommended Revisions

Pew recommends that TCEQ updates the TCEQ PFAS SR as follows:

1. Expand the literature search to include databases beyond PubMed and to capture relevant grey literature and non-English studies.
2. Strengthen quality control over AI-assisted screening of literature search results.
3. Extract and report all study outcomes including null findings and conduct sensitivity analyses to evaluate effects of including or excluding non-statistically significant findings.
4. Systematically consider and evaluate mechanistic evidence to fully capture the body of evidence and to support integration across evidence streams.
5. Include epidemiological evidence in the identification and characterization of hazard.
6. Revise the systematic review protocol to include a clear framework for translating biomarker changes (e.g., antibody titers, cholesterol) into adversity determinations, and to include a structured approach to evidence synthesis and integration.

PFOA/PFOS Toxicity Factor Recommendations

The limitations identified in the TCEQ PFAS SR have direct implications for the PFOA/PFOS toxicity factors presented in the Draft PFOA/PFOS DSD. Conclusions from the TCEQ PFAS SR may reflect methodological artifacts rather than a true capture of the scientific evidence. As a result, the proposed toxicity factors lack adequate justification and risk undermining health protection. Specifically, Pew is concerned that the proposed toxicity factors for PFOA, PFOS, and their salts are not protective of the most sensitive endpoint, immunotoxicity, as supported by the scientific evidence.

Pew recommends that TCEQ revise the TCEQ PFAS SEM and TCEQ PFAS SR to address the concerns described in these comments and to allow for public comment on the revisions. TCEQ should then revise the Draft PFOA/PFOS DSD accordingly and again allow for public comment.

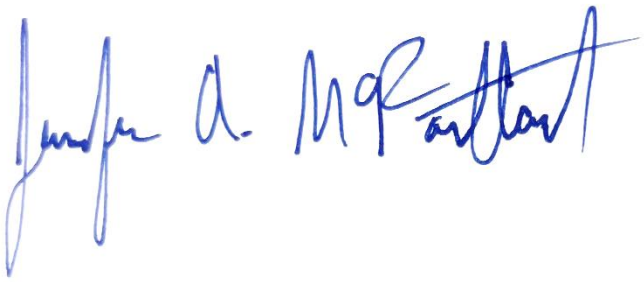
Conclusions

We appreciate TCEQ's efforts to prioritize and pursue action on PFAS based on the best available science. The approach described in the TCEQ PFAS SR reflects an intention to introduce consistency, rigor, and transparency into the evidence review process. However, this aim is undermined by significant deviations from best practices in systematic review. TCEQ should revise the TCEQ PFAS SR to align with best practices in systematic review and update the Draft PFOA/PFOS DSD accordingly.

Pew generally recommends that TCEQ allow for public comment on systematic review protocols supporting chemical assessments in advance of carrying out systematic evidence mapping exercises and systematic reviews. Finally, TCEQ rightly points to the importance of cumulative and mixture effects in PFAS risk assessments. TCEQ should use this as an opportunity to invest resources, and coordinate with other government agencies, to advance risk assessment approaches that better address cumulative and mixture effects.

Pew appreciates the opportunity to provide input to the TCEQ PFAS SR and Draft PFOA/PFOS DSD, and for the TCEQ's continued attention to this important subject. Please contact myself (jmcpartland@pewtrusts.org) or Kyle Kinner (kkinner@pewtrusts.org) in our Government Relations department for additional information or questions.

Sincerely,



Jennifer McPartland
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