August 15, 2023

Comments from Academics, Scientists and Clinicians on the Perchloroethylene Rulemaking under TSCA section 6(a)

Submitted online via Regulations.gov to docket EPA-HQ-OPPT-2020-0720-0024

These comments are submitted on behalf of the undersigned academics, scientists, health professionals, and clinicians. We declare collectively that we have no direct or indirect financial or fiduciary interest in any chemical or product that is the subject of these comments. The co-signers' institutional affiliations are included for identification purposes only and do not imply institutional endorsement or support, unless indicated otherwise.

We appreciate the opportunity to provide written comments on the proposed risk management rule[1] ("Proposed Rule") for perchloroethylene ("PCE"), issued under EPA's Toxic Substances Control Act ("TSCA"). PCE is a high-production volume solvent with widespread industrial and consumer uses as a metal degreaser, lubricant, mold remover, and stain/spot cleaner. EPA estimated a "…yearly aggregate production volume for PCE ranged from 388 to 324 million pounds between 2012 and 2015 according to CDR."[2] Nearly 65% of this production volume is "used as an intermediate in industrial gas manufacturing and producing fluorinated compounds"[3], such as hydrofluorocarbons (HFCs) and hydrochlorofluorocarbons (HCFCs), and around 15% is used as a dry cleaning solvent.[4] PCE exposures are linked to serious and irreversible health harms, including neurotoxicity, liver and kidney toxicity, and certain types of cancer such as kidney and bladder.[5]

EPA previously determined that PCE poses unreasonable risk of injury to human health,[6] and is therefore required under TSCA section 6(a) to promulgate the Proposed Rule to ensure that "the chemical no longer presents [unreasonable] risk."[7] EPA has now proposed to ban all consumer uses of PCE and many industrial and commercial uses, while allowing others to continue, subject to a Workplace Chemical Protection Program ("WCPP"). Under the Proposed Rule, 17 conditions of use, which "comprise more than an estimated 80% of the current production volume of PCE", would continue based on EPA's conclusion that unreasonable risks for those conditions of use can be "eliminated" through a WCPP and an expected gradual "decline over time" in PCE production volume.[8] Among the allowed conditions of use are high-

[1] Perchloroethylene (PCE); Regulation Under the Toxic Substances Control Act (TSCA), 88 Fed. Reg. 39,652 (proposed June 16, 2023) (to be codified at 40 C.F.R. 751)
[2] US EPA. (2020). Tetrachloroethylene (perchloroethylene); TSCA Review and Risk Evaluation. Risk Evaluation for Perchloroethylene. pp. 35. Available: https://www.regulations.gov/document/EPA-HQ-OPPT-2016-0732-0113
[3] Perchloroethylene (PCE); Regulation Under the Toxic Substances Control Act (TSCA), 88 Fed. Reg. 39,652 (proposed June 16, 2023) (to be codified at 40 C.F.R. 751)
[4] US EPA. (2020). Tetrachloroethylene (perchloroethylene); TSCA Review and Risk Evaluation. Risk Evaluation for Perchloroethylene. pp. 48. Available: https://www.regulations.gov/document/EPA-HQ-OPPT-2016-0732-0113
[5] Guyton, K. Z., Hogan, K. A., Scott, C. S., Cooper, G. S., Bale, A. S., Kopylev, L., Barone, S., Makris, S. L., Glenn, B., Subramaniam, R. P., Gwinn, M. R., Dzubow, R. C., & Chiu, W. A. (2014). Human health effects of tetrachloroethylene: key findings and scientific issues. Environmental health perspectives, 122(4), 325–334. https://doi.org/10.1289/ehp.1307359
[6] US EPA. (2022). Final Risk Evaluation for Perchloroethylene (PCE). Available: https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/final-risk-evaluation-perchloroethylene-pce#docs
[7] 15 U.S.C. §2605(a)
[8] Perchloroethylene (PCE); Regulation Under the Toxic Substances Control Act (TSCA), 88 Fed. Reg. 39,652 pp 39655 (proposed June 16, 2023) (to be codified at 40 C.F.R. 751)

risk uses like conveyorized vapor degreasing. [9] It is not enough that such standards "reduce exposures to PCE" to eliminate unreasonable risk,[10] they must, and EPA has the legal obligation to ensure they do.[11]

We strongly support all prohibitions of PCE proposed by EPA, which are necessary to eliminate unreasonable risk. We also have several concerns about ongoing unreasonable risks to workers and fenceline communities that may result from the continued uses of PCE that would be allowed by the Proposed Rule—uses that comprise the vast majority of current PCE production volume. Even with application of the WCPP, there may be excessive occupational exposures to tens of thousands of workers under the allowed conditions of use.[12] EPA has not conducted a sufficient analysis to determine if unreasonable risks to fenceline communities are eliminated by the Proposed Rule. Moreover, the limited analysis EPA has conducted found that the continuation of certain PCE conditions of use could result in high cancer risks to some fenceline communities that would constitute an unreasonable risk. EPA could address these shortcomings of the Proposed Rule by a near-term prohibition on all conditions of use, which would also eliminate unreasonable risk to fenceline communities. Alternatively, EPA could specify a time-limited period of continued use for the allowed conditions of use to be followed by prohibition. In addition, EPA's decisions, including the determination of a workplace exposure limit and assessment of health benefits to workers, consumers, and fenceline communities, should be informed by a quantitative analysis of non-cancer health effects, as recommended by the National Academies.[13] This approach is more scientifically appropriate and better accounts for risks.

Our detailed comments address the following issues:

1. **EPA should pursue the most comprehensive and health-protective regulatory action for PCE.**
2. **EPA should apply existing methods to generate quantitative estimates of non-cancer effects from chronic PCE exposures.**
3. **EPA's Proposed Risk Management strategy does not fully address the unreasonable risk of continued use of PCE.**
    a. **EPA should adopt a structured framework for determining the importance of maintaining current uses of chemicals undergoing risk management.**
    b. **EPA's Workplace Chemical Protection Program (WCPP) will fail to control any unreasonable risks from ongoing uses of PCE.**
    c. **EPA's proposed Existing Chemical Exposure Limit ("ECEL") does not eliminate unreasonable risk to workers.**
    d. **EPA should not promulgate open-ended allowances for continued use of PCE.**

[9] Perchloroethylene (PCE); Regulation Under the Toxic Substances Control Act (TSCA), 88 Fed. Reg. 39,652 pp 39700 (proposed June 16, 2023) (to be codified at 40 C.F.R. 751)

[10] Perchloroethylene (PCE); Regulation Under the Toxic Substances Control Act (TSCA), 88 Fed. Reg. 39,652 (proposed June 16, 2023) (to be codified at 40 C.F.R. 751)

[11] 15 U.S.C. § 2605(a).

[12] US EPA (2023). Economic Analysis of the Proposed Regulation of Perchloroethylene Under TSCA Section 6(a),Table ES-3. Available: https://www.regulations.gov/document/EPA-HQ-OPPT-2020-0720-0125

[13] National Research Council. (2009). Toward a unified approach to dose-response assessment. In Science and decisions: Advancing risk assessment. https://doi.org/10.17226/12209

    e. **EPA's proposed *de minimis* level is not protective and may result in continued unreasonable risks from PCE-containing products.**
4. **EPA has not adequately evaluated and addressed unreasonable risk to fenceline communities.**
5. **EPA's economic analysis should not use a "lowering factor" to reduce cancer risk reduction estimates without rigorous scientific review.**

We appreciate the opportunity to provide public input. Please do not hesitate to contact us with any questions regarding these or any of our previous comments on PCE.

Sincerely,

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DETAILED COMMENTS

1. EPA should pursue the most comprehensive and health-protective regulatory action for PCE.

In the Proposed Rule, EPA presents a proposed regulatory action in addition to primary and second alternative actions. While we find that all the proposed regulatory actions could be strengthened to better protect human and environmental health, the second alternative action would yield the greatest benefits by prioritizing prohibitions. We provide additional comments on the second alternative action proposal regarding the two TSCA section 6(g)(1)(B) exemptions in point 3d below.

The primary alternative action, on nearly every front, is less protective than the proposed regulatory action and would not protect workers, the general population, or fenceline communities from PCE exposures. This alternative action should not be considered as viable if EPA is to meet its statutory mandate to eliminate unreasonable risks to human health. Among other inadequacies, the primary alternative action proposes increased use of WCPP for conditions of use prohibited under the proposed action, recommends less protective prescriptive controls such as PPE where the proposed action employs a WCPP, and incorporates longer compliance timeframes.[14]

EPA's second alternative action shares more similarities with EPA's proposed regulatory action but prohibits several additional conditions of use that the proposed regulatory action proposes to regulate via a WCPP, and incorporates shorter compliance timeframes overall, including a shorter compliance timeframe of 5 years for the prohibited use of PCE in dry cleaning. Scientifically-supported methods for risk management, such as the NIOSH hierarchy of controls, demonstrate that eliminating or prohibiting hazardous chemicals, as detailed in the points below and outlined in the second alternative regulatory action, is the most effective method for reducing exposures and addressing unreasonable risk to human and environmental health.

Compared to the second alternative action, both the proposed regulatory and primary alternative actions propose longer compliance timelines for the use of PCE in dry cleaning due to the presumed age of existing dry cleaning machines and an assumption that machines are not used past their lifetimes. However, EPA presents no justification for this assumption. As a result of the state-level activity to phase-out PCE, particularly the enactment of California's phase out which took effect in January 2023, newer technologies have been adopted nationwide to transition dry cleaners away from PCE.[15] Therefore, the shorter compliance timeframe of 5 years proposed in the second alternative action seems feasible. In addition to the proposed mitigation strategies in the second alternative action, we recommend that EPA explore scientifically-supported safer alternatives strategies[16] that prioritize the use of less hazardous

[14] Perchloroethylene (PCE); Regulation Under the Toxic Substances Control Act (TSCA), 88 Fed. Reg. 39,652 pp 39682 (proposed June 16, 2023) (to be codified at 40 C.F.R. 751)

[15] Ceballos DM, Fellows KM, Evans AE, Janulewicz PA, Lee EG and Whittaker SG. (2021).Perchloroethylene and Dry Cleaning: It's Time to Move the Industry to Safer Alternatives. Front. Public Health 9:638082. doi:10.3389/fpubh.2021.638082

[16] National Research Council. (2014). Identifying, Comparing, and Implementing Alternatives. In A Framework to Guide Selection of Chemical Alternatives. https://doi.org/10.17226/18872.

alternatives and utilize a participatory stakeholder outreach approach with an equity and social justice lens.[17]

2. EPA should apply existing methods to generate quantitative estimates of non-cancer health effects from chronic PCE exposures.

EPA's methods for non-cancer risk assessment do not provide a quantitative estimate of risk at all exposure levels, and therefore the magnitude of risk reduction or benefits provided by the proposed action and the alternative actions cannot be calculated for non-cancer endpoints.

The analyses supporting EPA's Proposed Rule for PCE maintain the risk characterization methods used for non-cancer effects in the PCE risk evaluation, which rely on calculation of a margin of exposure ("MOE"), defined as:

Margin of Exposure = Non-cancer point of departure / Human exposure.[18]

The MOE approach is a scientifically inappropriate approach for characterizing risk and is inconsistent with TSCA's requirements to use the "best available science" and to ensure protection of "potentially exposed and susceptible subpopulations" ("PESS"). Use of the MOE, which relies on a point of departure ("POD") with no extrapolation to lower doses, is a simplistic approach that only compares the POD to the exposure level and judges whether this ratio "was interpreted as a human health risk" or "indicated negligible concerns for adverse human health effects."[19] The MOE does not estimate the proportion of the exposed population projected to experience a specified health endpoint or the number of individuals affected, and it perpetuates the scientifically flawed notion that a "safe" or "no risk" level of chemical exposure can be identified for a diverse exposed population.[20,21] In addition, the values used to determine whether there is a "sufficient" MOE are not scientifically supported; for example, the 10-fold factor used to represent human variability is an underestimate and insufficient to protect the population from chemical exposures.[22,23] The National Academies of Sciences, Engineering, and Medicine ("NAS")[24] and the World Health Organization ("WHO")[25] have outlined superior methods for

[17] Ceballos DM, Fellows KM, Evans AE, Janulewicz PA, Lee EG, Whittaker SG. Perchloroethylene and Dry Cleaning: It's Time to Move the Industry to Safer Alternatives. Front Public Health. 2021 Mar 5;9:638082. doi: 10.3389/fpubh.2021.638082. PMID: 33748070; PMCID: PMC7973082.

[18] US EPA (2020). Tetrachloroethylene (perchloroethylene); TSCA Review and Risk Evaluation. Risk Evaluation for Perchloroethylene. pp.369. Available: https://www.regulations.gov/document/EPA-HQ-OPPT-2016-0732-0113

[19] US EPA (2020). Tetrachloroethylene (perchloroethylene); TSCA Review and Risk Evaluation. Risk Evaluation for Perchloroethylene. pp.369-370. Available: https://www.regulations.gov/document/EPA-HQ-OPPT-2016-0732-0113

[20] Woodruff, T. J., Rayasam, S. D. G., Axelrad, D. A., Koman, P. D., Chartres, N., Bennett, D. H., Birnbaum, L. S., Brown, P., Carignan, C. C., Cooper, C., Cranor, C. F., Diamond, M. L., Franjevic, S., Gartner, E. C., Hattis, D., Hauser, R., Heiger-Bernays, W., Joglekar, R., Lam, J., . . . Zeise, L. (2023). A science-based agenda for health-protective chemical assessments and decisions: overview and consensus statement. Environ Health, 21(Suppl 1), 132. https://doi.org/10.1186/s12940-022-00930-3

[21] McGartland, A., Revesz, R., Axelrad, D. A., Dockins, C., Sutton, P., & Woodruff, T. J. (2017). Estimating the health benefits of environmental regulations. Science, 357(6350), 457-458. https://doi.org/10.1126/science.aam8204

[22] National Research Council. (2009).Table 4-1. In Science and decisions: Advancing risk assessment. https://doi.org/10.17226/12209

[23] Varshavsky, J. R., Rayasam, S. D. G., Sass, J. B., Axelrad, D. A., Cranor, C. F., Hattis, D., Hauser, R., Koman, P. D., Marquez, E. C., Morello-Frosch, R., Oksas, C., Patton, S., Robinson, J. F., Sathyanarayana, S., Shepard, P. M., & Woodruff, T. J. (2023). Current practice and recommendations for advancing how human variability and susceptibility are considered in chemical risk assessment. Environmental health : a global access science source, 21(Suppl 1), 133. https://doi.org/10.1186/s12940-022-00940-1

[24] National Research Council. (2009). Toward a unified approach to dose-response assessment. In Science and decisions: Advancing risk assessment. https://doi.org/10.17226/12209

[25] WHO. (2017). Guidance document on evaluating and expressing uncertainty in hazard characterization. Harmonization project document 11, 2nd edition. https://www.who.int/publications/i/item/9789241513548

risk estimation that have been demonstrated in published case studies.[26,27 28,29] A recent study by Nielsen et al. applied these methods to estimate risks of neurotoxic effects from chronic PCE exposure, using a study by Echeverria et al.[30] that is one of the key studies in EPA's risk evaluation. The Nielsen et al. study constitutes "reasonably available information" on the "effects of the chemical substance" and the "benefits of the proposed regulatory action"[31] that EPA has not used in preparing its statement of the effects of the Proposed Rule. Additionally, it represents the "best available science" for setting the level of a chronic workplace exposure standard.

We applied the WHO methodology and the analysis of Nielsen et al. to estimate risks of adverse neurotoxic effects from PCE exposure at doses relevant to the Proposed Rule. The neurotoxic effects examined include decrements in visual memory function, which can occur in certain neurodegenerative diseases like Parkinson's disease and multiple sclerosis, and which may have solvent exposure as an etiological component.[32] Our analysis finds that the risks of neurotoxic effects (in particular decrements in visual memory function) at existing occupational exposure levels reported in the PCE risk evaluation are extremely high, as multiple conditions of use have estimated exposures well in excess of the level associated with 1% incidence of effects. EPA should use this type of analysis in the TSCA program to inform its unreasonable risk determinations, the analysis of benefits of regulatory alternatives, and (when workplace chemical protections are proposed for uses that are not prohibited) to determine the level of an Existing Chemical Exposure Limit ("ECEL").

Nielsen et al. (2023) provides separate risk estimates for two approaches – one using as POD the exposure level identified by EPA as a lowest-observed-adverse-effect-level (LOAEL) in the Echeverria study (Nielsen et al. Table 3), and the second using an estimated benchmark dose ("BMD") for a 5% effect level as the POD (Nielsen et al. Table 4). The following summary results use only the second approach (POD is estimated 5% effect level). In addition, while the Nielsen et al. analysis is based on continuous exposures, the analysis we present in these comments is based on 8-hour time-weighted average (TWA) exposure, for direct comparison to the ECEL, which is similarly expressed as an 8-hour TWA. Detailed calculations are provided in the Technical Appendix (Appendix 1) to these comments.

[26] Nielsen, G. H., Heiger-Bernays, W. J., Levy, J. I., White, R. F., Axelrad, D. A., Lam, J., Chartres, N., Abrahamsson, D. P., Rayasam, S. D. G., Shaffer, R. M., Zeise, L., Woodruff, T. J., & Ginsberg, G. L. (2023). Application of probabilistic methods to address variability and uncertainty in estimating risks for non-cancer health effects. Environ Health, 21(Suppl 1), 129. https://doi.org/10.1186/s12940-022-00918-z

[27] Blessinger, T., Davis, A., Chiu, W. A., Stanek, J., Woodall, G. M., Gift, J., Thayer, K. A., & Bussard, D. (2020). Application of a unified probabilistic framework to the dose-response assessment of acrolein. Environ Int, 143, 105953. https://doi.org/10.1016/j.envint.2020.105953

[28] Ginsberg, G. L. (2012). Cadmium risk assessment in relation to background risk of chronic kidney disease. J Toxicol Environ Health A, 75(7), 374-390. https://doi.org/10.1080/15287394.2012.670895

[29] Nielsen, G. H., Heiger-Bernays, W. J., Levy, J. I., White, R. F., Axelrad, D. A., Lam, J., Chartres, N., Abrahamsson, D. P., Rayasam, S. D. G., Shaffer, R. M., Zeise, L., Woodruff, T. J., & Ginsberg, G. L. (2023). Application of probabilistic methods to address variability and uncertainty in estimating risks for non-cancer health effects. Environ Health, 21(Suppl 1), 129. https://doi.org/10.1186/s12940-022-00918-z

[30] Echeverria D, White RF, Sampaio C. A behavioral evaluation of PCE exposure in patients and dry cleaners: a possible relationship between clinical and preclinical effects. Journal of Occupational and Environmental Medicine. 1995;37(6):667–80.

[31] 15 USC §2625 (c)(2)(A)

[32] Nielsen, G. H., Heiger-Bernays, W. J., Levy, J. I., White, R. F., Axelrad, D. A., Lam, J., Chartres, N., Abrahamsson, D. P., Rayasam, S. D. G., Shaffer, R. M., Zeise, L., Woodruff, T. J., & Ginsberg, G. L. (2023). Application of probabilistic methods to address variability and uncertainty in estimating risks for non-cancer health effects. Environ Health, 21(Suppl 1), 129. https://doi.org/10.1186/s12940-022-00918-z

Our analysis finds that:

- 0.21 ppm is the lower bound (95% confidence) human dose at which 1% of the exposed worker population would experience decrements in visual memory function.
- 0.06 ppm is the lower bound (95% confidence) human dose at which 0.1% of the exposed worker population would experience decrements in visual memory function.
- At the proposed ECEL of 0.14 ppm (8-hour time-weighted average), the upper bound risk of decrements in visual memory function is 0.5%, or 1-in-200.
- The level of an ECEL necessary to protect workers from a 1-in-1000 risk of decrements in visual memory function with 95% confidence would be 0.06 ppm.
- The level of an ECEL necessary to protect workers from a 1-in-10,000 risk of decrements in visual memory function with 95% confidence would be 0.02 ppm.
- The level of an ECEL necessary to protect workers to a 1-in-100,000 risk of decrements in visual memory function with 95% confidence would be 0.01 ppm.

These results are just a brief illustration of the information that can be obtained from the application of the WHO methodology and should be a critical input to EPA's risk management decisions under TSCA. The results provided above can be applied to continuous exposure scenarios (e.g., fenceline communities) by multiplying each dose by 5 days/7 days (days of exposure per week) and 10 meters^3 per day / 20 meters^3 per day (breathing rate) [33] – for example, the continuous dose with an upper bound risk of 1-in-10,000 is: 0.02 ppm x 5/7 x 10/20 = 0.008 ppm. It is important to note that the data used for human variability in this analysis, a critical input for risk estimation, may understate the extent of human variability and thus underestimate risk (see Technical Appendix for discussion).

EPA's PCE risk evaluation indicates that there are multiple conditions of use with exposure levels well in excess of the level associated with 1% (1-in-100) risk, or 0.21 ppm (8-hr TWA). Some select examples are shown in the following table.

[33] U.S. EPA (2012). Toxicological review of Tetrachloroethylene (Perchloroethylene), Table 5-1. Available: https://cfpub.epa.gov/ncea/iris_drafts/recordisplay.cfm?deid=192423

Table 1. Occupational exposure summary for selected perchloroethylene occupational conditions of use with exposures greater than level (0.21 ppm) associated with 1% risk of neurological effects

Condition of Use	Number of Workers[a]	Exposure: Central Tendency (ppm, 8-hr TWA)[b]	Exposure: High-End (ppm, 8-hr TWA)[b]	EPA's Proposed Risk Management Action[c]
Adhesives and Sealants	25,596	0.088	0.8	WCPP
Aerosol Degreaser/ Lubricants	12,504[d]	5.5	17	Prohibition
Maskant	497	2.2	57	WCPP
Conveyorized Vapor Degreasing	14[e]	78	186	WCPP

WCPP = Workplace Chemical Protection Program
[a]U.S. EPA (2023). Economic Analysis of the Proposed Regulation of Perchloroethylene Under TSCA Section 6(a), Table ES-3.
[b]US EPA (2020). Risk Evaluation for Perchloroethylene, Table 2-61.
[c]Perchloroethylene (PCE); Regulation Under the Toxic Substances Control Act (TSCA). Proposed Rule. June 16, 2023, 88 FR 39652, Table 2.
[d]A single set of exposure estimates is presented in the Risk Evaluation for Perchloroethylene for two conditions of use: aerosol degreasers and aerosol lubricants. The value shown represents the combined number of workers for the two conditions of use, as reported in the Economic Analysis: 9450 workers for aerosol degreasers and 3054 workers for aerosol lubricants. The PCE risk evaluation (Table 2-40) provides a much greater estimate of 250,000 workers.
[e] The PCE risk evaluation (Table 2-33) provides a much greater estimate of up to 4000 workers.

These numbers show a significant number of workers with very high risk of adverse neurological effects at baseline exposures; EPA can use the risk calculations presented in the Technical Appendix to these comments along with the reported exposure levels and number of workers to estimate the number of workers with adverse neurological effects, and the reduction in affected workers due to the proposed risk management actions (and the alternative actions). This analysis would be particularly important to conduct for this rulemaking since EPA determined that neurotoxicity is "the most sensitive adverse effects driving the unreasonable risk of PCE." [34] It is also important to note that baseline exposures for some conditions of use are greater than the exposures to the medium exposure group (23 ppm) in the Echeverria study that EPA identified as a LOAEL and was used for characterizing risks in the PCE risk evaluation, again indicating a high likelihood of workers experiencing adverse effects – a risk that can be quantified with reasonably available information.

[34] Perchloroethylene (PCE); Regulation Under the Toxic Substances Control Act (TSCA), 88 Fed. Reg. 39,652 pp 39652 (proposed June 16, 2023) (to be codified at 40 C.F.R. 751)

3. EPA's proposed risk management strategy does not fully address the unreasonable risk of continued use of PCE.

In the Proposed Rule, EPA proposes to regulate continued PCE conditions of use primarily through WCPPs, however this approach only accounts for a narrow set of occupational exposures and would not protect the communities that surround facilities where PCE is manufactured, processed, and used. Similarly, it would not protect workers who are exposed to PCE from multiple routes and pathways. Unreasonable risks to workers and fenceline communities would be best addressed by a full prohibition on all conditions of use.

TSCA requires EPA to regulate PCE "to the extent necessary so that [it] no longer presents [unreasonable] risk."[35] If EPA cannot prohibit all uses of PCE, it must, at minimum, improve its proposed measures to eliminate PCE exposures from allowed conditions of use. EPA should start by adopting a framework that determines essentiality of PCE conditions of use. Only if essential uses are identified should EPA pursue science-based methods that increase worker protections, issue time limitations, and prohibit *de minimis* exemptions for allowed uses.

a. EPA should adopt a structured framework for determining the importance of maintaining current uses of chemicals undergoing risk management.

EPA claims to have "compelling reasons not to prohibit" each of several PCE conditions of use, but for many of these conditions of use no rationale is presented in the Federal Register notice. [36] Even for conditions of use with some provided rationale, EPA based these on industry claims (e.g. Spirit AeroSystems regarding the maskant condition of use, The Boeing Company regarding vapor degreasing) and failed to rely on the alternatives assessment it has conducted for PCE.

In place of the unsystematic approach EPA has taken to discussing the importance of selected ongoing uses of PCE, EPA should adopt a structured framework to carefully and consistently consider the importance of specific conditions of use for any chemical subject to risk management. Such a framework would help EPA determine whether a condition of use is critical for reasons of health and safety or is otherwise essential to the functioning of society. As an example, a recent publication by Balan et al.[37] proposed three questions for making such a judgment:

(a) Is the function of the chemical necessary for the product?
(b) Is use of the chemical the safest feasible option?
(c) Is use of the chemical in the product justified because such use is necessary for health, safety, or the functioning of society?

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[35] 15 U.S.C. § 2605(a).

[36] Perchloroethylene (PCE); Regulation Under the Toxic Substances Control Act (TSCA), 88 Fed. Reg. 39,652 pp 39692 (proposed June 16, 2023) (to be codified at 40 C.F.R. 751)

[37] Bălan, S. A., Andrews, D. Q., Blum, A., Diamond, M. L., Fernández, S. R., Harriman, E., Lindstrom, A. B., Reade, A., Richter, L., Sutton, R., Wang, Z., & Kwiatkowski, C. F. (2023). Optimizing Chemicals Management in the United States and Canada through the essential-use approach. Environmental Science & Technology, 57(4), 1568–1575. https://doi.org/10.1021/acs.est.2c05932

Incorporation of this approach into the development of TSCA risk management rules would help EPA make more systematic judgments in determining whether there are "compelling reasons" not to prohibit a condition of use and would also improve EPA's explanation of the rationale for its risk management decisions to the public. Further, early implementation of the "essential-use" approach (e.g., premarket registration) is the most effective way to prevent harmful chemicals from ever entering the marketplace or environment, thus minimizing potential human and environmental harms and the risk of regrettable substitutions.

In the Proposed Rule, EPA proposed a TSCA 6(g) exemption for the National Aeronautics and Space Administration (NASA), and even proposed to create "a Federal agency category of use"[38] for additional agencies like the Department of Defense ("DOD"). We strongly recommend against exceptions for Federal agencies who are chemical users, as that puts their needs, which are very similar to the regulated industry, in a higher priority status than agencies with primary interests in health and regulatory policy. Additionally, the draft rule identifies that "there may be instances where an ongoing use of PCE that has implications for national security or critical infrastructure as it relates to other Federal agencies (e.g., DOD, NASA) is identified after the PCE rule is finalized, but the final rule prohibits that use."[39] However, Federal agencies like DOD and NASA are a part of the interagency review process conducted by the Office of Management and Budget ("OMB"), and the agencies as well as their contractors have more than adequate notification to manage their ongoing uses of PCE. The proposition to create an expedited process to prioritize the needs of Federal agencies that are chemical users would leave thousands of workers and fenceline communities unnecessarily exposed to PCE from allegedly regulated uses with limited to no recourse. The proposition of this exception in the Proposed Rule underscores the previous point on the importance of not equating Federal health agencies and agencies that are chemical users.

b. EPA's Workplace Chemical Protection Program ("WCPP") will fail to control any unreasonable risks from ongoing uses of PCE

EPA's Proposed Rule leaves more workers and workplaces subject to ECELs than previous risk management rules, ultimately leaving workers at continued risk of harm from PCE exposure. The Proposed Rule would allow 80% of PCE production and numerous conditions of use for PCE to continue, including high-risk uses like conveyorized vapor degreasing, based on EPA's conclusion that unreasonable risks for those conditions of use can be eliminated by a WCPP that includes a limitation on chronic exposure (Existing Chemical Exposure Limit – ECEL):

> EPA has determined as a matter of risk management policy that ensuring exposures remain at or below the ECEL will eliminate any unreasonable risk of injury to health from occupational inhalation exposures.[40]

[38] Perchloroethylene (PCE); Regulation Under the Toxic Substances Control Act (TSCA), 88 Fed. Reg. 39,652 pp 39669(proposed June 16, 2023) (to be codified at 40 C.F.R. 751)
[39] Perchloroethylene (PCE); Regulation Under the Toxic Substances Control Act (TSCA), 88 Fed. Reg. 39,652 pp 39669 (proposed June 16, 2023) (to be codified at 40 C.F.R. 751)
[40] Perchloroethylene (PCE); Regulation Under the Toxic Substances Control Act (TSCA), 88 Fed. Reg. 39,652 pp 39659 (proposed June 16, 2023) (to be codified at 40 C.F.R. 751)

There are critical flaws in EPA's determination that the WCPP will control any unreasonable risks from ongoing PCE uses. First, application of probabilistic risk assessment methods indicates a high risk of non-cancer neurological effects at the proposed ECEL of 0.14ppm (as described above). Second, EPA has not sufficiently evaluated whether ongoing uses pose unreasonable risks to fenceline communities. Third, EPA failed to consider the likelihood that there would be instances of non-compliance with the ECEL. This is critical especially for a chemical as hazardous as PCE, where exposures resulting from any violations of the WCPP – particularly exposures above the ECEL – may have serious health consequences.

If EPA proceeds with a rule allowing some conditions of use to continue subject to a WCPP, it should do so sparingly and should revisit the ECEL using the WHO methodology detailed above to provide stronger worker protections. Our calculations (see Technical Appendix) find that protection of workers from a 1-in-100,000 risk of neurological effects would require an ECEL (8-hr TWA) of 0.01 ppm. This calculation could understate true risks because it does not consider the additive impact to workers who also experience non-workplace exposures to PCE, it could underestimate risk and the potential health burden to workers from acute exposure, and it considers neurological effects of PCE in isolation, without accounting for other chemicals that workers are exposed to (whether on the job or through consumer and general population exposure pathways) with neurological effects that are dose-additive with PCE.[41,42] Regarding acute exposures, the Proposed Rule doesn't include a short term exposure limit ("STEL"), unlike the previous risk management Proposed Rule for methylene chloride, and contrary to American Conference of Governmental Industrial Hygienists (ACGIH) and states like California.[43,44] EPA has identified numerous health effects resulting from acute high-level inhalation exposure to PCE such as respiratory tract irritation, kidney dysfunction, and neurological effects. As STELs are evaluated over shorter periods of time (usually 15 minutes), they have the benefit of being able to estimate the burden to workers from acute exposure events compared to an ECEL (8-hr TWA), which can only account for chronic effects. A failure to include STELs could result in a significant underestimation of risk to potentially exposed or susceptible subpopulations, including fenceline communities who could experience acute PCE exposures through accidental spills or releases to the air, soil, or water.

c. EPA's proposed Existing Chemical Exposure Limit (ECEL) does not eliminate unreasonable risk to workers.

As described above, EPA could use the WHO methodology for risk estimation to provide a more quantitative and rigorous basis for setting the ECEL[45] that would also be aligned with its mandate under TSCA to rely on methods consistent with the "best available science". Our analysis, detailed in the Technical Appendix, finds that risk of adverse neurological effects at the

[41] US EPA (2000). Supplementary guidance for conducting health risk assessment of chemical mixtures. https://cfpub.epa.gov/ncea/risk/recordisplay.cfm?deid=20533

[42] US EPA (2023). Science Advisory Committee on Chemicals (SACC) - Notice of Public Meeting and Request for Nominations for a Proposed Approach for Cumulative Risk Assessment of High-Priority Phthalates and a Manufacturer Requested Phthalate. Draft principles of CRA Under TSCA. Available: https://www.regulations.gov/document/EPA-HQ-OPPT-2022-0918-0008

[43] CalOSHA. (2023) Permissible Exposure Limits for Chemical Contaminants. Table AC-1. Available: https://www.dir.ca.gov/title8/5155table_ac1.html

[44] OSHA. (2022). Occupational Chemical Database: Perchloroethylene. Available: https://www.osha.gov/chemicaldata/190

[45] EPA derived the proposed 0.14 ppm (8-hour time weighted average – TWA) ECEL using the same MOE methodology that was used for risk characterization in the PCE risk evaluation. The chronic POD for neurotoxic effects in the risk evaluation is 14.5 ppm (8-hr TWA). The ECEL was calculated by dividing the POD of 14.5 ppm by a benchmark MOE of 100, resulting in an ECEL of 0.14 ppm (14.5/100, rounded down).

proposed ECEL of 0.14ppm may be as high as 0.5 percent, or 1-in-200. A standard with risks as high as 1-in-200 would not eliminate unreasonable risk to workers; this risk level is orders of magnitude greater than the target level for carcinogenic risks as acknowledged by EPA, which is as low as 1-in-1,000,000 (10^{-6}).[46] To eliminate unreasonable occupational risk, the ECEL needs to be set to protect workers from a target risk level of 1-in-1,000,000, which equates to an ECEL that is at or below 0.01 ppm—a limit more than 10 times lower than EPA's proposed ECEL. If EPA fails to quantify worker risks using health-protective scientific methods that represent the "best available science", it will set an unreasonable risk standard that is at least 10 times higher than health-protective levels.

d. EPA should not promulgate open-ended allowances for continued use of PCE.

EPA's Proposed Rule would allow many PCE conditions of use to continue indefinitely, including:[47]

- industrial and commercial use as a processing aid in catalyst regeneration in petrochemical manufacturing;
- industrial and commercial use in paints and coatings in maskants for chemical milling;
- industrial and commercial use as solvent for vapor degreasing (including open-top, closed loop, conveyorized, and web vapor degreasing);
- industrial and commercial use in solvent-based adhesives and sealants;
- domestic manufacturing;
- import;
- processing as a reactant;
- processing into a formulation, mixture, or reaction product in paint and coating products, cleaning and degreasing products, and adhesive and sealant products;
- repackaging;
- recycling;
- disposal; and
- industrial and commercial use as a laboratory chemical.

EPA says it had "compelling reasons not to prohibit" these conditions of use, but for many, little or no rationale is provided in the Federal Register notice. [48]

i. **Processing as a reactant.** EPA proposes to allow continued processing of PCE as a reactant because PCE is used in the manufacturing of the refrigerant chemicals HFC-134a and HFC-125. No time limit is proposed for this use, even though EPA considers continued manufacture of HFC-134a and HFC-125 for refrigerant use to be transitional:

> HFC-134a and HFC-125, while being regulated substances subject to the overall phasedown in production and consumption of regulated substances

[46] Perchloroethylene (PCE); Regulation Under the Toxic Substances Control Act (TSCA), 88 Fed. Reg. 39,652 pp 39700 (proposed June 16, 2023) (to be codified at 40 C.F.R. 751)
[47] Perchloroethylene (PCE); Regulation Under the Toxic Substances Control Act (TSCA), 88 Fed. Reg. 39,652 pp 39700 (proposed June 16, 2023) (to be codified at 40 C.F.R. 751), Table 2.
[48] Perchloroethylene (PCE); Regulation Under the Toxic Substances Control Act (TSCA), 88 Fed. Reg. 39,652 pp 39692 (proposed June 16, 2023) (to be codified at 40 C.F.R. 751)

> under the AIM Act, are likely to be used in blends to facilitate the transition from other HFCs and HFC blends with higher global warming potential in certain applications. [49]

EPA should specify a time-limit on this use, since there will not be a long-term need to produce refrigerants that are intended to be phased out after a transitional period. Without such a time-limit, the Agency opens the potential for the use of PCE and PCE-derived refrigerants to increase over time.

ii. **Industrial and commercial use in paints and coatings in maskants for chemical milling.** EPA discusses the chemical maskant condition of use only in the context of the second alternative regulatory action. Based on information provided by industry, EPA concludes that feasible alternatives are not currently available for use of PCE as a maskant in manufacturing of commercial and military aircraft:

> Representatives from the facility that comprises 85% of the U.S. market for PCE-based maskant chemical milling have described to EPA how efforts to develop new maskant have been ongoing for over 30 years but have not yet found a substitute that meets all of the necessary performance requirements.[50]

EPA then states that 10 years would be sufficient period for exemption of this use from a TSCA prohibition:

> as part of the second alternative regulatory action, EPA would grant a 10-year exemption from prohibition for the industrial and commercial use of PCE as maskant for chemical milling. EPA believes that the information provided by industry on the time needed to identify and qualify substitutes supports a 10-year exemption period.[51]

Instead of adopting the 10 year time-limit for the maskant use in the proposed regulatory action, EPA proposes to allow this condition of use to continue without time limitation. Rather than allowing open-ended use of PCE as a chemical maskant, it should apply a time limitation that would clearly signal a need for elimination of this use and move towards reducing worker and fenceline community exposures resulting from continuation of this use.

iii. **Industrial and commercial use in solvent-based adhesives and sealants.** EPA does not present any rationale for why PCE is necessary for industrial and commercial uses in solvent-based adhesives and sealants. EPA's PCE alternatives assessment identified numerous adhesives and sealants that do not contain PCE. As shown in Table 1, more than

[49] Perchloroethylene (PCE); Regulation Under the Toxic Substances Control Act (TSCA), 88 Fed. Reg. 39,652 pp 39695 (proposed June 16, 2023) (to be codified at 40 C.F.R. 751)
[50] Perchloroethylene (PCE); Regulation Under the Toxic Substances Control Act (TSCA), 88 Fed. Reg. 39,652 pp 39687 (proposed June 16, 2023) (to be codified at 40 C.F.R. 751)
[51] Perchloroethylene (PCE); Regulation Under the Toxic Substances Control Act (TSCA), 88 Fed. Reg. 39,652 pp 39687 (proposed June 16, 2023) (to be codified at 40 C.F.R. 751)

25,000 workers are exposed through this condition of use, and baseline high-end exposure estimates are 4 times the level that may pose a 1-in-100 risk of neurological harm. To ensure protection of these workers from unreasonable risks, as well as protection of neighboring communities, EPA should prohibit these uses.

iv. **Industrial and commercial use as solvent for vapor degreasing**. EPA also proposes to allow continued use of PCE for all forms of vapor degreasing (batch and in-line methods), with no supporting rationale. EPA only observes that in addition to PCE, other hazardous solvents are used for vapor degreasing without connecting this point to the regulatory decision, and without discussing whether safer chemicals are available for vapor degreasing:

> TCE, 1-bromopropane, PCE, and trans-1,2-dichloroethylene are solvents used in vapor degreasing and have or are currently undergoing risk evaluation or risk management under TSCA. In selecting among the TSCA section 6(a) requirements for the proposed approach for conditions of use where alternative substances to PCE may include other solvents undergoing risk evaluation and risk management under TSCA section 6, EPA considered whether technically and economically feasible alternatives that benefit health or the environment will be reasonably available as a substitute. [52]
>
> "[p]rohibition may not be suitable for conditions of use where alternative substances to PCE are more or equally hazardous, in particular for other solvents undergoing risk evaluation and risk management under TSCA section 6."

Despite acknowledging EPA's requirement to consider the availability of safer alternatives under TSCA, the Proposed Rule provides no discussion on safer alternatives (except regarding vapor degreasing of aerospace parts, based on information from a single corporation requesting a 10-year exemption from prohibition, in a separate section of the preamble). This approach poses a significant obstacle to moving the industry generally toward less hazardous chemicals in vapor degreasing and prolongs existing risks to workers and communities from not just PCE but also from other hazardous chemicals. Further, EPA's decision could lead to an endless cycle of failure to prohibit hazardous chemicals in vapor degreasing, especially other TSCA chemicals that are also undergoing risk evaluation. The same argument presented here could be used in future TSCA rules – that is, since PCE continues to be available for vapor degreasing, EPA may decline to prohibit other chemicals in vapor degreasing since such actions could lead to increased use of PCE. A separate PCE Alternatives Assessment conducted by EPA identified numerous non-PCE products for vapor degreasing, and found that:

[52] Perchloroethylene (PCE); Regulation Under the Toxic Substances Control Act (TSCA), 88 Fed. Reg. 39,652 pp 39692 (proposed June 16, 2023) (to be codified at 40 C.F.R. 751)

> 90 percent of the 68 alternative products did not contain any solvent that EPA has determined presents an unreasonable risk under TSCA section 6 and is currently undergoing risk management. [53]

This Alternatives Assessment also cites a 2006 report by the Toxic Use Reduction Institute ("TURI") and says that:

> TURI conducted technical performance testing on available formulations with lower hazard profiles. Generally, these assessments concluded that there were available vapor degreasers that performed well and may possess lower hazard.[54]

EPA's Proposed Rule has not given appropriate consideration to the findings of the alternatives assessment and does not provide "compelling reasons" for allowing this condition of use.

In the absence of scientifically supported reasons that a use of PCE is essential, EPA should prohibit all PCE uses to ensure that unreasonable risks to workers and fenceline communities are eliminated. If there are any cases where EPA can scientifically substantiate not to prohibit a condition of use in the near-term, it should allow continued use for only a specified period of time, to be followed by prohibition. A defined time limitation would allow for the development of necessary alternatives or changes in technologies, while committing to reduced worker and community PCE exposures. In addition, during the period of continued use, EPA should apply PCE concentration and/or volume limitations to ensure that the amount of PCE used and released does not increase.

e. EPA's proposed *de minimis* level is not protective and may result in continued unreasonable risks from PCE-containing products.

EPA proposal to prohibit PCE uses in all consumer products and several industrial/consumer products is not a full prohibition; EPA is proposing to allow up to 0.1% PCE by weight (referred to as a *de minimis* level) in **all** of these products. EPA's justification for this is that it needs to "account for impurities that do not drive the unreasonable risk" [55] and explains the allowed 0.1% level as follows:

> EPA examined the Consumer Exposure Model for the 2020 Risk Evaluation for PCE and found that…consumer use of products that are 0.124% PCE or less by weight would not drive the unreasonable risk from PCE…EPA also conducted an analysis using the Brake Servicing Near-Field/Far-Field exposure model in the 2020 Risk Evaluation for PCE and calculated that a PCE concentration of 0.7% in aerosol brake degreasing products would achieve exposure concentrations at or below the ECEL…Based on these analyses, EPA is

[53] US EPA. (2023). An Alternatives Assessment for Use of Perchloroethylene, pp. 56. Available: https://www.regulations.gov/document/EPA-HQ-OPPT-2020-0720-0104

[54] US EPA. (2023). An Alternatives Assessment for Use of Perchloroethylene, pp. 56. Available: https://www.regulations.gov/document/EPA-HQ-OPPT-2020-0720-0104

[55] Perchloroethylene (PCE); Regulation Under the Toxic Substances Control Act (TSCA), 88 Fed. Reg. 39,652 pp. 39693 (proposed June 16, 2023) (to be codified at 40 C.F.R. 751)

proposing to exclude from prohibition products containing PCE at less than 0.1% by weight.[56]

EPA's determination that products with a 0.1% concentration will not pose unreasonable risks is based on faulty analysis and assumptions. First, the analyses quoted above uses the MOE approach to risk characterization to determine a level without unreasonable risk. As discussed above, the MOE is not a scientific or sensitive method, and EPA's continued use of it will mean that the Agency's actions will underestimate risk. Better methods for risk estimation are reasonably available and these methods demonstrate that the exposure levels judged by EPA to indicate "negligible concerns for adverse human health effects" [57] actually pose a substantial risk of adverse neurological effects (Point 2; Technical Appendix). Second, EPA's analysis, fails to consider aggregate exposure, assuming that consumers and workers are exposed to the *"de minimis"* levels of PCE from only a single product. This assumption underestimates risk as individuals may use multiple PCE-containing products, like spot cleaners, adhesives, and lubricants, at work and/or at home. Additionally, individuals can be consumers, workers, and may also be exposed to through other exposure scenarios that EPA attributes to "general population exposures," for example residents of fenceline communities that have not been adequately assessed by EPA and are not subject to adequate risk management controls in the Proposed Rule.[58]

We strongly recommend against the use of this *de minimis* level and recommend the Agency issue full prohibitions on PCE to eliminate unreasonable risk, particularly to potentially exposed or susceptible subpopulations.

4. EPA has not adequately evaluated and addressed unreasonable risk to fenceline communities.

We support EPA's decision to consider impacts to fenceline communities when regulating PCE under the Proposed Rule, which is needed to comply with TSCA. We also support EPA's decision to consider multiple years of TRI-reported chemical releases to support this analysis, which underscored the "year-to-year variability that exists in the release data and illustrates the potential impact of considering multiple years of TRI data on risk calculations."[59] However, as currently drafted, the Proposed Rule fails to comprehensively account for the ways that fenceline communities are exposed to and harmed by PCE, and thus understates the harm that fenceline residents face from PCE exposures. EPA failed to consider all relevant exposure pathways, aggregate exposures, cumulative risks, non-chemical stressors, and reasonably available chemical release data when evaluating risk to fenceline communities in the Proposed Rule, which was recommended by EPA's Scientific Advisory Committee on Chemicals ("SACC"). Together, these critical omissions result in an underestimation of risk to fenceline community

[56] Perchloroethylene (PCE); Regulation Under the Toxic Substances Control Act (TSCA), 88 Fed. Reg. 39,652 pp. 39693 (proposed June 16, 2023) (to be codified at 40 C.F.R. 751)

[57] US EPA (2020). Tetrachloroethylene (perchloroethylene); TSCA Review and Risk Evaluation. Risk Evaluation for Perchloroethylene. pp.369-370. Available: https://www.regulations.gov/document/EPA-HQ-OPPT-2016-0732-0113

[58] Rayasam, S. D. G., Koman, P. D., Axelrad, D. A., Woodruff, T. J., & Chartres, N. (2022). Toxic Substances Control Act (TSCA) Implementation: How the Amended Law Has Failed to Protect Vulnerable Populations from Toxic Chemicals in the United States. *Environmental science & technology*, *56*(17), 11969–11982. https://doi.org/10.1021/acs.est.2c02079

[59] US EPA (2022). Perchloroethylene: Fenceline Technical Support—Air Pathway. https://www.regulations.gov/document/EPA-HQ-OPPT-2020-0720-0092

residents. EPA found that certain conditions of use pose high cancer risk (greater than 1-in-1,000,000) to fenceline community residents living 1000m from facilities releasing PCE even without including the full analysis. To address these risks and the potential underestimation of risk due to critical methodological flaws in the fenceline assessment approach, EPA should prohibit all uses of PCE which would ensure that all unreasonable risks are eliminated. Alternatively, EPA could more comprehensively account for fenceline community risk by making easily implemented revisions during the risk management stage that would not delay the finalization of the Proposed Rule. For example, EPA could also use existing chemical release data and the same models and information included in the fenceline analysis to better account for all relevant PCE exposure routes, pathways, and combinations thereof in fenceline communities.[60] As detailed below, EPA could also utilize science-based adjustment factors to better account for known but unquantified risks to fenceline communities, including the increased risks from cumulative exposures to multiple chemical and non-chemical stressors.

a. EPA's Proposed Rule fails to comprehensively and accurately reflect fenceline communities' exposures and risks.

In the Proposed Rule, EPA evaluated risk to fenceline communities from PCE exposures largely based on methodologies outlined in its Draft TSCA Screening Level Approach for Assessing Ambient Air and Water Exposures to Fenceline Communities Version 1.0 (the "Fenceline Assessment Approach").[61] This methodology, however, does not accurately capture fenceline communities' exposures and risks. This is particularly significant given EPA's intended use of the Fenceline Assessment Approach as a "screening" tool that can be used to support a finding that a chemical does not present unreasonable risk to a fenceline community and to justify the absence of any regulatory action under TSCA.[62]

EPA's SACC identified several flaws in EPA's Fenceline Assessment Approach, including a failure to consider all relevant exposure pathways, aggregate and cumulative exposures, non-chemical stressors, and reasonably available chemical release data when evaluating fenceline community risk, which EPA failed to address in the Proposed Rule.[63] Under TSCA, EPA's risk management processes must consider and address the real-world risks to fenceline communities from PCE exposures. TSCA further requires EPA to evaluate and regulate chemicals "in a manner consistent with the best available science"[64] and determine whether a chemical presents unreasonable risk to any "potentially exposed or susceptible subpopulation," which is defined as a group that "may be at greater risk than the general population" due to greater chemical exposures, greater susceptibility, or both.[65] The best available scientific protocols and methodologies for conducting risk assessments require consideration of all exposure pathways, taking into account aggregate and cumulative exposures, as well as increased susceptibility to

[60] US EPA. (2022) *Draft TSCA Screening Level Approach for Assessing Ambient Air and Water Exposures to Fenceline Communities Version 1.0*. Document No. EPA-744-D-22-001. Available: https://www.regulations.gov/document/EPA-HQ-OPPT-2021-0415-0012
[61] US EPA. (2022) *Draft TSCA Screening Level Approach for Assessing Ambient Air and Water Exposures to Fenceline Communities Version 1.0*. Document No. EPA-744-D-22-001. Available: https://www.regulations.gov/document/EPA-HQ-OPPT-2021-0415-0012
[62] US EPA. (2022) *Draft TSCA Screening Level Approach for Assessing Ambient Air and Water Exposures to Fenceline Communities Version 1.0*. Document No. EPA-744-D-22-001. Available: https://www.regulations.gov/document/EPA-HQ-OPPT-2021-0415-0012
[63] US EPA. (2022). Final Report on Draft TSCA Screening Level Approach for Assessing Ambient Air and Water Exposures to Fenceline Communities Version 1.0.Available: https://www.epa.gov/system/files/documents/2022-01/draft-fenceline-report_sacc.pdf.
[64] 15 U.S.C. § 2625(h).
[65] 15 U.S.C. § 2605(b)(4)(A); 15 U.S.C. § 2602(12).

harm. [66] Residents of fenceline communities must be considered a "susceptible subpopulation" because they face greater chemical exposures due to their proximity to polluting facilities and contaminated sites, and they often experience greater harm from those exposures due to their cumulative exposures to multiple chemicals as well as other non-chemical stressors such as poverty and racial discrimination.

i. EPA's Proposed Rule fails to examine real-world exposures to PCE

In its Proposed Rule, EPA fails to comprehensively consider real-world PCE exposures in fenceline communities. For example, EPA did not consider complete chemical release data to support its fenceline exposure assessment. While we support EPA's decision to evaluate chemical release data reported to the Toxics Release Inventory ("TRI") for multiple reporting years—the only change EPA has made to address SACC and public comments on the draft fenceline methodology—EPA's Proposed Rule does not consider other sources of chemical release data, including but not limited to data reported to the National Emissions Inventory ("NEI"), or data indicating chemical accidents, spills, and other peak emission events. EPA also failed to examine all relevant routes and pathways, and combinations thereof, through which fenceline communities are exposed to PCE. For example, when evaluating air releases, EPA considers inhalation of PCE, but not potential deposition of the chemical from the air into surface water or soil, which can result in additional fenceline community exposures via drinking water. This omission is of particular concern for fenceline communities located alongside rivers or other surface water bodies, who could be exposed to PCE in their air and surface water.

In addition, EPA separately calculated risks from PCE releases to air and surface water, but it did not combine exposure pathways or consider the risks to communities that both breathe polluted air and drink contaminated water in the Proposed Rule. EPA also considered fenceline community risks only from exposure to PCE from either outdoor air or surface water, even though many community residents may also be exposed to the same chemical in their workplaces and their homes.[67]

The impacts of chemical accidents, spills, or releases that can result in acute risks to fenceline communities were also not considered in the Proposed Rule. These events are "known" and "reasonably foreseen" consequences of chemical manufacturing, transportation, use, and disposal, and therefore, they must be considered under TSCA.[68] EPA also failed to account for the peak exposures that fenceline communities experience during facility start-up, shutdown, and malfunction conditions; as this administration has acknowledged, "*[start-up, shutdown, and malfunction]* events have the potential to lead to higher *emissions* and endanger public health."[69] While the Proposed Rule did provide mitigation strategies for "start-up, shutdown, spills, leaks,

[66] Rayasam, S. D. G., Koman, P. D., Axelrad, D. A., Woodruff, T. J., & Chartres, N. (2022). Toxic Substances Control Act (TSCA) Implementation: How the Amended Law Has Failed to Protect Vulnerable Populations from Toxic Chemicals in the United States. *Environmental science & technology*, *56*(17), 11969–11982. https://doi.org/10.1021/acs.est.2c02079

[67] PCE; Regulation Under the Toxic Substances Control Act (TSCA), 88 Fed. Reg. 28,284 (proposed May 3, 2023) (to be codified at 40 C.F.R. 751); US EPA (2022). *PCE: Fenceline Technical Support—Water Pathway* [Memorandum]. https://www.regulations.gov/document/EPA-HQ-OPPT-2020-0465-0095.

[68] 15 U.S.C. § 2602(4).

[69] Memorandum from Janet McCabe, Deputy Adm'r, EPA, to Reg'l Adm'rs, EPA 2 (Sept. 30, 2021), https://www.epa.gov/system/files/documents/2021-09/oar-21-000-6324.pdf (withdrawing Oct. 9, 2020, memorandum addressing startup, shutdown, and malfunctions in state implementation plans).

ruptures, or other breakdowns"[70] that lead to worker exposures, EPA failed to evaluate how these events may impact nearby fenceline communities. In addition, EPA's modeling effectively erases facilities' peak chemical releases by using a "continuous exposure scenario" that averages a facility's annual emissions over its entire period of operations.[71] Data on peak emissions releases are available from chemical incident reports, stack and facility monitoring records, and other sources that are "reasonably available" to EPA. EPA should also consider the off-site consequences analyses in facilities' Risk Management Plans to estimate the impacts of foreseen but unintended releases of PCE.[72]

The SACC raised many of these concerns in its evaluation of the Fenceline Assessment Approach and stated that "[t]he accuracy and/or completeness of the data used to develop the screening analysis was not adequately supported in the document" and "it did not defensibly represent actual exposure of fenceline communities." The SACC further recommended that EPA consider "multiple source exposures, aggregate exposures, and double aggregate and occupational exposures from workers living near and working at the facilities" where chemicals like PCE are released.[73]

ii. EPA's Proposed Rule fails to account for increased susceptibility to harm from PCE exposures

People living in fenceline communities are more likely to experience adverse health effects from chemical exposures than the general population due to a variety of factors that make them more susceptible to harm.[74,75] These factors can include biological traits like age, genetic makeup, and pre-existing health conditions, which are collectively considered *intrinsic* factors.[76] For example, studies examining air pollution exposure found that underlying diabetes increased the risk of cardiovascular disease from exposure to particulate matter.[77] Susceptibility to harm from chemical exposures can also be increased by external stressors, which include psychosocial stress from experiencing income inequality, violence, racism, healthcare inequity, or food

[70] Perchloroethylene (PCE); Regulation Under the Toxic Substances Control Act (TSCA), 88 Fed. Reg. 39,652 pp 39693 (proposed June 16, 2023) (to be codified at 40 C.F.R. 751)
[71] *E.g.*, Fenceline Assessment Approach, *supra* note 35, at 90.
[72] US EPA. (2009). Risk Management Program Guidance for Offsite Consequence Analysis. Rep. No. EPA 550-B-99-009. Available: https://19january2017snapshot.epa.gov/sites/production/files/2013-11/documents/oca-chps.pdf.
[73] US EPA. (2022). Final Report on Draft TSCA Screening Level Approach for Assessing Ambient Air and Water Exposures to Fenceline Communities Version 1.0 pp 15.Available: https://www.epa.gov/system/files/documents/2022-01/draft-fenceline-report_sacc.pdf
[74] McHale, C. M., Osborne, G., Morello-Frosch, R., Salmon, A. G., Sandy, M. S., Solomon, G., Zhang, L., Smith, M. T., & Zeise, L. (2018). Assessing health risks from multiple environmental stressors: Moving from G×E to I×E. Mutation research. Reviews in mutation research, 775, 11–20. https://doi.org/10.1016/j.mrrev.2017.11.003
[75] Rayasam, S. D. G., Koman, P. D., Axelrad, D. A., Woodruff, T. J., & Chartres, N. (2022). Toxic Substances Control Act (TSCA) Implementation: How the Amended Law Has Failed to Protect Vulnerable Populations from Toxic Chemicals in the United States. Environmental science & technology, 56(17), 11969–11982. https://doi.org/10.1021/acs.est.2c02079.
[76] National Academies of Sciences, Engineering, and Medicine. 2023. Building Confidence in New Evidence Streams for Human Health Risk Assessment: Lessons Learned from Laboratory Mammalian Toxicity Tests. Washington, DC: The National Academies Press. https://doi.org/10.17226/26906.
[77] Zanobetti, A., & Schwartz, J. (2001). Are diabetics more susceptible to the health effects of airborne particles?. American journal of respiratory and critical care medicine, 164(5), 831–833. https://doi.org/10.1164/ajrccm.164.5.2012039; Zanobetti, A., Schwartz, J., & Gold, D. (2000). Are there sensitive subgroups for the effects of airborne particles?. Environmental health perspectives, 108(9), 841–845. https://doi.org/10.1289/ehp.00108841.

insecurity.[78, 79,80,81,82,83,84] In general, people of color in the United States experience disproportionately high levels of these external stressors, collectively known as *extrinsic* susceptibility factors, and as a result, people of color are more susceptible to negative health outcomes from chemical exposures.[85,86]

While any individual internal or external factor can enhance susceptibility, people living in fenceline communities often experience multiple intrinsic and extrinsic factors simultaneously, which increases the potential for even greater susceptibility to adverse effects from chemical exposures.[87] A study examining nine fenceline communities across the United States found that people living within three miles of a polluting facility were more likely to be low-income people of color with reduced access to quality healthcare and healthy foods. In addition, the risk of developing cancer or respiratory illness from air pollution exceeded national averages in all but one of these communities.[88]

In the Proposed Rule, EPA does not consider increased susceptibility when assessing risks to fenceline communities. EPA thus fails to use risk assessment methodologies that are "consistent with the best available science,"[89] and understates the risks posed to fenceline communities. It is well established in the scientific literature that both intrinsic and extrinsic factors can increase susceptibility and thus must be taken into consideration when evaluating

[78] Morello-Frosch, R., Zuk, M., Jerrett, M., Shamasunder, B., & Kyle, A. D. (2011). Understanding the cumulative impacts of inequalities in environmental health: implications for policy. Health affairs (Project Hope), 30(5), 879–887. https://doi.org/10.1377/hlthaff.2011.0153;

[79] McHale, C. M., Osborne, G., Morello-Frosch, R., Salmon, A. G., Sandy, M. S., Solomon, G., Zhang, L., Smith, M. T., & Zeise, L. (2018). Assessing health risks from multiple environmental stressors: Moving from G×E to I×E. Mutation research. Reviews in mutation research, 775, 11–20. https://doi.org/10.1016/j.mrrev.2017.11.003

[80] Payne-Sturges, D. C., Scammell, M. K., Levy, J. I., Cory-Slechta, D. A., Symanski, E., Carr Shmool, J. L., Laumbach, R., Linder, S., & Clougherty, J. E. (2018). Methods for Evaluating the Combined Effects of Chemical and Nonchemical Exposures for Cumulative Environmental Health Risk Assessment. International journal of environmental research and public health, 15(12), 2797. https://doi.org/10.3390/ijerph15122797

[81] Gee, G. C., & Payne-Sturges, D. C. (2004). Environmental health disparities: a framework integrating psychosocial and environmental concepts. Environmental health perspectives, 112(17), 1645–1653. https://doi.org/10.1289/ehp.7074

[82] Solomon, G. M., Morello-Frosch, R., Zeise, L., & Faust, J. B. (2016). Cumulative Environmental Impacts: Science and Policy to Protect Communities. Annual review of public health, 37, 83–96. https://doi.org/10.1146/annurev-publhealth-032315-021807

[83] Koman, P. D., Singla, V., Lam, J., & Woodruff, T. J. (2019). Population susceptibility: A vital consideration in chemical risk evaluation under the Lautenberg Toxic Substances Control Act. PLoS biology, 17(8), e3000372. https://doi.org/10.1371/journal.pbio.3000372

[84] National Academies of Sciences, Engineering, and Medicine. 2023. Building Confidence in New Evidence Streams for Human Health Risk Assessment: Lessons Learned from Laboratory Mammalian Toxicity Tests. Washington, DC: The National Academies Press. https://doi.org/10.17226/26906.

[85] Gee, G. C., & Payne-Sturges, D. C. (2004). Environmental health disparities: a framework integrating psychosocial and environmental concepts. Environmental health perspectives, 112(17), 1645–1653. https://doi.org/10.1289/ehp.7074

[86] Payne-Sturges, D. C., Scammell, M. K., Levy, J. I., Cory-Slechta, D. A., Symanski, E., Carr Shmool, J. L., Laumbach, R., Linder, S., & Clougherty, J. E. (2018). Methods for Evaluating the Combined Effects of Chemical and Nonchemical Exposures for Cumulative Environmental Health Risk Assessment. International journal of environmental research and public health, 15(12), 2797. https://doi.org/10.3390/ijerph15122797.

[87] Environmental Justice Health Alliance for Chemical Policy Reform et al. (2018). Life at the Fenceline: Understanding Cumulative Health Hazards in Environmental Justice Communities. https://ej4all.org/assets/media/documents/Life%20at%20the%20Fenceline%20-%20English%20-%20Public.pdf.

[88] Environmental Justice Health Alliance for Chemical Policy Reform et al. (2018). Life at the Fenceline: Understanding Cumulative Health Hazards in Environmental Justice Communities. https://ej4all.org/assets/media/documents/Life%20at%20the%20Fenceline%20-%20English%20-%20Public.pdf.

[89] 15 U.S.C. § 2625(h).

risks to "potentially exposed or susceptible subpopulations,"[90,91,92,93] including fenceline communities. Further, the National Academy of Sciences has warned that failing to account for both intrinsic and extrinsic susceptibility factors could lead to a vast underestimation of risks from chemical exposures in the human population.[94] The SACC raised similar concerns in its evaluation of EPA's proposed Fenceline Assessment Approach, and stressed the importance of considering the impact of non-chemical stressors in chemical risk evaluation.[95] The SACC further recommended that EPA could apply safety factors to account for factors like co-occurrence of multiple chemical and non-chemical stressors.[96] To comply with TSCA and adhere to recommendations provided by EPA's own scientific peer reviewers, EPA must consider not only fenceline communities' increased exposures but also their heightened susceptibility to PCE as a result of intrinsic and extrinsic susceptibility factors. In the near term, we urge EPA to apply adjustment factors during the risk management stage to account for the unquantified increase in fenceline communities' susceptibility to PCE. To account for increased susceptibility to harm in younger age groups, California EPA's Office of Environmental Health Hazard Assessment ("OEHHA") now relies on a 30X intra-species adjustment factor that is three times higher than the one currently used by EPA.[12] We recommend that EPA apply an expanded intra-species adjustment factor of 42X, consistent with the 42-fold human variability in toxicokinetic and toxicodynamic responses to chemical exposures observed by the WHO using a probabilistic method.[97] Application of this expanded adjustment factor will more adequately capture human variability in the response to PCE exposures, including in highly exposed or susceptible subpopulations, and is consistent with recommendations made by scientific experts.[98]

iii. EPA's Proposed Rule fails to account for cumulative exposures to multiple chemicals

The Proposed Rule also fails to consider communities' cumulative exposures to other chemicals, in addition to PCE, from a variety of sources and pathways. In doing so, EPA is ignoring the real-world exposures and risks faced by many fenceline communities**.** EPA's failure to consider cumulative exposures is particularly problematic for chemicals that contribute towards common adverse health outcomes, which could increase the likelihood of harm to exposed

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[90] National Research Council. 2009. Science and Decisions: Advancing Risk Assessment. pp 110-111.Washington, DC: The National Academies Press. https://doi.org/10.17226/12209

[91] Morello-Frosch, R., Zuk, M., Jerrett, M, Shamasunder, B., & Kyle, A. D. (2011). Understanding the cumulative impacts of inequalities in environmental health: implications for policy. Health affairs (Project Hope), 30(5), 879–887. https://doi.org/10.1377/hlthaff.2011.0153

[92] McHale, C. M., Osborne, G., Morello-Frosch, R., Salmon, A. G., Sandy, M. S., Solomon, G., Zhang, L., Smith, M. T., & Zeise, L. (2018). Assessing health risks from multiple environmental stressors: Moving from G×E to I×E. Mutation research. Reviews in mutation research, 775, 11–20. https://doi.org/10.1016/j.mrrev.2017.11.003

[93] Payne-Sturges, D. C., Scammell, M. K., Levy, J. I., Cory-Slechta, D. A., Symanski, E., Carr Shmool, J. L., Laumbach, R., Linder, S., & Clougherty, J. E. (2018). Methods for Evaluating the Combined Effects of Chemical and Nonchemical Exposures for Cumulative Environmental Health Risk Assessment. International journal of environmental research and public health, 15(12), 2797. https://doi.org/10.3390/ijerph15122797.

[94] National Research Council. 2009. Science and Decisions: Advancing Risk Assessment. pp 9-10.Washington, DC: The National Academies Press. https://doi.org/10.17226/12209

[95] US EPA. (2022). Final Report on Draft TSCA Screening Level Approach for Assessing Ambient Air and Water Exposures to Fenceline Communities Version 1.0 pp 49.Available: https://www.epa.gov/system/files/documents/2022-01/draft-fenceline-report_sacc.pdf

[96] US EPA. (2022). Final Report on Draft TSCA Screening Level Approach for Assessing Ambient Air and Water Exposures to Fenceline Communities Version 1.0 pp 65.Available: https://www.epa.gov/system/files/documents/2022-01/draft-fenceline-report_sacc.pdf

[97] WHO IPCS. (2017). Guidance Document on Evaluating and Expressing Uncertainty in Hazard Characterization. Available: http://www.inchem.org/documents/harmproj/harmproj/harmproj11.pdf.

[98] Varshavsky, J. R., Rayasam, S. D. G., Sass, J. B., Axelrad, D. A., Cranor, C. F., Hattis, D., Hauser, R., Koman, P. D., Marquez, E. C., Morello-Frosch, R., Oksas, C., Patton, S., Robinson, J. F., Sathyanarayana, S., Shepard, P. M., & Woodruff, T. J. (2023). Current practice and recommendations for advancing how human variability and susceptibility are considered in chemical risk assessment. Environmental health : a global access science source, 21(Suppl 1), 133. https://doi.org/10.1186/s12940-022-00940-1

communities.[99,100,101, 102,103] For EPA to assess fenceline communities' risks without taking into account their cumulative exposures is not "consistent with the best available science,"[104] in violation of TSCA. The National Research Council has not only recommended the consideration of cumulative exposures in risk evaluations, but has also warned that "risk assessment might become irrelevant in many decision contexts" without it.[105,106] TSCA requires EPA to use scientifically supported approaches and methodologies to "integrate and assess available information on hazards and exposures"—including those that contribute to cumulative risks in fenceline communities.[107] This information includes a recent study that outlined methods for identifying cumulative exposures to chemicals that contribute to similar adverse health effects in highly exposed and susceptible groups.[108] Consistent with recommendations made by scientific experts,[109] EPA should apply additional adjustment factors during the risk management stage to account for any cumulative risks that were not measured in EPA's prior risk evaluation of PCE.

b. EPA fails to propose methods to reduce risks already identified for fenceline communities

EPA found that certain conditions of use pose high cancer risk to fenceline communities that constitutes unreasonable risk, even without appropriately accounting for all exposures and risks. For example, in its Fenceline Technical Support Analysis for the air pathway, EPA found that PCE ambient air exposures resulting from 6-year average releases reported to the TRI for 29 facilities were associated with cancer risk (more than 1×10^{-6}) to fenceline residents for nine conditions of use, six of which are allowed under the Proposed Rule.[110] However, EPA failed to propose adequate measures to mitigate these risks. Instead, EPA concluded that the prohibited uses and WCPP "is expected to reduce the risks identified in the screening analysis to any general population or fenceline communities close to facilities engaging in PCE use."[111] While

[99] National Research Council. 2008. Phthalates and Cumulative Risk Assessment: The Tasks Ahead. pp 4-11. Washington, DC: The National Academies Press. https://doi.org/10.17226/12528.

[100] Solomon, G. M., Morello-Frosch, R., Zeise, L., & Faust, J. B. (2016). Cumulative Environmental Impacts: Science and Policy to Protect Communities. Annual review of public health, 37, 83–96. https://doi.org/10.1146/annurev-publhealth-032315-021807;

[101] Rayasam, S. D. G., Koman, P. D., Axelrad, D. A., Woodruff, T. J., & Chartres, N. (2022). Toxic Substances Control Act (TSCA) Implementation: How the Amended Law Has Failed to Protect Vulnerable Populations from Toxic Chemicals in the United States. *Environmental science & technology*, *56*(17), 11969–11982. https://doi.org/10.1021/acs.est.2c02079

[102] Vandenberg, L. N., Rayasam, S. D. G., Axelrad, D. A., Bennett, D. H., Brown, P., Carignan, C. C., Chartres, N., Diamond, M. L., Joglekar, R., Shamasunder, B., Shrader-Frechette, K., Subra, W. A., Zarker, K., & Woodruff, T. J. (2023). Addressing systemic problems with exposure assessments to protect the public's health. Environmental health : a global access science source, 21(Suppl 1), 121. https://doi.org/10.1186/s12940-022-00917-0

[103] Pullen Fedinick, K., Yiliqi, I., Lam, Y., Lennett, D., Singla, V., Rotkin-Ellman, M., & Sass, J. (2021). A Cumulative Framework for Identifying Overburdened Populations under the Toxic Substances Control Act: Formaldehyde Case Study. International journal of environmental research and public health, 18(11), 6002. https://doi.org/10.3390/ijerph18116002.

[104] 15 U.S.C. § 2625(h).

[105] National Research Council. 2009. Science and Decisions: Advancing Risk Assessment. pp 9-10.Washington, DC: The National Academies Press. https://doi.org/10.17226/12209

[106] National Research Council. 2008. Phthalates and Cumulative Risk Assessment: The Tasks Ahead.pp 4-11. Washington, DC: The National Academies Press. https://doi.org/10.17226/12528.

[107] 15 U.S.C. § 2605(b)(4)(F)(i).

[108] Pullen Fedinick, K., Yiliqi, I., Lam, Y., Lennett, D., Singla, V., Rotkin-Ellman, M., & Sass, J. (2021). A Cumulative Framework for Identifying Overburdened Populations under the Toxic Substances Control Act: Formaldehyde Case Study. International journal of environmental research and public health, 18(11), 6002. https://doi.org/10.3390/ijerph18116002.

[109] Varshavsky, J. R., Rayasam, S. D. G., Sass, J. B., Axelrad, D. A., Cranor, C. F., Hattis, D., Hauser, R., Koman, P. D., Marquez, E. C., Morello-Frosch, R., Oksas, C., Patton, S., Robinson, J. F., Sathyanarayana, S., Shepard, P. M., & Woodruff, T. J. (2023). Current practice and recommendations for advancing how human variability and susceptibility are considered in chemical risk assessment. Environmental health : a global access science source, 21(Suppl 1), 133. pp.3. https://doi.org/10.1186/s12940-022-00940-1

[110] US EPA (2022). Perchloroethylene: Fenceline Technical Support—Air Pathway. Available: https://www.regulations.gov/document/EPA-HQ-OPPT-2020-0720-0092

[111] Perchloroethylene (PCE); Regulation Under the Toxic Substances Control Act (TSCA), 88 Fed. Reg. 39,652 pp 39693 (proposed June 16, 2023) (to be codified at 40 C.F.R. 751)

EPA highlighted that "[u]nder the proposed WCPP, facilities would need to monitor PCE air concentrations by taking personal breathing zone air samples of potentially exposed persons, which would allow facilities to better understand and manage the total releases of PCE within the facility and potentially stack and fugitive emissions", EPA later requested comment on whether these controls could actually result in "increased air releases of PCE from the workplace".[112] In doing so, EPA is acknowledging that WCPP mitigation strategies could potentially *increase* facility releases, putting fenceline communities at higher risk of harm from PCE exposures. EPA must issue a prohibition on all PCE conditions of use to ensure that the chemical no longer presents unreasonable risk to fenceline communities. If EPA does not broadly ban PCE, it must more comprehensively account for fenceline community risks by making near-term revisions during the risk management stage, as detailed above, that would not delay the finalization of the Proposed Rule.

5. EPA's economic analysis should not use a "lowering factor" to reduce cancer risk reduction estimates without rigorous scientific review

EPA's economic analysis uses two methods for calculating the estimated cancer risk reduction from the Proposed Rule. One method applies a scientifically unsupported "lowering factor" method to reduce the projected cancer benefits of the Proposed Rule with a particular impact on older populations.[113] The explanation of the lowering factor is extremely brief and unclear, but it appears that this method applies novel and scientifically unsupported assumptions that the cancer risk reduction per year of reduced or eliminated exposure declines as age increases. This is not only incorrect, as advanced age is a risk factor for many cancers,[114] but it results in underestimation of the cancer benefits and, depending on the cancer type, this adjustment reduces cancer risk reduction estimates by as much as two-thirds. This novel method does not appear to be scientifically-based, as the only citation provided for this approach is EPA's 2013 economic analysis of standards for formaldehyde in composite wood products,[115] which like the PCE Proposed Rule, was issued by the Office of Chemical Safety and Pollution Prevention. EPA does not cite any scientific publications, and there is no indication that this proposed "lowering factor" approach has been peer reviewed or otherwise subject to scrutiny by scientific experts. This goes directly against EPA's mandate under TSCA to evaluate risk in a manner consistent with the "best available science." The flawed application of a "lowering factor" disproportionately reduces estimated benefits to older populations, a subgroup that EPA considers a "potentially exposed or susceptible subpopulation (PESS)." EPA should not apply this approach to its benefits analysis, or any other assessment, until it has been reviewed and supported by a rigorous scientific review. Additionally, EPA should apply the excess lifetime risk regardless of age when determining the benefits from the Proposed Rule, as has been standard practice.

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[112] Perchloroethylene (PCE); Regulation Under the Toxic Substances Control Act (TSCA), 88 Fed. Reg. 39,652 pp 39701 (proposed June 16, 2023) (to be codified at 40 C.F.R. 751).

[113] US EPA (2023). Economic Analysis of the Proposed Regulation of Perchloroethylene Under TSCA Section 6(a), pp 8-20. Available: https://www.regulations.gov/document/EPA-HQ-OPPT-2020-0720-0125

[114] National Cancer Institute. (2021). Age and Cancer Risk. Available: https://www.cancer.gov/about-cancer/causes-prevention/risk/age

[115] US EPA (2013). Economic Analysis of the Formaldehyde Standards for Composite Wood Products Act Implementing Regulations Proposed Rule. Office of Chemical Safety and Pollution Prevention.Available: https://www.regulations.gov/document/EPA-HQ-OPPT-2016-0461-0037

Technical Appendix: Analysis of perchloroethylene neurological effects (decrements in visual memory) risk using WHO/IPCS methodology

In the TSCA perchloroethylene (PCE) risk evaluation, EPA identified neurotoxicity as a key endpoint for estimation of risks from chronic exposures. The TSCA evaluation used the dose-response analysis developed in the IRIS assessment of PCE, [116] which found neurotoxicity to be the most sensitive endpoint based on the epidemiological studies of Cavalleri et al., 1994 and Echeverria et al., 1995. Both the IRIS and TSCA assessments calculated a point of departure (POD) by identifying a lowest-observed-adverse-effect-level (LOAEL) for each of the two studies, and calculating a midpoint of these LOAELs. The TSCA point of departure is 14.5 ppm (8-hour time-weighted average - TWA).

For risk characterization of non-cancer health effects, the TSCA risk evaluation calculates a "margin of exposure" (MOE) for each exposure scenario, which is the ratio of the point of departure (POD) to the exposure level. For neurological effects of PCE, the TSCA risk evaluation concluded that an MOE greater than 100 "indicated negligible concerns for adverse human health effects." [117] EPA's approach to risk characterization does not actually estimate risks of adverse neurological effects in the population with chronic exposure to PCE, but instead simply applies a "bright line" judgment of whether or not the MOE is adequate. A more informative approach for both risk characterization and risk management would be to apply the probabilistic dose-response assessment methods of the International Programme on Chemical Safety (IPCS), part of the World Health Organization (WHO), to estimate the risk of liver effects at various levels of exposure.

Nielsen et al. (2023)[118] applied the WHO/IPCS approach for continuous endpoints and the "approximate probabilistic" calculation (see IPCS report Fig 3.5, panel C)[119] to estimate risks of adverse neurological effects from chronic PCE exposure. Although the IPCS has provided the spreadsheet APROBA tool to facilitate calculations using the "approximate probabilistic" method, APROBA is designed for use of animal data and was not used for in the analysis by Nielsen et al. which was based on data from a human epidemiological study.

Point of Departure

Nielsen et al. derived two alternate points of departure (PODs) from the study by Echeverria et al. for application of the IPCS methodology. In the first analysis, the POD is based on the LOAEL identified by EPA. In the second analysis, Nielsen et al. estimate a 5% effect level, with uncertainty, from the data reported by Echeverria et al. All methods and results discussed below are based on the second method, using the estimated 5% effect level as POD. Results from the

[116] U.S. EPA (2012). Toxicological review of Tetrachloroethylene (Perchloroethylene), Table 5-1. Available: https://cfpub.epa.gov/ncea/iris_drafts/recordisplay.cfm?deid=192423

[117] US EPA (2020). Tetrachloroethylene (perchloroethylene); TSCA Review and Risk Evaluation. Risk Evaluation for Perchloroethylene. pp.370. Available: https://www.regulations.gov/document/EPA-HQ-OPPT-2016-0732-0113

[118] Nielsen, G. H., Heiger-Bernays, W. J., Levy, J. I., White, R. F., Axelrad, D. A., Lam, J., Chartres, N., Abrahamsson, D. P., Rayasam, S. D. G., Shaffer, R. M., Zeise, L., Woodruff, T. J., & Ginsberg, G. L. (2023). Application of probabilistic methods to address variability and uncertainty in estimating risks for non-cancer health effects. Environ Health, 21(Suppl 1), 129. https://doi.org/10.1186/s12940-022-00918-z

[119] WHO. (2017). Guidance document on evaluating and expressing uncertainty in hazard characterization. Harmonization project document 11, 2nd edition. https://www.who.int/publications/i/item/9789241513548

first method, for incidence levels of 1% and 0.1%, are available in the Nielsen et al. publication.[120]

In the second method, Nielsen et al. estimate a 5% effect level (i.e., benchmark dose, or BMD) by extrapolation from results reported by Echeverria et al. for the medium exposure group. Nielsen et al. converted the exposure levels presented by Echeverria et al., which represented an occupational exposure scenario, to continuous exposure. For presentation here, exposures for the occupational exposure scenario, representing an 8-hour time-weighted average (TWA) are used to enable easy comparison to EPA's proposed existing chemical exposure limit (ECEL), which is 0.14 ppm (8-hr TWA).

Data from Echeverria et al. indicate that an incremental exposure of 12 ppm was associated with a central estimate reduction of 6% on a visual memory test, with a 95% upper confidence limit (UCL) of 11%. The central estimate BMD for a 5% effect level (BMD_{05}) was determined by linear extrapolation from the 6% effect level (12 ppm) as follows: BMD_{05} = (5%/6%) x 12 ppm = 10 ppm. The BMD lower confidence limit ($BMDL_{05}$) was calculated by similar extrapolation using the UCL on the effect size (11%) for the medium exposure group in place of the central estimate of the effect size (6%): $BMDL_{05}$ = (5%/11%) x 12 ppm = 5.5 ppm.

The IPCS methodology requires expression of the POD as a P50 (50^{th} percentile) value and its uncertainty as a P95/P50 value (ratio of 95^{th} percentile to P50). The P50 is the BMD_{05} of 10 ppm, and the P95/P50 is the ratio of the BMD to the BMDL: P95/P50 = BMD_{05}/ $BMDL_{05}$ = 10 ppm / 5.5 ppm = 1.8.

In the IPCS approximate probabilistic calculation template, those values are entered as follows:

Aspect	P50	P95/P50
BMD_{05}	10 ppm	1.8

Adjustment factor for human variability

In the IPCS methodology, the value of the human variability adjustment factor ($AF_{intraspecies}$) varies depending on the incidence of the adverse effect in the exposed population – with a larger adjustment factor necessary to extrapolate to lower levels of incidence. The IPCS report provides $AF_{intraspecies}$ for several incidence (I) values. As with the POD, the IPCS methodology uses the P50 as a central estimate and the P95/P50 as a measure of uncertainty for each value of I. $AF_{intraspecies}$ values provided by IPCS for several values of I, along with an additional value of I of interest for this analysis, are provided in the following table:

[120] Nielsen, G. H., Heiger-Bernays, W. J., Levy, J. I., White, R. F., Axelrad, D. A., Lam, J., Chartres, N., Abrahamsson, D. P., Rayasam, S. D. G., Shaffer, R. M., Zeise, L., Woodruff, T. J., & Ginsberg, G. L. (2023). Application of probabilistic methods to address variability and uncertainty in estimating risks for non-cancer health effects. Environ Health, 21(Suppl 1), 129, Table 3. https://doi.org/10.1186/s12940-022-00918-z

Lognormal approximation of uncertainty distributions for intraspecies variability for varying levels of population incidence (I)		
Incidence (I)	**$AF_{intraspecies}$**	
	P50	**P95/P50**
1%[a]	9.69	4.32
0.5%[a]	12.36	5.06
0.1% (1-in-1,000)[a]	20.42	6.99
0.01% (1-in-10,000)[a]	37.71	10.39
0.001% (1-in-100,000)[b]	64.25	14.65

[a] IPCS Table 4.5
[b] Calculated for this analysis using the same methods that were used to derive IPCS Table 4.5

Calculation of HD_M^I

The output of the IPCS methodology is generically described as an HD_M^I value – the human dose (HD) associated with a particular magnitude of effect M at a particular population incidence I. For this analysis, the "M" represents a 5% decrement is visual memory test scores, corresponding to the benchmark response used in calculating the POD (i.e., BMD_{05}). The IPCS approach is a probabilistic method, so the HD_M^I is a distribution; selected values from that distribution are presented as follows:

- P05: 5th percentile estimate (lower confidence limit) of HD_M^I (this value is shown in **bold**)
- P50: 50th percentile estimate (median) of HD_M^I
- P95: 95th percentile estimate (upper confidence limit) of HD_M^I

The following tables present the results for I = 1%, 0.5%, 0.1%, 0.01% and 0.001% using the POD and $AF_{intraspecies}$ values shown above. Because the point of departure is a BMD derived from a human study, other adjustment factors (for interspecies extrapolation, LOAEL-to-NOAEL) are not applied in this analysis.

Calculation of $HD_M^{1\%}$ for risk of decrements in visual memory from chronic perchloroethylene exposure (Incidence = 1%; 8-hour time-weighted average)			
Aspect	**P50**	**P95/P50**	**Comments**
BMD_{05}	10 ppm	1.8	POD – derived from Echeverria et al.
$AF_{intraspecies\ (I=1\%)}$	9.69	4.32	IPCS human variability distribution, I=1%
$HD_M^{1\%}$	1.03 ppm	4.85[a]	*Median* = 10 ppm/9.69
	P05	**P95**	
$HD_M^{1\%}$	**0.21 ppm**	5 ppm	*Lower and Upper Confidence Limits*[b]
[a](Composite P95/P50) = 10^[(log 1.8)^2 + (log 4.32)^2]$^{0.5}$ = 4.85 [b]P05 = P50 / (Composite P95/P50); P95 = P50 x (Composite P95/P50)			

Calculation of $HD_M^{0.5\%}$ for risk of decrements in visual memory from chronic perchloroethylene exposure (Incidence = 0.5%; 8-hour time-weighted average)			
Aspect	**P50**	**P95/P50**	**Comments**
BMD_{05}	10 ppm	1.8	POD – derived from Echeverria et al.
$AF_{intraspecies\ (I=0.5\%)}$	12.36	5.06	IPCS human variability distribution, I=0.5%
$HD_M^{0.5\%}$	0.81	5.61[a]	*Median* = 10 ppm/12.36
	P05	**P95**	
$HD_M^{0.5\%}$	**0.14 ppm**	4.5 ppm	*Lower and Upper Confidence Limits*[b]
[a](Composite P95/P50) = 10^[(log 1.8)^2 + (log 5.06)^2]$^{0.5}$ = 5.61 [b]P05 = P50 / (Composite P95/P50); P95 = P50 x (Composite P95/P50)			

Calculation of $HD_M^{0.1\%}$ for risk of decrements in visual memory from chronic perchloroethylene exposure (Incidence = 0.1%; 8-hour time-weighted average)			
Aspect	**P50**	**P95/P50**	**Comments**
BMD_{05}	10 ppm	1.8	POD – derived from Echeverria et al.
$AF_{intraspecies\ (I=0.1\%)}$	20.42	6.99	IPCS human variability distribution, I=0.1%
$HD_M^{0.1\%}$	0.49 ppm	7.62[a]	*Median* = 10 ppm/20.42
	P05	**P95**	
$HD_M^{0.1\%}$	**0.06 ppm**	3.7 ppm	*Lower and Upper Confidence Limits*[b]

[a](Composite P95/P50) = 10^[(log 1.8)^2 + (log 6.99)^2]$^{0.5}$ = 7.62
[b]P05 = P50 / (Composite P95/P50);
P95 = P50 x (Composite P95/P50)

Calculation of $HD_M^{0.01\%}$ for risk of decrements in visual memory from chronic perchloroethylene exposure (Incidence = 0.01%; 8-hour time-weighted average)			
Aspect	**P50**	**P95/P50**	**Comments**
BMD_{05}	10 ppm	1.8	POD – derived from Echeverria et al.
$AF_{intraspecies\ (I=0.01\%)}$	37.71	10.39	IPCS human variability distribution, I=0.01%
$HD_M^{0.01\%}$	0.27 ppm	11.17[a]	*Median* = 10 ppm/37.71
	P05	**P95**	
$HD_M^{0.01\%}$	**0.02 ppm**	3.0 ppm	*Lower and Upper Confidence Limits*[b]

[a](Composite P95/P50) = 10^[(log 1.8)^2 + (log 10.39)^2]$^{0.5}$ = 11.17
[b]P05 = P50 / (Composite P95/P50);
P95 = P50 x (Composite P95/P50)

Calculation of $HD_M^{0.001\%}$ for risk of decrements in visual memory from chronic perchloroethylene exposure (Incidence = 0.001%; 8-hour time-weighted average)			
Aspect	**P50**	**P95/P50**	**Comments**
BMD_{05}	10 ppm	1.8	POD – derived from Echeverria et al.
$AF_{intraspecies\ (I=0.001\%)}$	64.25	14.65	IPCS human variability distribution, I=0.001%
$HD_M^{0.001\%}$	0.16 ppm	15.61[a]	*Median* = 10 ppm/64.25
	P05	**P95**	
$HD_M^{0.001\%}$	**0.01 ppm**	2.4 ppm	*Lower and Upper Confidence Limits*[b]
[a](Composite P95/P50) = 10^[(log 1.8)^2 + (log 14.65)^2]$^{0.5}$ = 15.61 [b]P05 = P50 / (Composite P95/P50); P95 = P50 x (Composite P95/P50)			

Interpretation of results

Based on these calculations, we find that:

- 0.21 ppm (8-hr TWA) is the lower bound (95% confidence) human dose at which 1% of the exposed worker population would experience decrements in visual memory function.
- 0.06 ppm (8-hr TWA) is the lower bound (95% confidence) human dose at which 0.1% of the exposed worker population would experience decrements in visual memory function.
- At EPA's proposed ECEL of 0.14 ppm (8-hr TWA), the upper bound risk of decrements in visual memory function is 0.5%, or 1-in-200.
- This model can also be used to calculate values for an ECEL necessary to provide confidence that risk of decrements in visual memory function is no greater than 0.01% (1-in-10,000 or 10^{-4} risk), or 0.001% (1-in-100,000 or 10^{-5} risk). The values are:
    - 0.01% risk: 0.02 ppm (8-hr TWA); and
    - 0.001% risk: 0.01 ppm (8-hr TWA).

Risk of visual memory decrements can also be estimated for continuous exposures scenarios, e.g. for fenceline communities. Per the EPA IRIS assessment, values for continuous exposure can be obtained by multiplying the 8-hour time weighted average by 5 days/7 days (days of exposure per week) and 10 meters^3 per day /20 meters^3 per day (breathing rate),[121] which simplifies to a factor of (5/7) x (10/20) = 0.36. The resulting continuous exposure doses associated with various levels of risk are therefore:

[121] U.S. EPA (2012). Toxicological review of Tetrachloroethylene (Perchloroethylene), Table 5-1. Available: https://cfpub.epa.gov/ncea/iris_drafts/recordisplay.cfm?deid=192423

- 0.08 ppm (continuous exposure) is the lower bound (95% confidence) human dose at which 1% of the exposed population would experience decrements in visual memory function.
- 0.05 ppm (continuous exposure) is the lower bound (95% confidence) human dose at which 0.5% of the exposed population would experience decrements in visual memory function.
- 0.02 ppm (continuous exposure) is the lower bound (95% confidence) human dose at which 0.1% of the exposed population would experience decrements in visual memory function.
- 0.008 ppm (continuous exposure) is the lower bound (95% confidence) human dose at which 0.01% of the exposed population would experience decrements in visual memory function.
- 0.004 ppm (continuous exposure) is the lower bound (95% confidence) human dose at which 0.001% of the exposed population would experience decrements in visual memory function.

An important caveat to these calculations is that the values used to represent human variability may be understated. The IPCS default human variability distribution is based on 37 data sets for human toxicokinetic variability and 34 data sets for human toxicodynamic variability. Most of these data sets were obtained from controlled human exposure studies of pharmaceuticals conducted in small samples of healthy adults, representing considerably less variability than found in the general population.[122,123,124] If human variability is underestimated, then the actual dose associated with each incidence level (e.g. I =1%, I = 0.1%) will be lower than the values obtained from this analysis – or in other words, risk at each dose will be underestimated. These caveats would be particularly important for application of the risk estimates to the general population (including residents of fenceline communities) rather than workers exposed on the job; however even for workers the magnitude of human variability is very likely to be understated.

[122] WHO. (2017). Guidance document on evaluating and expressing uncertainty in hazard characterization. Harmonization project document 11, 2nd edition. https://www.who.int/publications/i/item/9789241513548

[123] Hattis, D. & Lynch, M.K. (2007). Empirically observed distributions of pharmacokinetic and pharmacodynamic variability in humans—Implications for the derivation of single-point component uncertainty factors providing equivalent protection as existing reference doses. In Lipscomb, J.C. & Ohanian, E.V. (Eds.), Toxicokinetics in risk assessment. pp. 69-93. Taylor & Francis Group. https://doi.org/10.1201/b14275

[124] Axelrad, D. A., Setzer, R. W., Bateson, T. F., DeVito, M., Dzubow, R. C., Fitzpatrick, J. W., Frame, A. M., Hogan, K. A., Houck, K., & Stewart, M. (2019). Methods for evaluating variability in human health dose-response characterization. Hum Ecol Risk Assess, 25, 1-24. https://doi.org/10.1080/10807039.2019.1615828