HSIA
halogenated solvents industry alliance, inc.

August 1, 2022

Kelly Summers
Office of Pollution Prevention and Toxics (7404M)
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460–0001

Re: Docket No. EPA-HQ-OPPT-2016-0732

Dear Ms. Summers:

These comments are submitted on Perchloroethylene (PCE); Draft Revision to Toxic Substances Control Act (TSCA) Risk Determination issued at 87 Fed. Reg. 39085 (June 30, 2022). They are submitted on behalf of the Halogenated Solvents Industry Alliance, Inc. (HSIA), an association of producers and users of PCE (also referred to as "Perc" below). TSCA Section 6(4)(A) requires that "The Administrator shall conduct *risk evaluations pursuant to this paragraph to determine* whether a chemical substance presents an unreasonable risk…" (emphasis added).

These comments describe how the PCE risk evaluation[1] was not conducted *pursuant to*, or in a manner that satisfies, the TSCA risk evaluation requirements in Section 6(4), and therefore do not provide an adequate basis for either the initial risk determination or this proposed revised risk determination.[2]

Particularly for conditions of use (COUs) evaluated in the manufacture and processing as a reactant/intermediate, the exposure assessments were not realistic and do not reflect current industrial hygiene (IH) practices. For the Risk Evaluation in general, the analysis of the Cavalleri *et al.* (1994) study was flawed, and EPA's evaluation of the mouse liver tumor mode-of-action (MOA) was inaccurate and did not represent the best available science. We request that EPA

[1] EPA-740-R1-8011 (December 2020) (hereafter "Risk Evaluation").

[2] These comments should be read in concert with HSIA's July 6, 2020, comments on the draft PCE Risk Evaluation. EPA-HQ-OPPT-2019-0502-0053.

correct the Risk Evaluation to incorporate realistic and best available science into both the final Risk Evaluation and prior to finalizing this proposed revised risk determination.

I. Risk Determinations for PCE are Based on Flawed Risk Evaluations

A. EPA Did Not Use Best Available Science in the Exposure Assessments

1. Dermal Exposure Assessment

In both the final Risk Evaluation and in the proposed revised draft risk determination for PCE, EPA finds unreasonable risks to workers from acute and chronic dermal exposure in the manufacture of PCE and its use in the production of other chemicals (feedstock or intermediate use), even with the most protective glove use (Protection Factor of 20). Although EPA assumed glove use in the Risk Evaluation for dermal protection, the models EPA used to estimate the amount of PCE that is retained by workers from dermal contact was not based on any supporting information and overestimated any potential exposure. These "worst-case scenarios" assumed unrealistic dermal exposure durations and failed to recognize basic industrial hygiene (IH) practices, including implementation of OSHA-compliant standard operating procedures (SOPs),[3] as well as engineering controls required by the National Emission Standards for Hazardous Air Pollutants (NESHAP) for Synthetic Organic Chemical Manufacturing Industry (SOCMI)[4] and Miscellaneous Organic Chemical Manufacturing (MON),[5] which require closed systems where exposure is tightly controlled. Thus, they are clearly inapplicable to facilities that manufacture PCE or use PCE as a process reactant or intermediate.

The manufacture of PCE and its use in the production of other chemicals (*i.e.*, refrigerants) are COUs that occur in closed system process units where potential dermal contact is limited to short-term tasks in the operation of unit activities. "Closed systems (including rigorous

[3] See SOPs for Personal Protection at CTC Manufacturing Sites, Appendix 1, Detailing the OSHA standards in place at CTC Manufacturing sites. These standards also apply to HSIA member-company manufacturing and processing sites as detailed in HSIA Response to EPA's Questions on Standard Operating Procedures (SOPs) at Carbon Tetrachloride and Other Solvent Manufacturing Sites, Appendix 2.

[4] 40 C.F.R. Part 63 Subparts F, G, H, I.

[5] 40 C.F.R. Part 63, Subpart FFFF.

containment by technical means) generally relate to high integrity plant/machinery where the opportunity for exposure is negligible, both in terms of frequency and magnitude".[6] Following several meetings with OPPT staff, HSIA submitted to an EPA docket for carbon tetrachloride several documents that provide comprehensive details on the typical tasks involved in the manufacturing of carbon tetrachloride and the SOPs for these tasks including personal protective equipment (PPE).[7] HSIA explained that these comments apply equally to the manufacture of the other chlorinated solvents, including PCE, and their use as intermediates in manufacturing fluorochemicals.[8] The typical short-term (5-30 minutes) tasks that could potentially involve contact with liquid phase PCE are loading transport equipment, conducting minor maintenance and line openings, packaging wastes, and collecting process samples. Although not expected, should accidental contact with PCE occur during the performance of these tasks, concentrations and amounts are minimal. Incidental, intermittent, or splash contact may only occur if there is an accidental spill, overspray conditions, or unexpected failure of a control device.

Despite the SOPs in place to prevent any exposure and potential for exposure limited to the short-term tasks described above, EPA estimated dermal exposure to PCE for workers in manufacturing and processing using Kasting and Miller (2006) with the following assumptions: (1) one dermal contact with undiluted PCE which coats fully one or both hands per work shift; (2) workers do not wash their hands at any point during the 8-hour work shift if gloves are not worn; and (3) a worker wears the same pair of gloves for the entire 8-hour work shift without stopping to wash their hands and/or change their gloves.[9] EPA provides no documentation or justification for these assumptions other than the intent to establish a theoretical "worst-case scenario." As a

[6] European Chemicals Agency (ECHA), Guidance on Information Requirements and Chemical Safety Assessment. Chapter R.14: Occupational Exposure Assessment, Version 3.0 (2016).

[7] See Appendices 1-4, including SOPs for Personal Protection at CTC Manufacturing Sites; HSIA Response to EPA's Questions on Standard Operating Procedures (SOPs) at Carbon Tetrachloride and Other Solvent Manufacturing Facilities (September 27, 2021). EPA Docket #EPA-HQ-OPPT-2020-0592-0003.

[8] HSIA Response to EPA's Questions on Standard Operating Procedures (SOPs) at Carbon Tetrachloride and Other Solvent Manufacturing Sites, Appendix 2, and Meeting with EPA on Chlorinated Feedstocks in HFC/HFO Production and Cross Cutting Issues, Appendix 3.

[9] Risk Evaluation, Supplemental Information on Releases and Occupational Exposure Assessment.

result of these assumptions, EPA very substantially overestimated worker exposure to PCE from dermal contact in facilities that manufacture and use PCE as a reactant or intermediate.

According to EPA, risk evaluations under TSCA § 6(b) are not screening level risk assessments, but are intended to "use scientific information, technical procedures, measures, protocols, methodologies and models consistent with the best available science." Therefore, instead of assuming a theoretical worst-case scenario, EPA should use in its dermal exposure models data and assumptions that are relevant and appropriate to actual workplace practices for the COUs being evaluated, information which EPA has had now for over a year.[10] Unfortunately, the Risk Evaluation fails to acknowledge basic IH practices.

As noted in the information provided to EPA on use of PPE at chlorinated solvent production facilities with closed systems, any potential dermal exposures are for short durations and, combined with the industry standards for good IH practices at these facilities which require removal and disposal of potentially contaminated gloves and hand washing after each task completion, do not justify an 8-hour period for absorption of PCE through skin.[11] Moreover, PCE will evaporate from the skin and gloves between exposure periods. A more realistic approach to estimating the dermal dose of PCE in workers in closed system facilities (manufacturing and process reactant/intermediate use) can be obtained using the IH Skin Perm model.[12] This tool is commonly used by practitioners of IH and exposure assessment to produce reliable estimates of dermal exposure. And, as noted in the Risk Evaluation, "this model takes into account losses to evaporation and estimates the mass that is absorbed." In addition, IH SkinPerm can be used to

[10] In this regard, the SACC concluded that "the worker exposures characterized in the draft risk evaluation are best described as a screening-level assessment. Due to the lack of readily available monitoring data and low confidence in the data sources, this assessment should not be used to decide whether health risks are reasonable or unreasonable. The results of a screening-level assessment can be used to determine if further refinement and more data are needed." See Summary of External Peer Review and Public Comments and Disposition for Perchloroethylene (PCE): Response to Support Risk Evaluation (epa.gov) at 217. In spite of having had very reliable monitoring data for these COUs for over a year, EPA has continued to ignore this comment.

[11] See, for example, Appendix 1, page 4, describing how gloves are inspected and donned before use for short-term tasks and removed after use; Appendix 2, page 4, responding to EPA's questions regarding glove evaluation, use and replacement for short term tasks; and Appendix 3, page 9, comparing the model assumptions to the actual condition of use potential for dermal exposure.

[12] IH SkinPerm is a peer-reviewed exposure assessment tool published by the American Industrial Hygiene Association (AIHA) Exposure Assessment Strategies Committee.

evaluate the impacts of differing patterns of exposure on fractional and total dose of absorption, *i.e*., it allows for the incorporation of realistic exposure patterns.

Recognition of standard work practices and reliance on reasonable and realistic exposure data are critical to meet the statutory requirements of TSCA, as well as the "objectivity" criterion of the Information Quality Act. EPA's reliance on hypothetical assumptions for modeling of the amount of PCE that is absorbed by workers from dermal contact cannot be justified. Assumptions used for estimating worker exposures should be as relevant as possible for the COUs being evaluated. EPA's use of unrealistic dermal exposure assumptions has led to erroneous conclusions regarding the health risks to workers using PCE in closed systems. Because the Risk Evaluation is intended to determine whether PCE presents an unreasonable risk of injury to workers under TSCA § 6(b), which requires rulemaking to mitigate risks found to be unreasonable, it is imperative that it be revised to reflect the "best available science" in advance of any risk management rulemaking.

2. Flawed Assumptions Regarding Use of PPE in Risk Determinations

In its justification for revising the risk determinations for all COUs of PCE in the Risk Evaluation, EPA states that this change "reflects EPA's recognition that unreasonable risk may exist for subpopulations of workers that may be highly exposed because they are not covered by OSHA standards, or their employers are out of compliance with OSHA standards, or because many of OSHA's chemical-specific permissible exposure limits largely adopted in the 1970's are described by OSHA as being 'outdated and inadequate for ensuring protection of worker health,' or because the OSHA Permissible Exposure Limit may be inadequate for ensuring protection of worker health."

EPA has generalized this concern to all COUs for PCE, yet it is not pertinent at all to the manufacture of PCE, or its use as a fluorochemicals feedstock, based on the information provided by HSIA to EPA over a year ago on industry best practices for industrial hygiene.[13] There are three PCE manufacturers in the United States. All three manufacturers have submitted to EPA

[13] HSIA described that OSHA standards apply to all member sites that manufacture CTC (Appendix 1), which also applies to all manufactures of other chlorinated organics, including PCE (see Appendix 2).

documentation on the level of required PPE for general nonspecific tasks in a manufacturing plant for any operations of maintenance personnel, visitors or contractors who enter designated process areas. (Appendices 1-4.) These documents also provide a summary of the extensive training that is in place for employees (new and seasoned) to ensure SOP requirements are followed. There are no exceptions – the SOPS and training apply to all workers.

In the case of the COU for the manufacture of PCE, EPA must evaluate in the Risk Evaluation the circumstances under which PCE is intended, known, or reasonably foreseen to be manufactured. Since all three U.S. manufacturers of PCE require PPE use for anyone entering the processing areas at a plant, and that information has been "clearly articulated" to EPA, then EPA "believes it is appropriate to also evaluate the levels of risk present in the scenarios considering" applicable OSHA requirements and industry or sector best practices into its risk evaluations as serve as the basis for the risk determinations and the risk management rules.[14]

B. Non-Cancer Point-of-Departure (POD) for Chronic Exposure: Evaluation of the Cavalleri *et al.* (1994) Study

In the final Risk Evaluation for PCE, EPA identified a Lowest-Observed-Adverse-Effect-Level (LOAEL) of 6 ppm for color confusion in the Cavalleri *et al.* (1994) study of 35 workers in dry cleaning facilities in Moderna, Italy,[15] one of two studies used to derive a POD for chronic non-cancer (neurotoxicity) effects in the risk characterization as well as in EPA's derivation of an Existing Chemical Exposure Limit (ECEL); the other study being Echeverria *et al.* (1995).[16] This LOAEL determination and POD approach was the same as for the RfC derivation in the 2012 PCE IRIS assessment, which was added after the peer review of the draft IRIS assessment by the National Academy of Sciences. A significantly higher color confusion index (CCI) was reported

[14] Asbestos Part 1: Chrysotile Asbestos; Regulation of Certain Conditions of Use Under Section 6(a) of the Toxic Substances Control Act (TSCA), Proposed Rule, 87 Fed. Reg. 21706 at 21712 (April 12, 2022).

[15] Cavalleri, A, Gobba, F, Paltrinieri, M, Fantuzzi, G, Righi, E, and Aggazzotti, G, Perchloroethylene exposure can induce colour vision loss, *Neurosci. Lett.* 179: 162-166.

[16] 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, *J. Occup. Environ. Med.* 37: 667-680 (1995).

for dry cleaners exposed to average PCE levels of 7.3 ppm as an 8-hr (mean CCI 1.19) vs. matched referents (mean CCI 1.09), but not for ironers exposed to mean PCE levels of 4.8 ppm (CCI 1.06), indicating a NOAEL of 5 ppm. Furthermore, neither duration of exposure nor cumulative exposure (ppm-year) was associated with CCI, suggesting a temporary or at least non-cumulative effect. The authors of the study concluded that "the mean exposure and the range of TWA levels of PCE in *ironers* and *dry-cleaners* (Table 2) suggest a mean threshold for colour vision effect of the solvent ranging approximately between 5 and 11 ppm."

In identifying 6 ppm as a LOAEL, EPA ignored not just HSIA's very relevant comments but also the peer review EPA had commissioned. The Cavalleri *et al.* (1994) study was reviewed in 2004 by a five-person expert panel convened for the EPA's National Center for Environmental Assessment (NCEA) to provide expert commentary on its document titled *Neurotoxicity of Tetrachloroethylene (Perchloroethylene)*.[17] The panel included scientists with expertise in epidemiology (studies of human neurological effects, specifically studies of visual function including visual contrast sensitivity); neurotoxicology and/or neurobehavioral evaluation (testing of human subjects for chemically induced deficits in nervous system performance, especially with solvents such as PCE); and studies of the relationship between neurobehavior and low-level chemical exposures in residential or occupational populations. In response to the charge question "Is there evidence of a dose response or an exposure effect gradient in the studies of Perc, and is there a threshold?," the expert panel concluded:

> **"**A dose-response relationship is supported by three findings: (a) *in a study of dry-cleaning workers, a deficit was observed in dry-cleaners who were highly exposed to Perc, but not in ironers, who had lower exposures (Cavalleri et al., 1994)* [emphasis added]; (b) a significant correlation ($r = 0.52$; $p<0.01$) observed between individual Perc exposure (environmental Perc levels measured using personal dosimeters) and colour vision impairment (quantitatively evaluated using the Color Confusion Index) (Cavalleri

[17] EPA/600/R-04/041, Summary Report of the Peer Review Workshop on the Neurotoxicity of Tetrachloroethylene (Perchloroethylene) Discussion Paper (2004).

et al. 1994); and (c) the progression of the impairment observed in dry-cleaners whose exposure was increased (Gobba et al, 1998)."

In contradiction to the study authors' conclusions and the neurotoxicity expert panel, EPA determined that there was no threshold for color vision effects in the PCE-exposed workers. EPA considered the dry-cleaners and ironers as a single group of workers even though the two groups of workers had different tasks with different exposure scenarios. It stated in the IRIS assessment that the mean exposure value of the ironers could not be considered a NOAEL because elevated CCI scores were seen in the dry cleaners at lower exposures. This is an extraordinary conclusion by EPA since it is completely at odds with the CCI values from the control (non-PCE-exposed) group where there were also elevated CCI scores similar to values seen in the ironers; the statistical analysis, in fact, showed no significance difference between the two groups (mean and standard deviations: 1.061 ± 0.058 for ironers versus 1.073 ± 0.079 for controls). In contrast to the ironers, there was a statistically significance difference between the dry cleaners and controls (mean and standard deviations: 1.197 ± 0.133 for dry cleaners versus 1.089 ± 0.117 for controls; $P = 0.007$).

Therefore, EPA cannot properly infer that the elevated CCI scores in the ironers are due to PCE exposure. EPA did not even acknowledge that the correlation between CCI scores and PCE exposure was dependent on three high values (>12.5 ppm, two of which were >20 ppm) involving just the dry-cleaners. In the absence of these three high values, there was no evidence of a linear association between mean CCI scores and PCE at exposures below 10 ppm. Moreover, EPA ignored the fact that there are task differences between the two groups of workers that can result in peak exposures not accounted for in the exposure assessment, which evaluated only 8-hr Time-Weighted Average (TWA) values. As noted by the study authors, peak exposures to PCE can occur with specific tasks involving the dry cleaners, such as the retrieval of just washed garments or maintenance, but not the ironers. In an example, the study authors reported on spot samples taken during retrieval of garments that resulted in a tenfold increase in PCE air concentrations (from 2 to 29 ppm nearly).

In conclusion, EPA needs to correct its flawed analysis and dose-response assessment of the Cavalleri *et al.* (1994) study which shows a NOAEL of 5 ppm for color vision effects.

2. The weight of the scientific evidence supports a peroxisome-proliferator activated receptor alpha (PPAR alpha) MOA for PCE-induced mouse liver tumors; thus they are not relevant to humans.

The calculation of the Inhalation Unit Risk (IUR) for PCE in the final Risk Evaluation did not fundamentally change from the derivation in the 2012 PCE IRIS assessment. PCE was tested for carcinogenicity in two mouse inhalation bioassays, and EPA used a linear non-threshold dose-response model on the male mouse liver tumors from the JISA (1993) two-year carcinogenicity study to derive the IUR.[18] EPA justifies both the choice of the tumor type and the linear extrapolation approach because, according to the EPA Cancer Guidelines, "a linear extrapolation approach is used when the mode of action information is supportive of linearity or mode of action is not understood." EPA states in the Risk Evaluation that it had conducted "a weight of scientific evaluation for several proposed MOAs for liver carcinogenicity" and concluded in the IRIS Assessment "that multiple modes of action were likely responsible for liver tumors induced by PCE." However, the Science Advisory Committee on Chemicals (SACC) in their peer-review of the Risk Evaluation did not appear to agree with EPA's evaluations of the proposed liver tumor MOAs and felt that "the supportive evidence for some of the proposed mouse liver cancer MOA was minimal and/or circumstantial."[19] It was also stated in the final report from the SACC peer-review that "the evidence for genotoxicity in the mouse liver stemming from PCE exposure was not convincing to most Committee members."

The mouse liver tumor MOA for PCE has been reviewed by Dr. James Klaunig, who is Professor Emeritus at Indiana University School of Public Health and is a well-recognized expert in liver carcinogenesis (see Appendix 5). He has concluded that PCE is a liver carcinogen in mice via a PPAR alpha MOA and that it is trichloroacetic acid (TCA), the oxidative metabolite of PCE, that is responsible for PPAR alpha activation. Liver tumor development in mice via PPAR

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[18] National Toxicology Program [NTP], Toxicology and Carcinogenesis Studies of Tetrachloroethylene (Perchloroethylene) (CAS No. 127-18-4) in F344 Rats and B6C3F$_1$ Mice (Inhalation Studies). (NTP TR 311). Research Triangle Park, NC: U.S. Department of Health and Human Services (1986); Japan Industrial Safety Association [JISA], Carcinogenicity Study of Tetrachloroethylene by Inhalation in Rats and Mice, Hadano, Japan (1993).

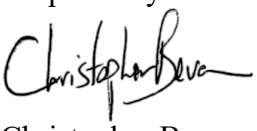
[19] TSCA Science Advisory Committee Meeting Minutes and Final Report No. 2020-5, EPA docket #EPA-HQ-OPPT-2019-0502, pages 80-81.

alpha activation is a non-genotoxic MOA with considerable evidence of little to no human relevance. Dr. Klaunig also provides in his review some critical comments of EPA's assessment of the PPAR alpha MOA in the Risk Evaluation. EPA discredits the PPAR alpha MOA in a manner that is incomplete and biased and fails to satisfy the requirements placed on EPA under TSCA § 26 with using the best available science and weight of scientific evidence.

II. Conclusion

In sum, TSCA mandates that EPA must complete a risk evaluation pursuant to the risk evaluation requirements in § 6(4) before it can proceed to § 6 risk management rulemaking. In this case, the underlying Risk Evaluation fails to comply with the § 6(b) risk evaluation requirements, including accounting for exposure under the conditions of use, describing the weight of the scientific evidence for the identified hazard and exposure, using scientific information employed in a manner consistent with the best available science, and considering of the extent of independent verification or peer review of the information. To maintain the credibility of its regulatory efforts under TSCA, it is imperative that EPA build upon the available information to construct a more realistic risk evaluation before proceeding with rulemaking.

Respectfully submitted,



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Appendices

SOPs for Personal Protection at CTC Manufacturing Sites

As conveyed to EPA during the Risk Evaluation process, carbon tetrachloride (CTC) is tightly controlled under the federal Clean Air Act and its use is regulated under Title VI of the Clean Air Act (implementing the Montreal Protocol). CTC is also the critical feedstock for US production of Low-Global Warming Potential (GWP) alternative fluorocarbon products which serve as the basis for the Kigali Amendment to the Montreal Protocol's phase down of hydrofluorocarbons (HFCs).

This summary discusses four topics relating to personal protection at CTC manufacturing sites that are in place in addition to the environmental regulations currently imposed upon and benefits generated by CTC manufacturing and processing. This information is provided to EPA for consideration during the Risk Management rule development process for carbon tetrachloride:

1) OSHA standards applicable to Personal Protective Equipment (PPE) selection for dermal protection that protect against potential dermal exposure, and inhalation protection that protect against vapor exposure.
2) Minimum PPE requirements for operational and maintenance personnel at CTC manufacturing facilities.
3) CTC manufacturing practices only present a potential risk of an intermittent, short term exposure (The CTC Risk Evaluation assumed an 8-hour potential exposure which overestimates any potential dermal risk.)
4) Standard Operating Procedures (SOPs) examples for short-term tasks such as loading, minor maintenance and sampling that document the required steps to ensure the safe operation of task and the proper use of the selected PPE to prevent potential dermal and vapor inhalation exposure.

1. OSHA STANDARDS FOR DERMAL AND INHALATION PROTECTION

OSHA standards have specific Hazard Assessment requirements for personal protection and training requirements for PPE selection and use. This section lists OSHA regulations relating to personal protection that are implemented at each CTC manufacturing site.

Glove selection must meet the OSHA Hazard Assessment requirements in 29 CFR Part 1910:

- 1910.1000 Toxic and Hazardous Substances
- 1910.132(a) General Requirements
- 1910.132(d) Hazard Assessment and PPE Equipment Selection
- 1910.132(e) Prohibition of use of defective or damaged equipment
- 1910.132(f) PPE Training
- 1910.133 Eye and Face Protection
- 1910.134 Respiratory Protection
- 1910.138 Hand Protection

As a part of the OSHA PPE regulations, OSHA Standard (29 CFR 1910.138) specifically addresses hand protection:

> (a) Appropriate hand protection must be worn when hands are exposed to hazards such as skin absorption of harmful substances, severe cuts, lacerations or abrasions, punctures, chemical or thermal burns and harmful temperature extremes.

(b) Employers must base the selection of appropriate hand protection on an evaluation of the performance characteristics of the hand protection relative to the task(s) to be performed, conditions present, duration of use and the hazards and potential hazards identified.

In addition to chemical protection, the OSHA regulation for hand protection, quoted above, requires that the glove selection must be appropriate for task. Selection of glove types and materials are based on the potential exposure risk and nature of the hazards that are likely to be encountered when performing job tasks. OSHA guidelines recognize that consideration should be given to other factors when selecting the appropriate PPE for a task. 29 CFR Part 1910 Subpart I Appendix B.11. The following list provides an example of factors that are evaluated when selecting the most appropriate glove for a particular application:

- Permeation/degradation/breakthrough data provided by the manufacturer or through independent testing
- Degree of dexterity required to perform task (i.e. use of fine motor skills)
- Expected contact with chemical (incidental with little or no direct contact with chemical or extended contact with chemical)
- Compatibility of glove type and material with one or more chemicals that may be encountered
- Feasibility (i.e. availability)
- Length of glove (i.e. gauntlet style)
- User fit, function, and comfort
- Reusability of glove
- Temperature considerations (i.e. glove textures, finishes, linings)
- Duration/frequency of job tasks requiring the use of gloves

Glove selection and use cannot be solely determined by permeation, degradation, and breakthrough data. All of the factors listed above may need to be considered when identifying a glove for a specific type of task.

Many manufacturers test glove materials by immersing the glove material in the chemical. Immersion data may provide the user with “worst case scenario” data. The assumption may be made that glove materials may perform for longer periods of time without permeation or degradation occurring in situations where incidental, intermittent, or splash contact is expected.

2. Minimum PPE Requirements

Chemical manufacturers conduct evaluations on hazards present in the workplace by knowledgeable experts to ensure that PPE used in the workplace will protect against the hazards present and work as expected. These evaluations address worker exposures to chemical, physical, biological and ergonomic hazards with potential health significance in the workplace. While the evaluations normally concentrate on specific facility tasks. Attention is also be paid to exposures resulting from general, non-specific tasks such as "making plant rounds".

The level of PPE required for general nonspecific tasks in a plant is often referred to as "plant minimum PPE". This is the minimum requirement for PPE specified for any Operations or Maintenance personnel, visitors or contractors, to enter designated process areas. See Figure 2.

Additional levels of PPE are then required based on the task to be conducted, or demarcation of specific areas within the facility that have been identified to contain increased risk (e.g. “acid handling area”, or "hearing protection required" area, etc.).

Access to the process area of each plant is controlled through the control room. Anyone needing to access the process area must inform the control room prior to entering the area. Minimum PPE is expected to be worn when entering the area. Any additional PPE would be specified by the control room.

Figure 2 – Typical Minimum PPE Requirements at CTC Manufacturing Facilities

(A.) Operations and Maintenance Personnel - Minimum Facility PPE Requirements:

- **Head:** Safety Glasses with side shields, Hard Hat, Monogoggles (must carry on person), Hearing Protection (muffs or ear plugs)
- **Respiratory Protection**: Mouthbit Organic Vapor Respirator (must carry on person) or Half Face Air Purifying Respirator
- **Body:** Fire Retardant Clothing (area or task specific requirement)
- **Feet:** Safety Shoes with Steel Toes
- ***Goggles and work gloves are required anytime valves are operated**

(B.) Line and Equipment Opening (LEO) Activities with minimal risk of exposure – PPE Requirements:

- **Head:** Safety Glasses with side shields, Hard Hat, Monogoggles (must carry on person), Hearing Protection (muffs or ear plugs)
- **Respiratory Protection**: Full or Half Face Air Purifying Respirator
- **Body:** Fire Retardant Clothing (area or task specific requirement)
- **Gloves**: Chemical Resistant Gloves (i.e. Nitrile)
- **Feet**: Chemical Resistant Boots with Steel Toes

(C.) Major LEO Activities or those with increased risk of exposure – PPE Requirements:

- **Head:** Safety Glasses with side shields, Hard Hat, Monogoggles (must carry on person), Hearing Protection (muffs or ear plugs)
- **Respiratory**: Full Face Respirator with Supplied Air Line (can also include a 5 minute Escape Pack)
- **Gloves**: Chemical Resistant Gloves (i.e. Nitrile)
- **Body**: Chemically Resistant Suit
- **Feet**: Chemical Resistant Boots with Steel Toes

3. INTERMITTENT TASKS

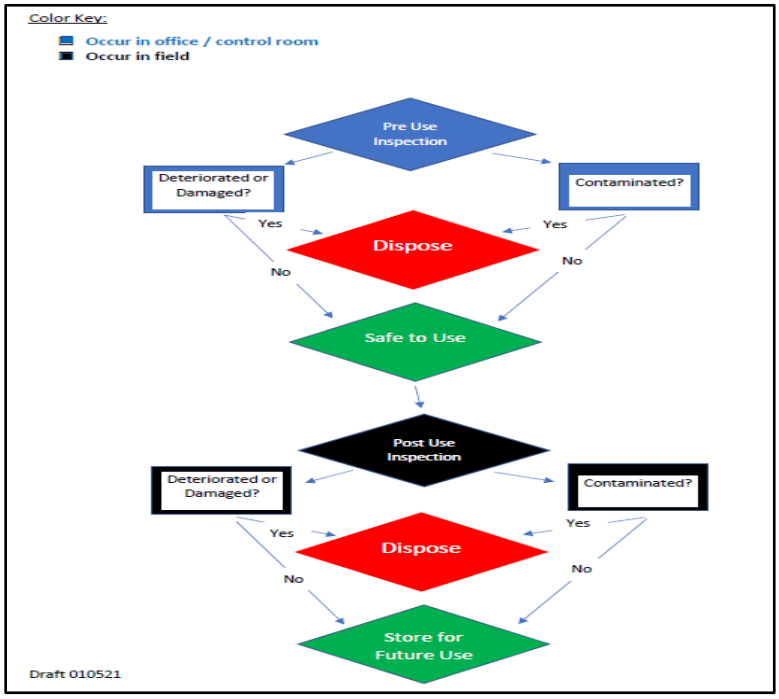
The glove use, and the hazard assessments, for manufacturing CTC are based upon activities where the potential risks for exposure are extremely short term (ranging from approximately 5 - 30 min.), *i.e.*, sampling, loading/unloading preparation, connections and disconnections. The CTC Risk Evaluation assumed a longer 8-hour glove use and/or exposure period for potential exposure which is not applicable to these tasks.

Tasks with potential CTC exposure in manufacturing, such as collecting samples, loading and unloading carbon tetrachloride, require the use of gloves for a duration of approximately 15 – 30 minutes. Sample collection occurs daily; gloves are donned before the sampling round begins and are removed after the round is completed. For loading/unloading activities, which varies weekly, the gloves are donned before the connection is made and are removed after disconnection. Although not expected, should accidental contact with carbon tetrachloride occur during the performance of these tasks, concentrations and amounts are minimal. Incidental, intermittent, or splash contact may only occur if there is an accidental spill, overspray conditions, or unexpected failure of a control device.

It is also important to note that employees are trained to inspect gloves before and after use to look for signs of swelling, cracking, shrinking, or discoloration of the material, as these are evidence of chemical contact and signs the glove material may no longer provide adequate chemical protection. Employees are trained to look for holes, tears, or punctures and remove the gloves from service if any are found. If an employee suspects any incidental or intermittent chemical contact, gloves will be discarded and replaced with new gloves. Refer to the PPE Pre and Post Task Inspection Process diagram in Figure 3.

The glove material must have the fit and thickness to protect against any potential intermittent exposure during these short term tasks, but just as importantly, the gloves must allow the appropriate dexterity to take samples and unhook loading lines without adding to the risk of exposure due to a reduced ability to conduct the task.

Figure 3: PPE Inspection Process



4. STANDARD OPERATING PROCEDURE EXAMPLES FOR TASKS IN CTC MANUFACTURING.

This section includes example Standard Operating Procedures (SOPs) for short-term tasks such as loading transport equipment, conducting minor maintenance and line openings, packaging wastes, and collecting process samples. These SOPs are provided to document examples of existing process steps taken and controls employed to safely conduct the task and prevent potential dermal and inhalation exposure. OSHA regulations require that the SOP include instructions for conducting activities safely, including the "Precautions necessary to prevent exposure, including engineering controls, administrative controls, and personal protective equipment." (40 CFR §68.69 and 29 CFR §1910.119(f)). Additionally, EPA regulates facilities that manufacture CTC through the National Emission Standards for Hazardous Air Pollutants (NESHAP) for the Synthetic Organic Chemical Manufacturing Industry (SOCMI). 40 C.F.R.§63 Subparts F, G, H, I.

The SOPs incorporate both the use of PPE and the procedures to properly operate the engineering controls for these tasks.

It is critical to note that these SOPs are examples only as each facility must account for specific protections for its unique facility operational footprint and process.

The various SOPs are listed in Appendix 1. Each section contains a flowchart of the SOP and an overview of the typical procedures employed by manufacturers.

Appendix 1

Standard Operating Procedures for CTC

A. Rail Tank Car Loading

B. Tank Truck Loading

C. Process Sampling

D. Waste Packaging

E. Minor Maintenance and Line Openings

Each section contains a flowchart of the SOP and an overview of the typical procedures employed by manufacturers.

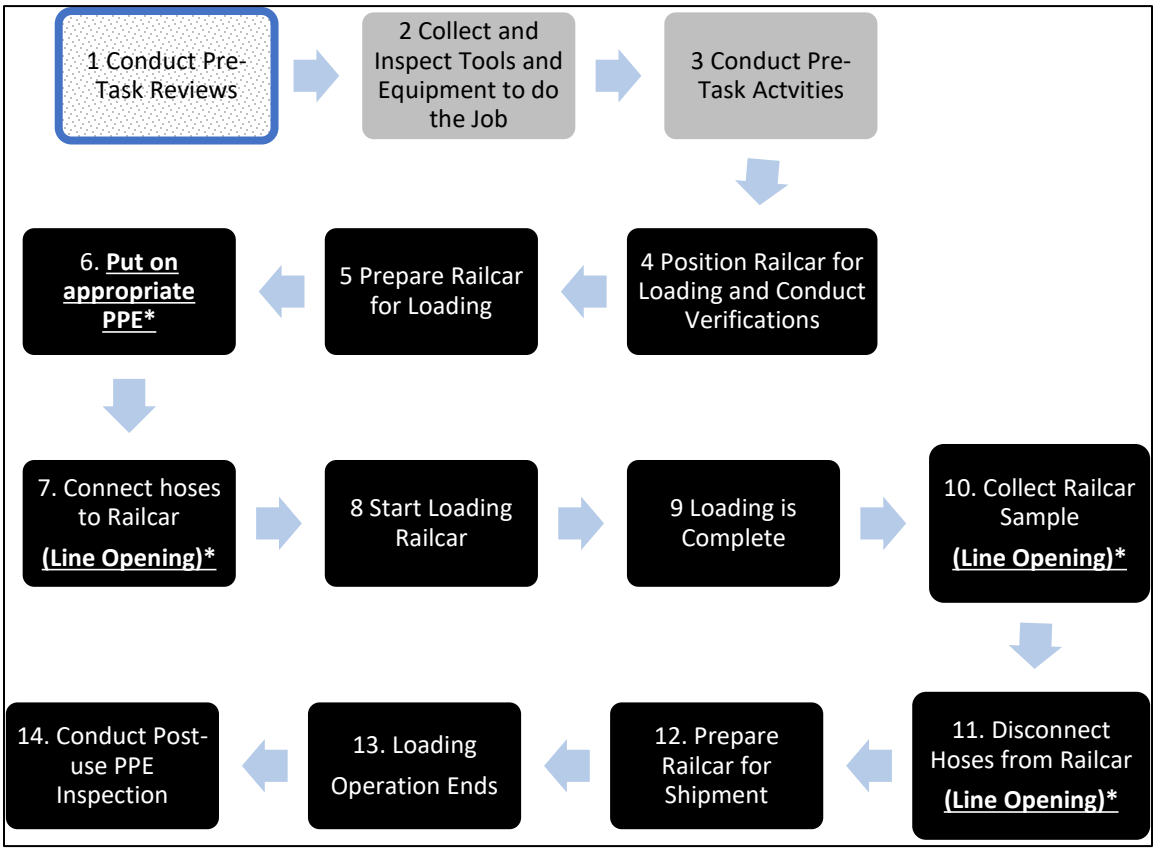
As stated above, it is critical to note that these SOPs are examples only as each facility must account for specific protections and procedures for its unique facility operational footprint and process. Due to the timeline of the Risk Management proposal, additional information may be necessary to provide details on a site-specific basis and/or address specific questions from EPA.

A. Rail Tank Car Loading SOP

1. SOP Flow Chart

Color Key:

- **Occur in office / control room**
- **Occur in both office/control and field**
- **Occur in field**



Underline text denotes steps that require additional PPE, and/or when additional PPE is donned or removed

A. Rail Tank Car Loading SOP (Continued)

2. SOP Overview

1. Conduct Pre-Task Reviews
    a. Scope & Risk Assessment
    b. Safety, Health and Environmental and Ergonomic Considerations
    c. Determine Proper PPE Requirements
    d. Consequences of Deviation from Procedure
2. Collect and inspect tools and equipment necessary to do the job
3. Conduct Pre-Task Activities
    a. Review Plant Safety Standards
    b. Visual inspections of rail tank car to be loaded
    c. Verify safety equipment operational
    d. Inspect tools, hoses, sample equipment
    e. Evaluate spill potential and verify emergency procedures in place (spill response, evacuation)
4. Position Railcar for loading
    a. Derail, Blue Flag & Light in place
    b. Chock Railcar and set Brake
    c. Conduct Railcar Verifications
        i. Car is spotted at correct spot to load CTC
        ii. Adequate CTC in storage tank to load rail tank
        iii. Correct rail car type for product, status, net weight
5. Prepare Railcar for loading
    a. Calculate weight of CTC to be loaded.
    b. Lower load ramp and platform onto railcar
    c. Conduct Elevated Work pre-task analysis
    d. Secure loading area and move all non-essential personnel outside of barricade
    e. Test high level probe and alarm (if equipped)
6. **Put on protective equipment (PPE) for loading operation***
7. **Connect loading hoses to Tank Car**
    a. Open railcar dome lid and inspect railcar valves
    b. Connect vent hose from railcar to Thermal Treatment Unit
    c. Depressurize railcar
    d. Connect CTC liquid loading hose to railcar
    e. Line opening ends – Extra PPE can be removed if conditions permit
    f. Pressure test the CTC liquid load line
    g. Set CTC load meter – it will close the automatic block valve when load amount has been reached.
8. Start loading Rail Tank Car
    a. Open manual liquid fill and vent valves on railcar. **The CTC is now loading**
    b. Inspect hoses, rail tank car and piping for leaks during the loading process
9. When load is complete:
    a. Close liquid loading valve
    b. Notify control room that loading is complete.
    c. Blow any remaining liquid in loading hose back into the railcar using nitrogen
    d. Close nitrogen valve
10. **Collect Railcar Sample**
    a. Put on protective equipment (PPE) for sample collection*
    b. Ensure all personnel are away from the railcar
    c. De-pressure sample point into a waste collection container
    d. If sample is taken from the load line, allow liquid to flow from railcar into load line
    e. Fill sample container 75% full from sample valve on load line.
    f. Blow any remaining liquid in loading hose back into the railcar using nitrogen (or air)and close nitrogen (or air)valve.
11. Disconnect load and vent hoses from railcar
    a. Remove high level probe
    b. Close railcar vent valve and manual load valve
    c. De-pressure vent and load hoses and disconnect from railcar
    d. Install plugs in all railcar valves
    e. Secure load and vent hoses to load rack
    f. Line opening ends – Extra PPE can be removed if conditions permit
12. Prepare railcar for shipment
    a. Inspect dome area for cleanliness
    b. Close dome
    c. Attach product tags
    d. Apply tamper evident seal to dome, Record seal numbers
    e. Raise and secure load ramp
    f. Attach DOT placards on railcar
    g. Remove derail, blue flag, blue light
    h. Remove chocks
    i. Input load data and note end time
13. Loading Operation ends
14. Conduct Post-Use PPE inspection and store for future use or discard PPE if not suitable for reuse

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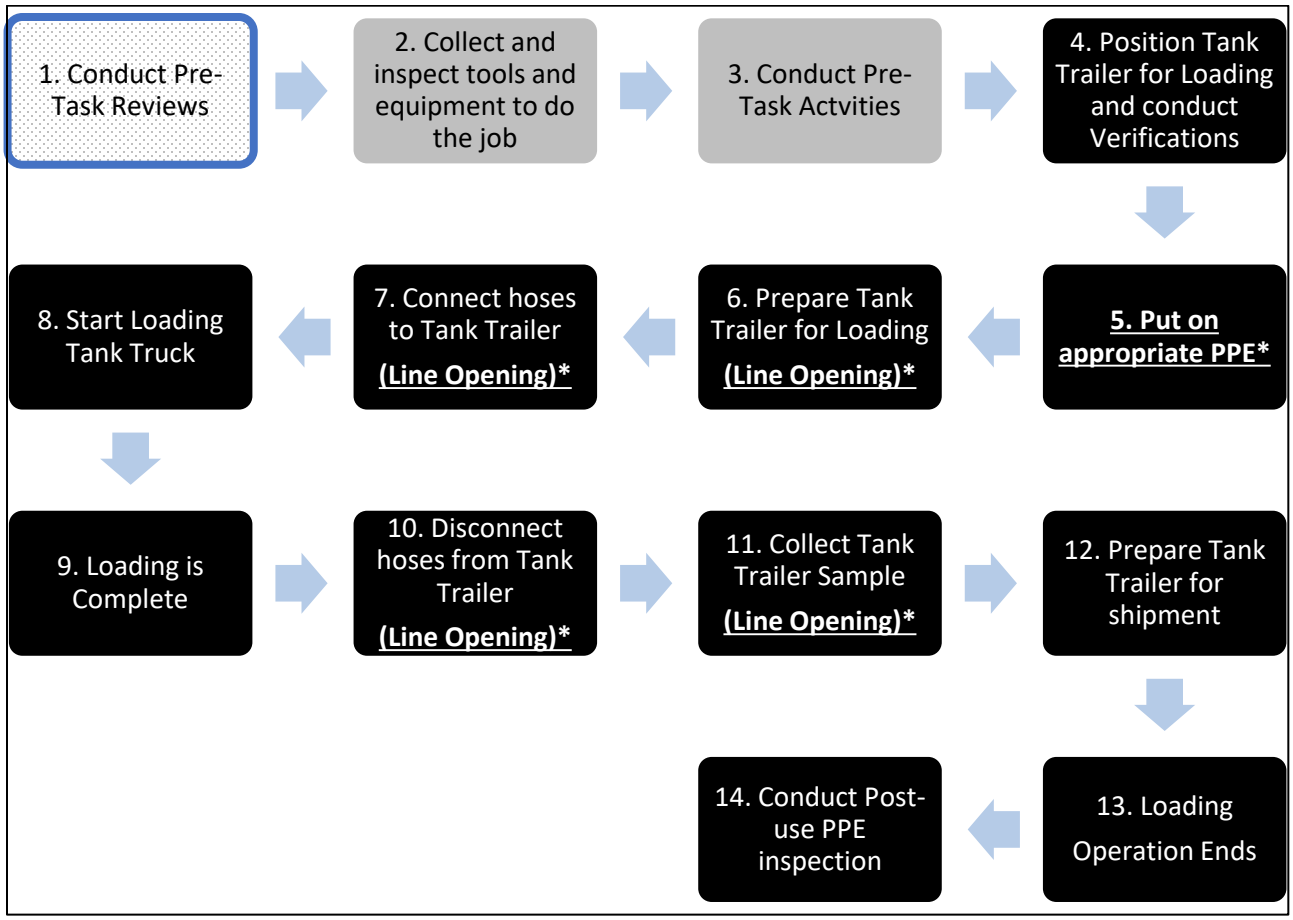
*At a minimum, Line and Equipment Opening Activities require additional PPE: Full or Half Face Air Purifying Respirator and Chemical Resistant Gloves. Some LEO tasks with higher risk of exposure require Chemical Suit and Supplied Air Respirator

B. Tank Truck Loading SOP

1. SOP Flow Chart

Color Key:

- Occur in office / control room
- Occur in both office/control and field
- Occur in field



Underline text denotes steps that require additional PPE, and/or when additional PPE is donned or removed

B. Tank Truck Loading SOP (Continued)

2. SOP Overview

1. Conduct Pre-Task Reviews
    a. Scope & Risk Assessment
    b. Safety, Health and Environmental and Ergonomic Considerations
    c. Determine Proper PPE Requirements
    d. Consequences of Deviation from Procedure
    e. Confirm current DOT training for loading personnel
2. Collect and inspect tools and equipment necessary to do the job
3. Conduct Pre-Task Activities
    a. Review Plant Safety Standards
    b. Verify safety equipment operational
    c. Inspect tools, hoses, sample equipment
    d. Evaluate spill potential and verify emergency procedures in place (spill response, evacuation)
    e. Conduct Elevated Work pre-task analysis
4. Collect general information prior to loading
    a. Verify that an order has been placed and the vehicle has arrived at CTC load area
    b. Review the trailing loading papers
    c. Spot tank truck at the CTC loading rack
    d. Verify correct DOT classification and capacity of the trailer.) Apply wheel chocks and place sign in windshield.
    e. Lower the ramp and fall protection in place over dome.
5. **Put on protective equipment (PPE) for loading operation***
6. **Prepare Tank Trailer to Load**
    a. Inspect dome area of tank trailer
    b. Check pressure on trailer
7. **Connect hoses to Tank Trailer**
    a. Connect vent hose and depressurize tank trailer to Vapor Recovery Unit (VRU)
    b. Connect load line to tank trailer.
    c. Verify pressure test of tank trailer and loading/vent hoses.
    d. Place CTC placards on trailer
    e. Line opening ends – extra PPE can be removed if conditions permit
    f. Set CTC load meter – automatic block valve closes once load amount reached.
8. Start loading Tank Trailer
    a. Open manual liquid fill and vent valves on tank trailer
    b. Notify control room ready to load CTC.
    c. Open CTC loading valves in field.
    d. **The CTC is now loading**
    e. Inspect hoses, tank trailer and piping for leaks during the loading process
9. When load is complete,
    a. Put on protective equipment (PPE) for loading and sampling operation*
    b. Close liquid loading valve
    c. Blow any remaining liquid in loading hose back into the tank trailer.
    d. Verify tank trailer is depressurized.
    e. Close vent valve to VRU
10. **Disconnect loading and loading hoses**
    a. Place caps on end of each hose.
11. **As needed, Collect Tank Trailer Sample**
    a. Ensure all personnel are away from the area
    b. Collect samples.
    c. Line opening ends – extra PPE can be removed if conditions permit
12. Prepare tank trailer for shipment
    a. Inspect dome area for cleanliness
    b. Close dome
    c. Attach product tags
    d. Apply tamper evident seal to dome, Record seal numbers
    e. Raise and secure load ramp
    f. Inspect tank trailer for leaks.
    g. Remove chocks and windshield sign
    h. Verify trailer sample analyses meet sales specifications
    i. Give completed load sheet and keys to driver
    j. Record end time.
13. Loading operation ends
14. Conduct Post-Use PPE Inspection and store for future use or discard PPE if not suitable for reuse

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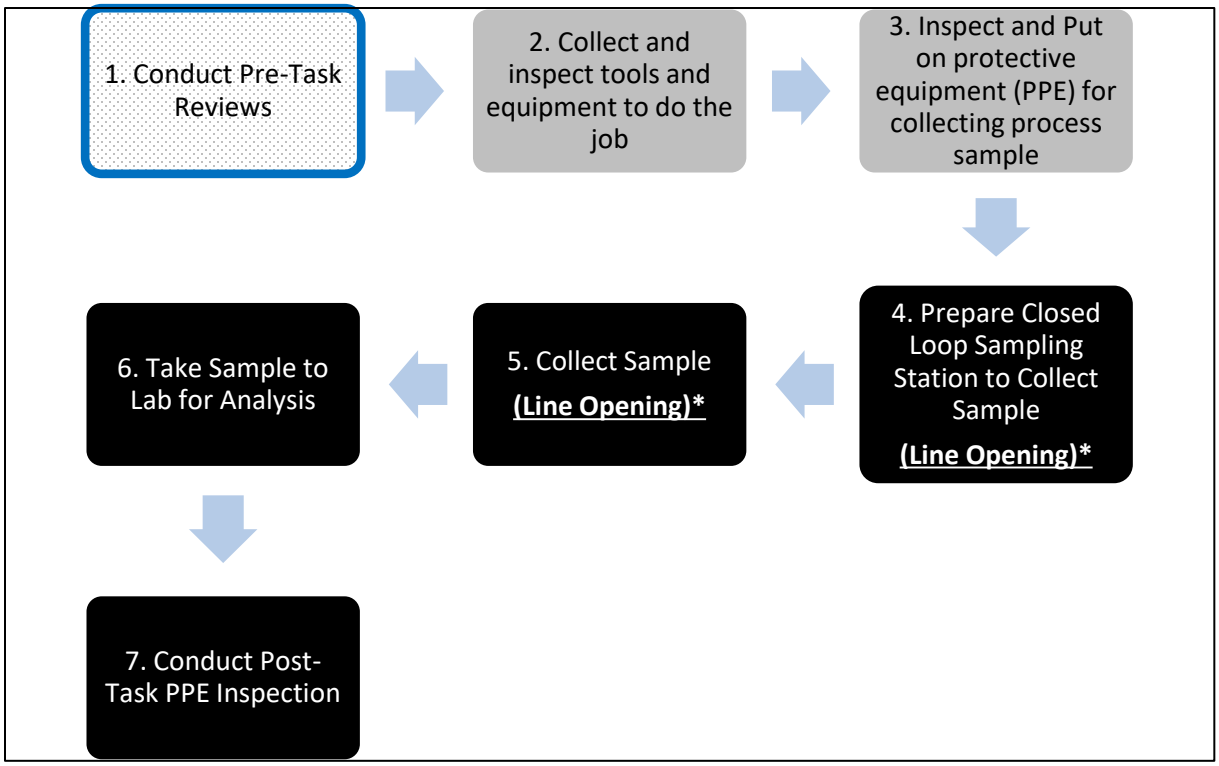
*At a minimum, Line and Equipment Opening Activities require additional PPE: Full or Half Face Air Purifying Respirator and Chemical Resistant Gloves. Some LEO tasks with higher risk of exposure require Chemical Suit and Supplied Air Respirator

C. CTC Process Sampling SOP

1. SOP Flow Chart

Color Key:

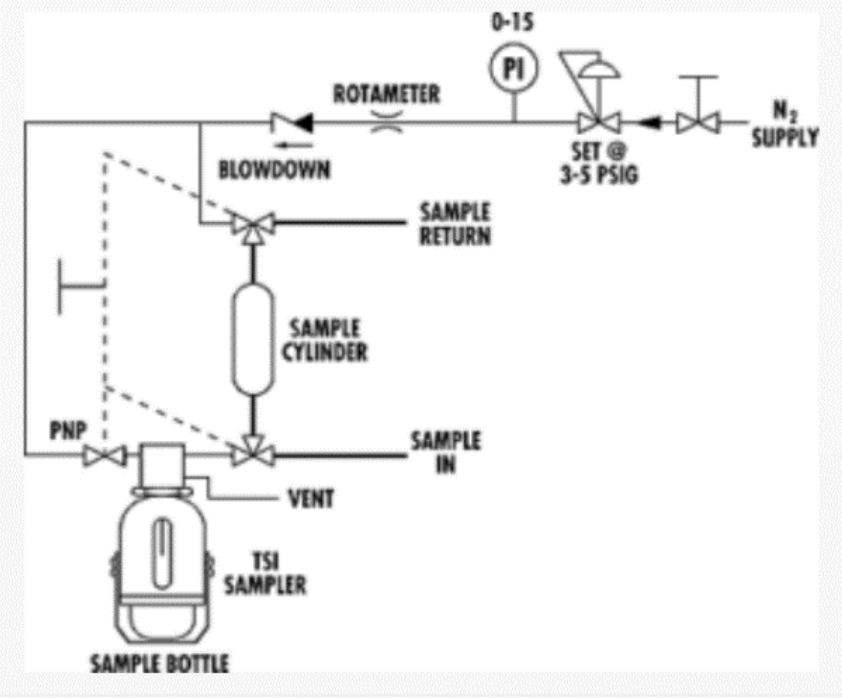
- Occur in office / control room
- Occur in field
- Occur in both office/control and field



Underline text denotes steps that require additional PPE, and/or when additional PPE is donned or removed

C. CTC Process Sampling SOP (Continued)

Note: This SOP example includes the use of a Closed Loop Sampling Station, such as those commercially available from Texas Sampling[1] or similar vendors. Diagram is shown below:



[1] https://www.texassampling.com/fixed-volume-sample-systems/#1587512857215-8489adfc-4187

C. CTC Process Sampling SOP (Continued)

2. SOP Overview

1. Conduct Pre-Task Reviews
    a. Scope & Risk Assessment
    b. Safety, Health and Environmental and Ergonomic Considerations
    c. Determine Proper PPE Requirements
    d. Consequences of Deviation from Procedure
2. Collect and inspect tools and equipment necessary to do the job
    a. Sample bottles
    b. Sample carrier
    c. Label bottles for each sample to be collected
3. **Inspect and put on protective equipment (PPE) for collecting process sample***
4. If closed loop, prepare Closed Loop Sampling Station to Collect Sample
    a. Verify valves on Sampling Station are in proper position to collect sample
    b. Circulate fresh material through the sampling system for 20-30 seconds
5. Collect Sample
    a. Insert clean sample bottle into the Sampling Station
    b. Fill the sample bottle through the septum, leaving adequate vapor space.
    c. Relieve pressure on sampling system back into the process
    d. Verify valves on Sampling Station are in proper closed positions
    e. Remove full sample bottle and place into Sample Carrier
    f. Line Opening Ends, additional PPE can be removed if conditions permit
6. Take samples to Lab for analyses
7. Conduct PPE post-use inspection and store for future use or discard PPE if not suitable for reuse

*At a minimum, Line and Equipment Opening Activities require additional PPE: Full or Half Face Air Purifying Respirator and Chemical Resistant Gloves. Some LEO tasks with higher risk of exposure require Chemical Suit and Supplied Air Respirator

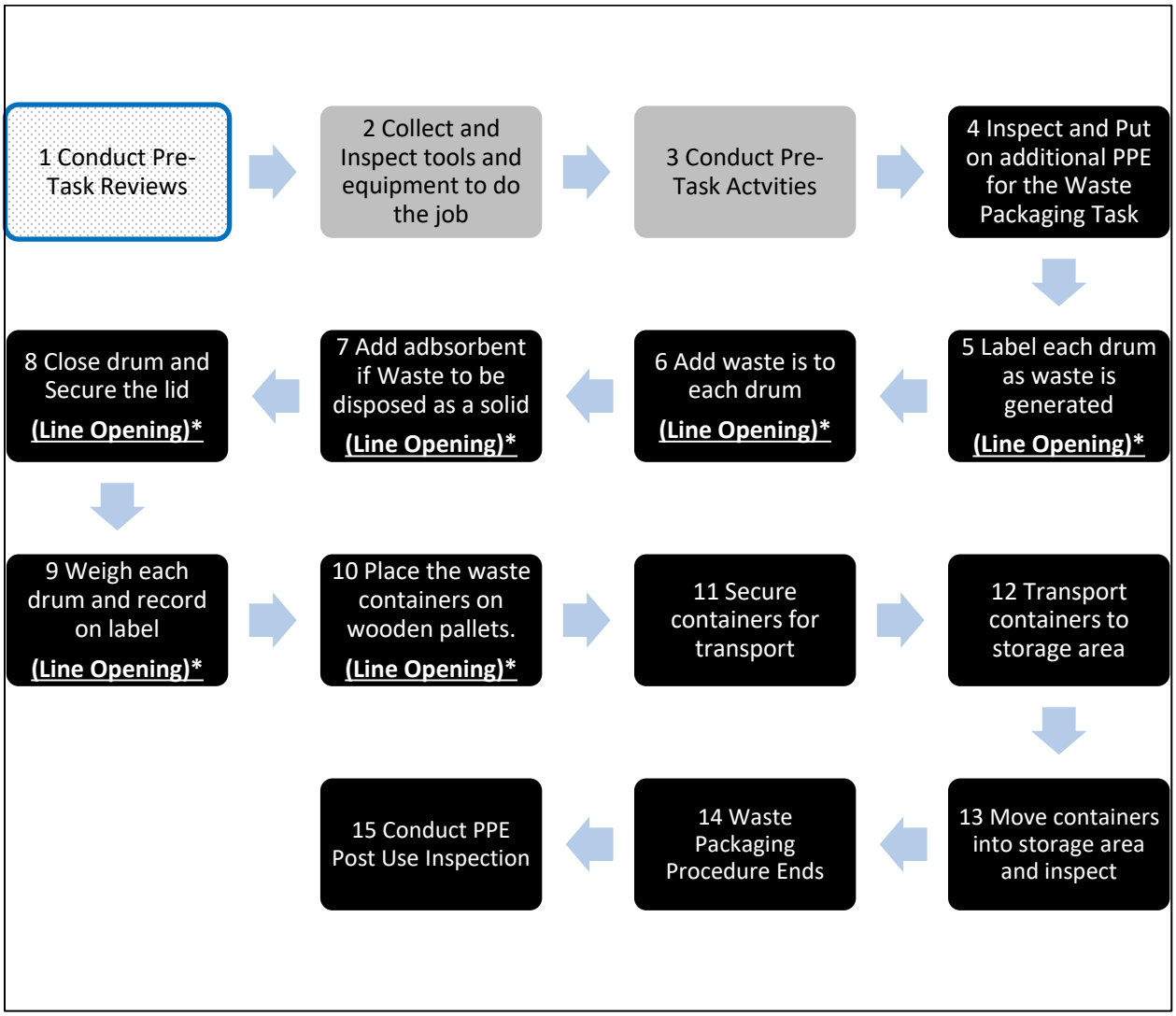
D. CTC Waste Packaging SOP (Solvent Waste/Retains)

1. SOP Flow Chart

Color Key:

Occur in office / control room **Occur in both office/control and field**

Occur in field



Underline text denotes steps that require additional PPE, and/or when additional PPE is donned or removed

D. CTC Waste Packaging SOP (Solvent Waste/Retains) (Continued)

2. SOP Overview

1. Conduct Pre-Task Reviews
    a. Scope & Risk Assessment
    b. Safety, Health and Environmental and Ergonomic Considerations
    c. Determine Proper PPE Requirements
2. Collect and inspect tools and equipment necessary to do the job
3. Conduct Pre-Task Activities – identify the following:
    a. Origin of the waste
    b. Waste Designation
    c. Container needed
    d. Compatible absorbent
    e. Intended disposal method
    f. Proper labels
4. **Inspect and Put on additional protective equipment (PPE) for Waste Packaging**
5. As the waste is generated, package and label the container as per the requirements determined in Step 1.
6. Add the waste to the drum.
    a. Note: The drum can only be open when waste being added or removed.
    b. If the waste will be disposed of as a solid offsite, all liquid must be completely absorbed.
    c. If the waste will be disposed of as a liquid, do not add any absorbent to the waste.
7. Close the drum and secure the lid.
8. If weighing the drum, write the weight on the drum or the drum label.
9. Place the waste containers on wooden pallets.
10. **Line Opening Ends – additional PPE can be removed if conditions permit**
11. Containers must be secured while in transport.
12. Transport the waste drums to the proper storage area.
13. Move the waste drums into the proper storage area and inspect the waste containers:
    a. If any part of the waste label is illegible or obscured in any form or fashion, re-label the drum
    b. If the label is not visible from the aisle space of the storage area, rotate the drum until the label is visible from the aisle space
    c. If the label is not dated, date the label with the date waste was generated
    d. If the exterior of the drum is contaminated, clean the exterior of the drum
    e. Ensure there is at least a minimum 24 inch aisle space between rows of drums
14. Conduct post-use PPE inspection and store for future use or discard PPE if not suitable for reuse

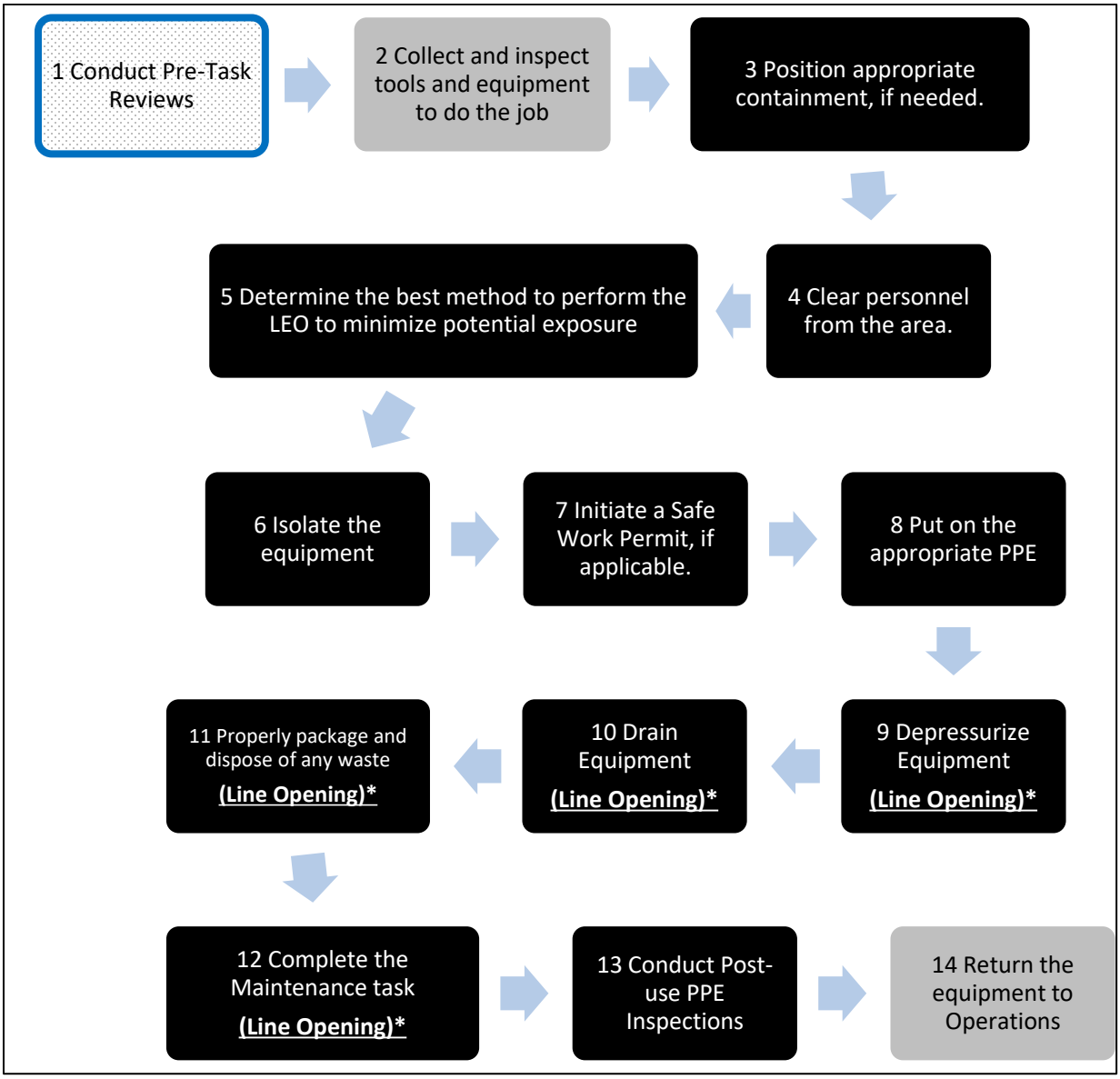
*At a minimum, Line and Equipment Opening Activities require additional PPE: Full or Half Face Air Purifying Respirator and Chemical Resistant Gloves. Some LEO tasks with higher risk of exposure require Chemical Suit and Supplied Air Respirator

E. CTC Minor Maintenance and Line Openings SOP

1. SOP Flow Chart

Color Key:

- Occur in office / control room
- Occur in field
- Occur in both office/control and field



Underline text denotes steps that require additional PPE, and/or when additional PPE is donned or removed

E. CTC Minor Maintenance and Line Openings SOP (Continued)

2. SOP Overview

1. Conduct Pre-Task Reviews
    a. Scope & Risk Assessment
    b. Safety, Health and Environmental and Ergonomic Considerations
    c. Determine Proper PPE Requirements
    d. Describe methods to Prepare and Confirm Line and/or Equipment is ready for Maintenance (Isolation, Depressurization, Draining/Disposal)
    e. Identify the exact location of the LEO.
2. Assemble and inspect equipment needed to perform the work.
3. Position appropriate containment, if needed.
4. Clear unnecessary personnel from the area.
5. Determine the best method to perform the LEO that minimizes potential exposure (regardless of PPE in use).
6. Isolate the process equipment.
7. Initiate a Safe Work Permit, if applicable.
8. **Don the appropriate PPE for the Line Opening Task***
9. As possible, clear process fluids from equipment into other process vessels
10. Perform the LEO.
    a. Depressurize equipment to vent recovery device
    b. Drain Equipment
11. Properly package and dispose of any waste associated with the LEO.
12. Complete the maintenance task associated with the LEO.
13. **Line Opening Task is complete – extra PPE can be removed if conditions permit**
14. Conduct Post-Use PPE inspection and store for future use or discard PPE if not suitable for reuse
15. Return the process equipment to Operations as per the plant policies

*At a minimum, Line and Equipment Opening Activities require additional PPE: Full or Half Face Air Purifying Respirator and Chemical Resistant Gloves. Some LEO tasks with higher risk of exposure require Chemical Suit and Supplied Air Respirator

HSIA halogenated solvents industry alliance, inc.

September 27, 2021

HSIA Response to EPA's Questions on Standard Operating Procedures (SOPs) at Carbon Tetrachloride and Other Solvent Manufacturing Sites

Carbon Tetrachloride Docket #EPA-HQ-OPPT-2020-0592; EPA-HQ-OPPT-2016-0733
Trichloroethylene Docket #EPA-HQ-OPPT-2020-0642; EPA-HQ-OPPT-2019-0500; EPA-HQ-OPPT-2016-0737
Perchloroethylene Docket #EPA-HQ-OPPT-2019-0502; EPA-HQ-OPPT-2016-0732
Methylene Chloride Docket #EPA-HQ-OPPT-2019-0437; EPA-HQ-OPPT-2016-0742

EPA posed several questions to HSIA on August 5, 2021 via email in preparation for meeting with HSIA and the EPA Carbon Tetrachloride (CTC) risk management team. As a part of that request, EPA asked for written responses that also noted when the information or answers applies to trichloroethylene, perchloroethylene, and methylene chloride. EPA's questions are presented in italics below followed by HSIA's response.

EPA: *What administrative controls (e.g., training, signs designating process areas, etc.) are in place to ensure SOP requirements are followed?*

HSIA: Employees, both new and seasoned, at our facilities are highly trained on a regular basis to ensure SOP requirements are followed. The following outline highlights some training sessions that focus on SOPs and information included in SOPs for new operator orientation, area training for experienced operators new to a process area, and additional training for specific tasks within a process area.

<u>Orientation Training of approximately 60 hours depending on the complexity of the unit and experience of the operator</u>

Orientation training for new operators includes, but is not limited to:

a. An overview of safety process systems and how employees will participate, be trained and tested on the safety systems;
b. Basic PPE requirements of the facility, the type of PPE used at the facility and how the task and/or area specific PPE is identified and required;
c. Training on the Hazard Communications Program required by 29 CFR 1910.1200, including the labeling system, how to obtain hazard information and review safety data sheets, the physical and health hazards they may encounter in the workplace, measures taken to prevent exposures such as work practices; and
d. Initial training on site-wide key procedures such as line break procedures.

Process specific area training of approximately 160 hours depending on the complexity of the unit and experience of the operator.

For experienced operators new to a process area, area training includes testing their knowledge of SOPs. This specific process training and testing requires that the operator demonstrates knowledge of:

a. The process area systems and operation guidelines;
b. The hazards of the process(es), and
c. The methods used to control those hazards specific to the plant area (e.g., information included in SOPs such as engineering controls, administrative controls, personal protective equipment).

The process specific area training is module-based training, followed by testing exercises to confirm process knowledge. A documented field walk through will be given by the unit process supervisor to determine if the trainee has the required knowledge of the unit.

Specific task training of approximately 360 hours depending upon the complexity of the unit and experience of the operator.

Additional job/task specific training is generally conducted on-the-job, on shift, on a one-on-one basis and focuses on the plant procedures and practices specific to the task expected to be performed within an area. Materials covered include training and testing an operator's knowledge of SOPs. Specific task training includes:

a. Field-based training with a transition towards taking the lead on specific tasks or duties based on demonstrated competence. Until a trainee reaches full qualification, the trainer maintains full accountability and responsibility for: 1.) the operation of the unit; 2.) the trainee's understanding; and 3.) managing the trainee's learning as they progress towards qualification;
b. Testing to ensure the operator can demonstrate an understanding of the training;
c. A job performance talk-thru must be performed or explained for every task. The walk-thru must be witnessed by a unit qualified technician and a supervisor. The trainer/supervisor will use a task check off list to verify that the trainee has completed all steps of the task correctly; and
d. Testing on each of the following applicable units: 1.) troubleshooting; 2.) safety procedures; and 3.) hazard assessments.

Refresher/Requalification Training

All employees who perform work under an SOP are trained on that SOP with refresher sessions on a regular basis. Retraining includes both a process-specific training refresher course that is conducted every six to twelve months after initial qualification and requalification and every three years at a minimum.

Additional Administrative Controls

Personnel entering certain process areas must sign in and out of the area. All personnel entering a process area must go through site orientation training that includes annual hazard communication/PPE training, which informs the employees about the hazards they work with in the facility, including all chemicals. The personnel must wear the minimum PPE required for entering the process area.

Signs are used within the plant to list the PPE required to enter a process area. In areas where additional PPE is routinely required, PPE requirements are posted in that area.

Finally, all SOPs must be readily available in hardcopy or electronically to employees that work in the unit.

EPA: *The SOP states that googles and work gloves are required anytime valves are operated and Figure 2 mentions nitrile gloves, which is consistent with some of the information provided during the risk evaluation process. Some work gloves do not offer chemical protection or offer limited protection. Are nitrile gloves the only gloves used? Is there a specific standard (e.g. ASTM) that is used or the manufacturer uses to determine the type of gloves?*

HSIA: Nitrile gloves are the primary gloves approved and listed in the PPE Hazard Assessments for tasks with potential exposure/contact with CTC. Nitrile gloves are also used for Perc and butyl gloves are used for TCE. In some cases, a specific PVC glove many be approved for tasks based on the hazard assessment. Other work gloves, such as cotton or leather, are not approved for any task where contact with CTC, Perc, Methylene Chloride or TCE is expected to occur (e.g., opening valves, etc.)

Glove permeation testing is typically performed by the glove manufacturers to make a preliminary decision of appropriateness of the glove materials for protection against chemical exposure. Chemical permeation testing is performed according to the American Society of Testing and Materials (ASTM) F739 total immersion and ASTA F1383 intermittent contact methods.

The ASTM F1383 is an intermittent test with one minute of immersion followed by nine minutes of no immersion, and then repeated up to a maximum of four hours or 240 minutes. The test was designed for showing reasonable use of gloves with highly volatile chemicals where limited contact was involved and not total immersion.

Other glove selection factors are considered such as length of task, type of task performed, and expected exposure. Many of the glove recommendations made are for tasks where incidental contact, i.e., no contact (or at worst very little contact), with a chemical is anticipated. The gloves specified are intended to prevent chemical contact with the skin during an unanticipated event – such as a spill or splash to the hand. Based upon the controls and standard operating practices in place, chemical contact is rarely seen with the glove, and these practices have been successful in

making actual hand contact with the chemical during the task practically unseen as a risk to hands protected by gloves. If there is a rare situation that creates contact with the glove or with gloved hand, the gloves are removed and the hands are washed.

EPA: *How are the PPE selections modified when the chemical hazard involves a mixture of chemicals compared to a single individual chlorinated solvent hazard?*

HSIA: The PPE is selected that best provides protection against the chemical of highest concern or the chemical that presents the most likelihood/potential for exposure to the worker in the mixture. The chemical hazard determination for each chemical in the mixture is made using the permeation data for that chemical published by the manufacturer (ATSM F739). This is the standard for liquids and gases. The Hazard Assessment provides the glove selection information to employees or those personal purchasing gloves.

EPA: *The document states that gloves are donned before sampling and loading/unloading activities. In addition, we understand tasks take 5-30 minutes. How many times are gloves reused and how is the number of reuses calculated based on breakthrough time and other workplace factors? How are the employees trained to recognize that a glove can no longer be used?*

HSIA: Employees are trained on how to inspect PPE used as part of unit orientation/SOP training as outlined in the PPE self-inspection guideline. If the gloves used for sampling/loading/unloading or line opening do not pass inspection (e.g., by showing any sign of discoloration or deformity) or have otherwise been in contact with a chemical, the gloves are disposed of per PPE policy.

Use or reuse of gloves vary based upon the task but are typically disposed of quickly. Cost is not considered in glove reuse. If the gloves do not pass inspection, they are disposed and replaced. In some cases, gloves are disposed of after a task or at the end of a shift. While there is training that requires when gloves should be disposed of, there are no restrictions on obtaining a new set of gloves after a single use or as needed or identified by the operator.

EPA: *If concentrations and amounts of accidental contact are minimal, how does the facility determine if the gloves should be replaced? Is it simply based on employee inspection or evidence? Have you considered using charcoal patch testing?*

HSIA: The PPE disposal decision is based on the employee's inspection or implemented policies, such as a single use for specific tasks. If the gloves used for sampling/loading/unloading or line opening do not pass inspection (e.g., by showing any sign of discoloration or deformity) or have otherwise been in contact with a chemical, the gloves are disposed of per PPE policy.
There are no incident trends that indicate the current methods of protection, inspection and glove replacement are not protective. Charcoal patch testing is not an industry standard.

In addition to the engineering controls and PPE use that prevents exposure, any minimal accidental exposure is also mitigated by the highly evaporative nature of the solvents. As mentioned above, although glove inspection and disposal in certain cases is mandatory, there are no restrictions on obtaining a new set of gloves after a single use.

EPA: *Can you clarify what is entailed in the step "extra PPE can be removed if conditions permit".*

HSIA: PPE can be removed if conditions permit although it is not typical to remove or downgrade PPE. For respiratory protection to be removed, it must be validated that exposures are below applicable exposure limits and/or within the protection factor of the respiratory protection type being downgraded to. Direct read instrumentation is often used to establish baseline concentrations during the performance of a task and/or to clean an area after a task has been performed. There must be sufficient evidence to suggest that exposures do not exceed exposure limits and PPE (including respiratory protection) is no longer needed. If there is any potential for the employee to come into contact with any liquid, splash, overspray, etc., then PPE would not be removed.

One example of when PPE requirements can be modified for a specific task, if conditions permit, would be a line opening task that requires full body PPE and a respirator for a "first break", when the individual begins to loosen bolts on a flange to break the line apart. Prior to this, the line has been cleared for maintenance. Once it has been verified using direct read instrumentation that the equipment is clear of all liquids, then the PPE requirements may be modified.

Other examples would be when a worker leaves the area where the potential exposure exists, a line opening task is completed and the equipment is closed up and returned to normal operations; or if the real time air monitoring with a direct reading instrument for specific chemicals shows that the level is below the exposure limit, then the PPE may be modified for that specific task. Permission from the environmental health and safety department, the operations permit writer or a supervisor may be required to make this decision. The full PPE must be put back on before the worker reenters the work area, for example, where the risk of solvent exposure exists until the specific task if completed and the risk of exposure no longer exists.

EPA: *Do you use any tools in addition to gloves, such as glove bags, tongs, funnels, SafeTainers®, etc. for any of the tasks that may lead to contact with CTC or other solvents? If not, have you considered these tools? If these tools are mot helpful or feasible, could you explain why not?*

HSIA: The tools listed in the question are not applicable to the CTC, TCE, Perc or Methylene Chloride manufacturing or feedstock processes. Closed loop sampling systems are used to collect process samples. Emission control devices are used to collect and dispose of vapors for rail car loading and unloading. If additional tools are used (wrenches, etc.), then they would need to be

evaluated for use on a task-by-task basis and decontaminated after the task is completed prior to reuse or be disposed of.

There are no incident trends that would lead us to research alternatives or additional methods of protection such as those listed. Our typical activities don't currently necessitate use of the tools listed in the question above.

EPA: *What circumstances trigger the need for the lower and the higher range of PPE when documentation suggests a range?*

HSIA: The potential for exposure to a chemical while performing a task determines the level of PPE required. This is based on the engineering controls in place for the task/process, the industrial hygiene data, and an assessment of the task to determine what the exposure level and frequency of exposure might be. In some cases, PPE may not be needed based on the exposure assessment, yet it is required by the hazard assessment to be worn as an additional backup layer to protect the worker.

EPA: *The waste packaging SOP has a step for cleaning. "If the exterior of the drum is contaminated, clean the exterior of the drum." Could you clarify how the drum is cleaned and what PPE is used during this step?*

HSIA: The drum is cleaned using a solvent chosen for the type of contamination. For CTC wastes, it would likely be perchloroethylene. In that instance, the required PPE would be full body protection and a full-face respirator with supplied air. For Perc wastes, it's most likely that perc is used to clean the drum. For methylene chloride wastes, it's most likely that methylene chloride is used to clean the drum, and for TCE wastes, it must likely that TCE is used.

EPA: *We understand that the NESHAPs require management practices consisting of quarterly inspection for leaks. Are there any additional inspections, for example, due to process changes or equipment updates, and if so, how often do they occur?*

HSIA: In addition to the quarterly inspections referenced above, HSIA's CTC, perc, TCE and methylene chloride manufacturing, processing and feedstock facilities implement the following multi-layered inspection program, management of change (MOC) procedures and pre-start up safety reviews (PSSR) requirements.

Operator Rounds
Operator audible, visual and olfactory (AVO) rounds occur at least twice each shift. During this time, operators are walking through the process area looking for leaks, drips and odors while they are taking readings from field instruments.

Mechanical Integrity Inspections
EPA's RMP (40 CFR 68.73) and OSHA's PSM (29 CFR 1910.119(j)

a. These regulations impose performance-based mechanical integrity programs that apply to the manufacturing and processing equipment. In certain cases, these standards allow/require site-specific inspection practices, maintenance and replacement based upon process knowledge and experience.

b. Industry standards for mechanical integrity incorporate Generally Accepted Good Engineering Practices (RSAGAGEP) for the process safety/mechanical integrity program (including design, fabrication, installation, inspection, testing and repair.

c. Performance-based standards and site-specific implementation for testing, inspection and repair begins with API industry standards. For example, (i.) API 653 for Tanks; (ii) API 570 and 574 for Pipes; and (iii) API 510 and API RP 572 for pressure vessels.

Management of Change (MOC)
(40 CFR 68.75) and (29 CFR 1910.119(1))

d. The MOC process reviews any changes proposed for existing processes prior to the implementation to minimize the occurrence of unplanned events. The MOC provides a mechanism for documenting changes and tracking all follow-up activities resulting from changes.

e. Supplemental training is implemented based upon each site's MOC program and training is presented when needed and upon the MOCs in place.

Pre-Startup Safety Review (PSSR)
(40 CFR 68.77) and (29 CFR 1910.119(i)

PSSR reviews the installation of new processes (new facilities), significant modification to processes, or a change to process safety information. This review is to ensure that all process safety system(s) affected by the change have been reviewed to verify that they are in place and adequate prior to the introduction of chemicals or energy to the process.

Reportable Quantity

The mechanical integrity inspections, quarterly inspections and AVO rounds described above are actions taken to both prevent and detect any releases early. The reportable quantity levels (per the Clean Water Act Section 311, CERCLA and DOT) represent additional regulatory programs in place to detect and end any potential release.

Reportable quantities for the substances discussed in this response are listed below.

	CWA Section 311 40 CFR § 117.3	**CERCLA 40 CFR § 302.4**	**DOT 40 CFR § 172.101 Table 1 to Appendix A**
Carbon Tetrachloride 56-23-5	Not listed	10 lbs	10 lbs
Perchloroethylene 127-18-4	Not listed	100 lbs	100 lbs
Methylene Chloride 75-09-2	Lot listed	1,000 lbs	1,000 lbs
Trichloroethylene 79-02-6	100 lbs	100 lbs	100 lbs

EPA: *Upon entering the production area or designed process area, at what point do respirator use requirements take effect?*

HSIA: The production areas for CTC, TCE, Perc and Methylene Chloride are all located outside and the equipment is a closed process system. Respirators are not required to be worn in the process area under normal operating conditions but are required per the task.

This is supported by the industrial hygiene data collected for employees working in the process area. Full shift and task-based samples are evaluated against the applicable occupational exposure limits. When precautionary protection is required for certain tasks, that requires respiratory protection. If another employee is going to enter the area where an SOP task is being conducted, they too would have to don the appropriate PPE for that SOP.

Appendix 3

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Meeting with EPA on Chlorinated Solvent Feedstocks in HFC/HFO Production and Cross Cutting Issues

May 25, 2021

Agenda

halogenated solvents industry alliance, inc.

1. Implications of Restricting Feedstock Use
2. Cross Cutting Concerns
    i. Hazard Assessment
    ii. Inhalation Exposure
    iii. Dermal Exposure
3. Examples: Conditions of Use should Consider existing Layers of Protections
    i. Manufacture
    ii. Feedstock Use

Overarching Issues

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1) The hazard assessments were not based upon best available science and weight of evidence. As an example, these concerns are documented in the Request for Correction submitted to EPA for CTC.

2) Conditions of Use in the Risk Evaluation did not incorporate standard engineering and workplace industrial requirements for dermal or inhalation potential exposure, as implemented under NESHAP and OSHA regulatory requirements.

3) These errors in the Risk Evaluations do not provide a scientific or practical basis for the Risk Management Rule and should be remedied before or during the Risk Management Phase.

Implications of Restricting Feedstock Uses

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- CTC, PERC and TCE are used as a feedstock for refrigerant gases and other critical uses such as automotive and stationary air conditioning.

- The implications of these unreasonable risk determinations are enormous for the environment as well as the US economy.
  - For example, the Kigali Amendment to the Montreal Protocol, which mandates a global phase down of HFCs, is predicated on the widespread availability of low-GWP alternatives such as HFO-1234yf and related HFOs which rely on these substances as feedstock.
  - The importance of this transition was recognized by the inclusion of HFC phase down provisions in the omnibus spending bill approved in December 2021, hailed as the most important measure to fight climate change ever enacted by Congress

- CTC feedstock is required for production of HFOs, the critical low-GWP alternatives.

- The transition to HFOs will take over a decade, and during this time HFCs will still be very much in demand. Restricting the use of TCE and perc as HFC feedstocks could cause severe disruptions in important user sectors such as refrigeration, HVAC, and mobile A/C.

Issues with Hazard Assessments

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- Decisions not based on weight of the scientific evidence
- Deficiencies in the use of best available science
- Carbon tetrachloride (CTC) cancer hazard assessment
  - EPA disregarded advice from scientific advisory committees (IRIS, SACC) on CTC cancer mode-of-action (MOA) and derivation approach for a cancer toxicity/risk value
  - EU concluded CTC acts as a carcinogen by a threshold MOA with a Derived-Minimal-Effect-Level (DMEL) based on a No-Observed-Adverse-Effect-Concentration (NOAEC) of 5 ppm for mouse liver tumors
- Similar problems also exist for the cancer hazard assessments of TCE and PCE

Issues with Hazard Assessment

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- Considerable objectivity concerns with the systematic review of TCE (and PCE) cancer epidemiology studies.
  - Similar view by the NAS committee review of the TSCA systematic review process.
- Significant scientific validity problems with key TCE autoimmune study (Keil *et al.*, 2009) for the chronic non-cancer toxicity endpoint.
- Inaccurate and misleading interpretation of one of the key PCE studies (Cavelleri *et al.*, 1994) for the chronic non-cancer toxicity endpoint.

Inhalation Exposure Assessment Concerns in TSCA Risk Evaluations

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- Lumping all worker exposure data together for a condition of use
  - Does not differentiate tasks or similar exposure groups (SEGs)
  - Tasks are combined having an array of exposure profiles: differences in processes, frequency of exposure, exposure duration, etc.
  - Matching non-routine vs. routine tasks with inappropriate health benchmarks
    - Impacts risk characterization and determination of Existing Chemical Exposure Limits (ECELs)
    - Workers/ONUs that have infrequent or rare exposure potential should be benchmarked with an 8-hr TWA based on acute effects, not an 8-hr TWA based on cancer and/or non-cancer effects that require repeated daily exposures.
- Bias due to considerable amount of worker/ONU monitoring data below the Level of Quantitation (LOQ)

Dermal Exposure Assessment Concerns in TSCA Risk Evaluations

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- Engineering controls (CAA MACT standards) are designed to prevent industrial emissions and exposures.
- TSCA risk evaluations excluded consideration of EPA-mandated MACT standards in dermal exposure models for closed system production/feedstock use facilities.
- Instead, EPA dermal exposure model assumed open process assuming both hands on both sides have liquid contact. Moreover, EPA assumed liquid stayed on unwashed hands (if gloves used, not removed) for the entire 8-hr work shift.
- Splash exposures are not allowed at these facilities and worst-case exposure (rare) are reduced to drops from, for example, transfer lines.

Dermal Exposure Assessment

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Closed, hard-piped systems, engineering controls and procedures for manufacturing and processing prevent the type of dermal exposure scenarios assumed in the risk evaluations.

EPA Assumption in dermal model	Actual Condition of Use for intermittent tasks such as loading, unloading, sampling and line openings with any potential dermal exposure
Undiluted, full hand CTC contact each shift.	Tasks are 15 min., approximately once a shift, engineering controls and PPE protect from potential exposure. Rare, worst-case exposures are reduced to drops, not full hand contact.
Workers do not wash hands during a shift.	Any liquid prompts immediate glove removal and hand washing. Hands are washed after the task. (Not an infinite dose).
Workers wear the same gloves for 8 hours.	The integrity of gloves are inspected both before the task and when removed immediately after the task.

The dermal assumptions used in the risk evaluation for manufacturing and processing do not reflect the actual condition of use.

Dermal Exposure Assessment

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- Final risk evaluation drastically overstates the dermal risk for chlorinated solvents in closed processes used in production and feedstock use.
  - Skin loading (2.1 vs. 0.2 mg/cm2)
  - Skin area for contact (1070 vs 134 cm2)
  - Fraction absorbed (versus evaporation)
- Dermal exposure in final risk evaluations does not account for rapid evaporation of these highly volatile substances. (evaporation time for 2 g ranges from 0.5- 2min at 25 degrees C)
- 2 grams deposited on the hand is more representative of dermal exposure to water from consumer washing dishes
- 2 grams deposited on the glove would evaporate in under 5 min. The gloves are impervious to the solvent for short exposure time
- Using a more realistic yet still conservative approach results in exposures 40-250x lower depending on the substance properties

The Manufacturing and Processing Conditions of Use should consider Existing Layers of Protection

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FACILITY DESIGN

ENGINEERING CONTROLS

- Closed Vent System – hard piping into control devices or recycled
- Emission controls such as scrubbers, thermal oxidizers or flares with a required destruction efficiency
- Vapor recovery units, vapor balancing to a control device
- Caps and/or double valves so no single layer to a potential open line
- Closed loop sampling
- Welding fittings

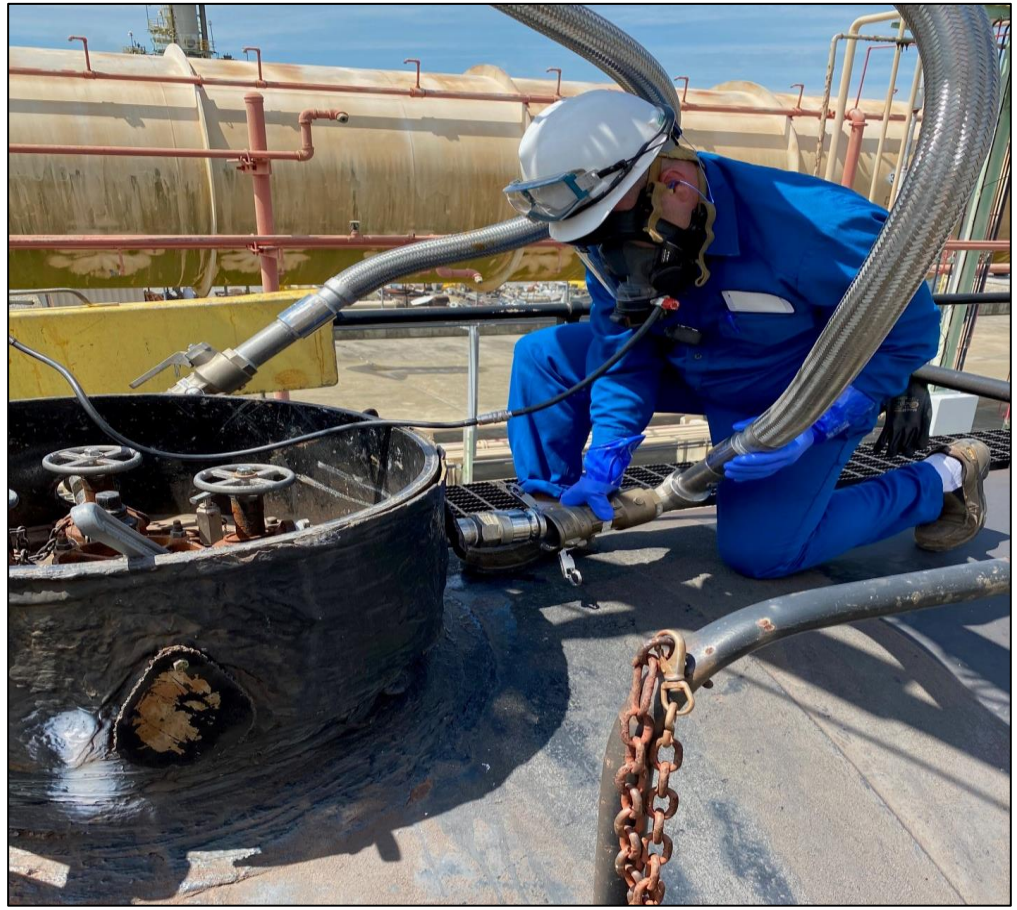
ADMINISTRATIVE CONTROLS

- Employee Training and Qualification
- Standard Operating Procedure
- Permitting Requirements
- Access Controls
- Leak Detection and Repair
- Distributive Control Systems

PERSONAL PROTECTIVE EQUIPMENT (PPE)

- Standard Plant PPE is typically hard hat, safety glasses, steel-toed shoes, earplugs (as required by signage). Chemical gloves, chemical resistant suit and respirator use is required based upon task.
- Full shift and task-based sampling confirms engineering controls and administrative controls are protective
- Monitored by Specific Exposure Groups
- Exposure data does not account for half-face or air-supplied respirator worn during monitoring periods (personal monitor device is worn “outside” PPE).

Layers of Protection Loading/Unloading



Engineering Controls: NESHAP Controls for loading/unloading, transfer racks (40 CFR 63.126-130, 2475, 2525) *e.g.*, vapor recovery units, vapor balancing, incineration with a required destruction efficiency.

Administrative Controls: Standard Operating Procedures includes the procedures to use the engineering controls and the necessary PPE for the task.

PPE: chemical resistant gloves, clothing and footwear; air supplied respirator.

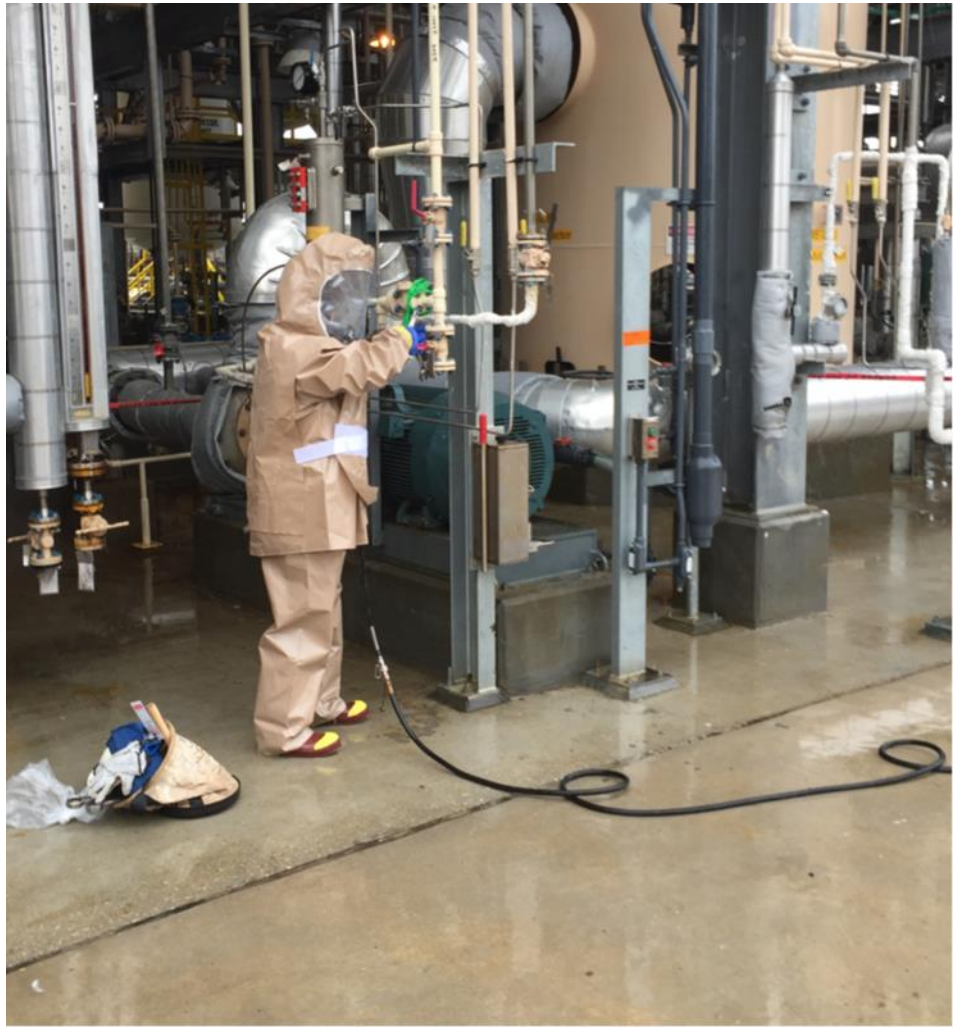
Layers of Protection Sampling

Engineering Controls: Process sampling systems for CTC prevents releases or potential personnel exposure.

Administrative Controls: Standard Operating Procedure (SOP) includes the procedures to use the engineering controls and the necessary PPE for the task.

PPE requirements: Goggles, hand protection and air purifying respirator

Layers of Protection Line Opening



Administrative Controls: Standard Operating Procedure and Permitting requirements before each task:

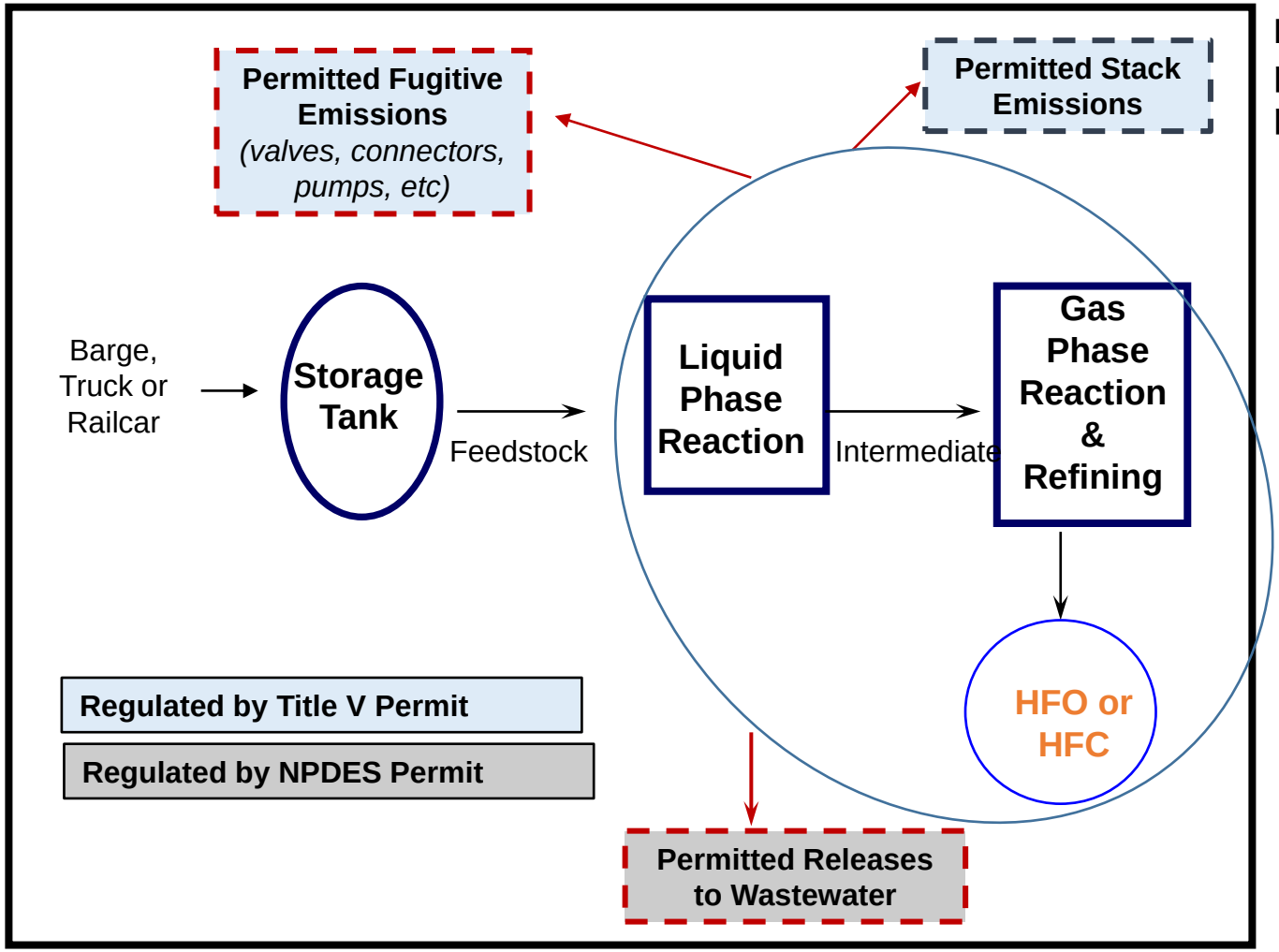
- Required hazard analysis
- Communication tool between maintenance and operations
- Ensure that work hazards are identified and mitigated prior to the work beginning
- Barricade

Engineering Controls: two layers of protection for the duration of the task for example, for a line break:

- Line clearing
- multiple layers of isolation

PPE: chemical resistant gloves, clothing and footwear; air supplied respirator

Use of Chlorinated Solvent as a Feedstock



Loading/unloading operations should include the following protections required by regulations in the manufacturing and processing condition of use:

i. **NESHAP regulations/Engineering Controls:** The HON NESHAP requires engineering controls such as vapor collection, balancing and/or controls to control emissions during unloading/loading. (40 CFR 63.126-130, 2475, 2525)

ii. **SOPs/Administrative Controls:** As required by OSHA, each site implements Standard Operating Procedures (SOPs) to ensure the engineering controls are effectively and safely used in the unloading/loading process. (29 CFR 1910.119(f))

iii. **PPE:** PPE (respiratory and dermal) is identified and required for unloading/loading operations. For dermal, gloves are selected based upon potential exposure and nature of potential hazards for the task. (OSHA 29 CFR 1910.138.) OSHA also recognizes factors, *e.g.,* required dexterity, length of glove, temperature, and duration of task, that may be evaluated for use when selecting the proper dermal protection. (29 CFR Subpart I Appendix B.11)

HFC Allocation Proposed Rule

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- Proposal published a week ago.
- EJ section is rooted in these TSCA evaluations: focus is entirely on solvent feedstocks: “known to present an unreasonable risk of injury to the health of workers or occupational non-users in processing as a reactant or intermediate in industrial gas manufacturing.”
- The TSCA Evaluations are also impeding transition to HFOs where solvents now presented as risk at fenceline as well as to workers.
- NESHAPs adopted under §112(d) of the Clean Air Act specifically “to provide an ample margin of error of safety to protect public health” in fenceline communities should be focus of EJ analysis but are not mentioned.

Key Takeaways

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- EPA must use the best available science in assessing risks, consistent with peer reviewer advice.
- Dermal exposure is not an issue for these conditions of use.
- EPA must look at NESHAP requirements in assessing workplace exposures and fence line risk.
- Failure to reflect foregoing will offshore HFO/HFC manufacturing.

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Carbon Tetrachloride Risk Management Rule August 17, 2021

Docket EPA-HQ-OPPT-2016-0733
EPA-HQ-OPPT-2019-0499

Carbon Tetrachloride Agenda

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1. Environmental Benefits
2. Federal CAA Emission Controls
3. Layers of Protection in Facilities
4. Risk Evaluation and Exposure Concerns
5. EPA Questions

CTC Feedstock Use Has Environmental Benefits

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- CTC is the feedstock for all the low GWP HFO alternatives that will enable compliance with the Kigali Amendment and the AIM Act, including the refrigerant HFO-1234yf.

- Example: HFO-1234yf, refrigerant replacing R-134a for auto A/C, has a low GWP:

  R-134a: 1,300 GWP

  HFO-1234yf: 4 GWP

TSCA Section 6(c)(A)(iii) considers the benefits of a chemical substance in the Risk Management Rule process.

CTC is a critical building block for low GWP refrigerants.

Implications of Restricting Feedstock Uses

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Eliminating CTC as a feedstock use would threaten major production facilities just opened in Louisiana and Texas, along with a projected additional 33,000 new American manufacturing jobs, $12.5 billion increase in direct output per year by 2027, and 25 percent boost in US exports of refrigerants and related equipment.

TSCA §6(c)(A)(iv) considers the economic consequences of a chemical substance in the Risk Management Rule process.

Industry has heavily invested in the transition to low GWP refrigerants using CTC.

The transition to low-GWP refrigerants will take over a decade, eliminating the manufacture or use of CTC as a feedstock would cause severe disruptions in the transition to low GWP refrigerants.

CTC Emissions Controlled by Federal CAA

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National Emission Standards for Organic Hazardous Air Pollutants (NESHAP) imposes standards and controls on CTC facilities.

- Synthetic Organic Chemical Manufacturing Industry (HON) 40 CFR Part 63 Subparts F, G, H, and I, and/or
- Miscellaneous Organic Chemical Manufacturing (MON) 40 CFR Part 63 Subpart F

CAA Title VI (Montreal Protocol)
Protection of Stratospheric Ozone

- 40 CFR Part 82

TCSA §6(c)(A)(i) requires consideration of exposure in the Risk Management Rule process.

Existing federal Clean Air Act requirements currently reduces exposure with controls, standards and use limitations.

NESHAP Emission Standards and Controls

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HON and MON NESHAPs. Impose standards and controls to prevent emissions and exposure from CTC manufacturing and processing facilities:

- Process Vents
- Wastewater
- Storage Tanks and Vessels
- Loading/Unloading transfer racks
- Fugitives - Leak Detection and Repair

CAA Residual Risk Review (CAA §112(f)(2)). EPA determined that no changes were required for CTC controls under the HON (71 Fed. Reg. 76603 (Dec. 21, 2006)) or the MON (85 Fed. Reg. 49084 (Aug. 12, 2020)) because the regulations impose CTC controls that:

- Reduces HAP emissions to levels that present an acceptable level of risk, and
- Protects the public health with an ample margin of safety.

Montreal Protocol Limits Uses of CTC

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Protection of Stratospheric Ozone, 40 CFR Part 82.3, limits the use of CTC to the following:

(1) the manufacture of a controlled substance that is subsequently 100% transformed (*i.e.,* used as a feedstock);
(2) the reuse or recycling of a controlled substance;
(3) amounts that are destroyed by approved technologies; and
(4) amounts of CTC that are unintentionally vented or spilled.

In addition to the HON and the MON NESHAPs, these use limitations require additional engineering and emission controls, as well as recordkeeping and reporting requirements, to maintain compliance.

Layers of Protection
CTC Manufacturing or Processing

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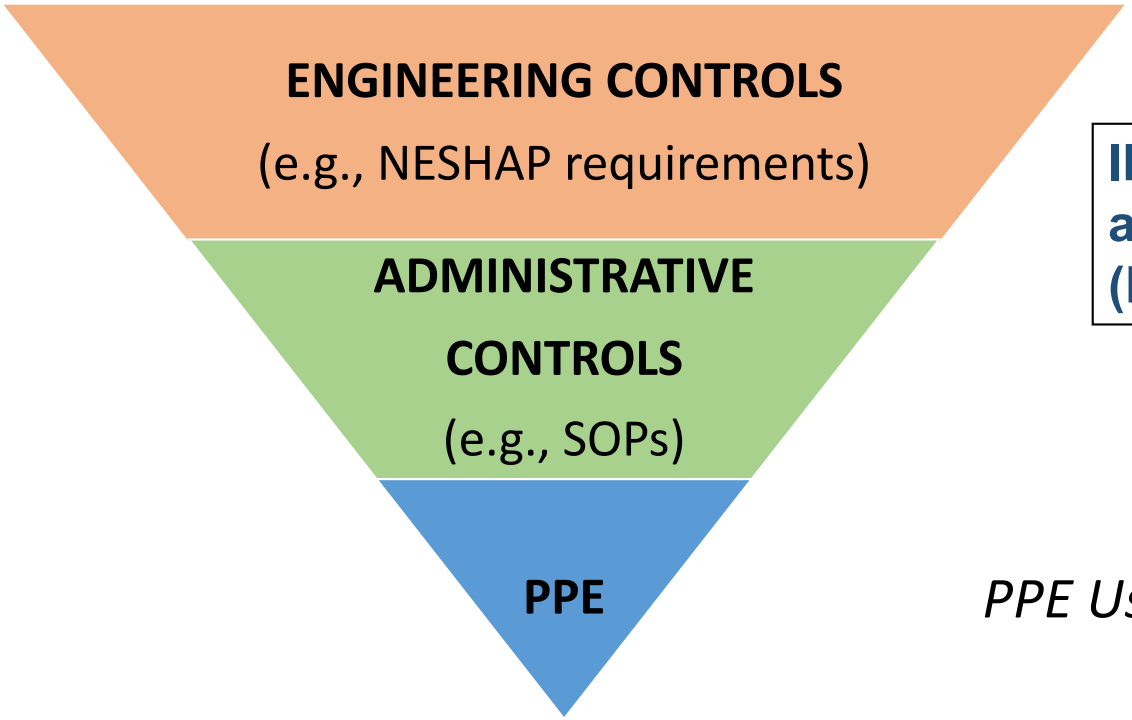
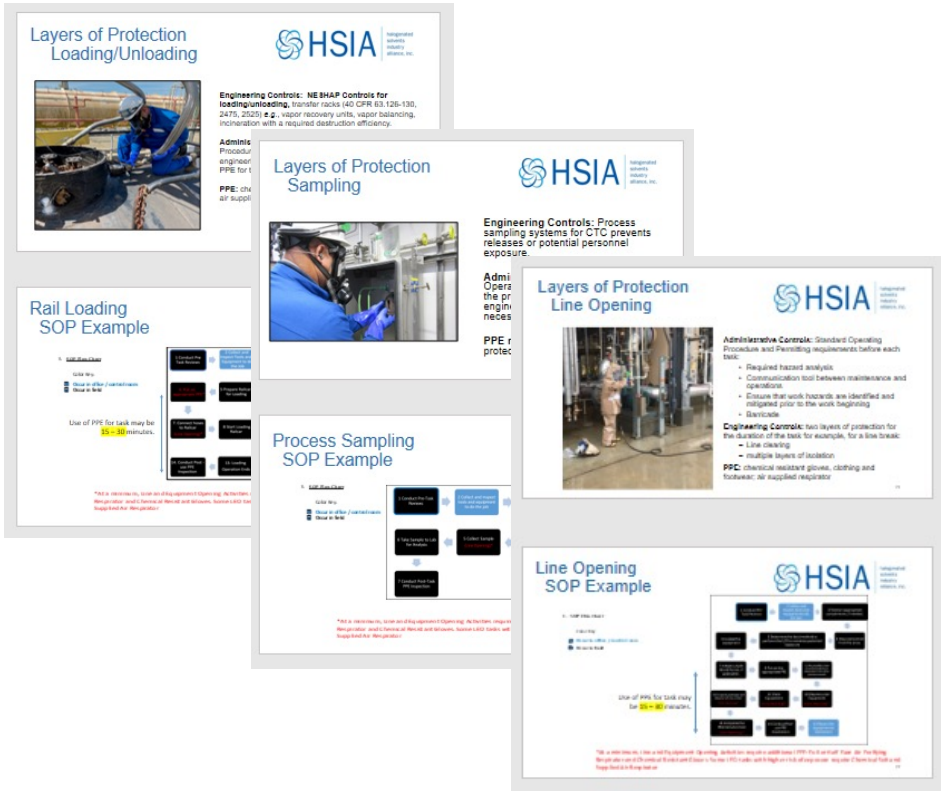


IH Monitoring Confirms Control and SOP Effectiveness. (Measured Outside of PPE.)

PPE Use Does Not Equal Exposure

Layers of Protection by Task



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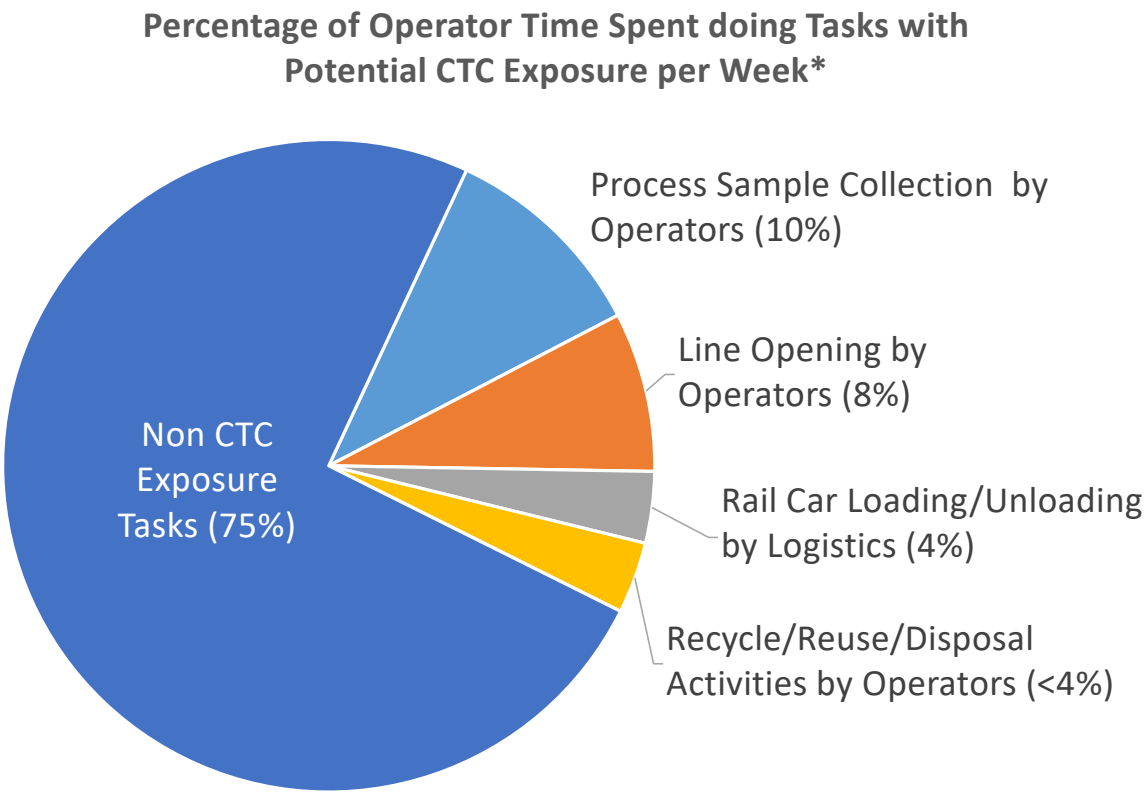
- Risks are mitigated by standard detailed SOPs for all tasks
- Operators in Manufacturing and Feedstock Facilities spend most of their time out of the process area

Analysis of CTC Tasks



Majority of Operator Task Time Don't Involve CTC Exposure Potential

**All tasks not necessarily conducted by a single operator; could be spread across multiple groups*

**Line Opening, Loading/Unloading, and Recycle etc tasks are performed weekly. Process Sampling is a daily task.*

Risk Evaluation Concerns

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Hazard Assessment

- The Risk Evaluation uses a linear non-threshold model coupled with an assumption that the principal study relied upon did not produce a no-observed-adverse-effect level (NOAEL) for mouse liver tumors.
- This approach disregards the advice provided by outside peer reviewers, resulting in estimates of risk thousands of times higher than reality.

ONUs as defined in the Risk Evaluation do not exist

- PPE is required by task, not job title.
- Any person/worker is subject to PPE requirements imposed on a specific location and/or task.

Exposure Assessment

- The ONU category is overestimated in Risk Evaluation.
- The CTC dermal exposure modeling overestimates exposure

Screening Assessment

- Fenceline assessments were conducted for the NESHAP HON and MON Residual Risk Review.
- The NESHAP Standards and Residual Risk Reviews should be utilized for the review in accord with TSCA §9.

"ONU" Risk Concerns

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"ONU" as defined in the Risk Evaluation does not exist in Manufacturing and Processing Facilities.

- PPE requirements are driven by task and potential exposure, not job classification.
- If a supervisor is in the area of a SOP-covered task, the supervisor must don appropriate PPE.
- SOPs implement a restricted area & removal of all nonessential personnel before tasks begin.

The Risk Evaluation overestimates exposure for ONU-like workers.

- All exposure values for ONU-like workers were less than the limit of detection (<LOD)
- For workers not performing certain SOP tasks, it is expected that exposure will be <LOD.

Dermal Modeling Overestimates Exposure

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- Facilities employ closed, hard-piped systems, engineering controls and procedures
- Tasks are infrequent and typically of short duration during a shift
  - Engineering controls and PPE protect from potential exposure.
  - Rare, worst-case exposures are reduced to drops, not full hand contact.
- Any liquid prompts immediate glove removal and hand washing. Hands are washed after the task. (Not an infinite dose).
- The integrity of gloves are inspected both before the task and when removed immediately after the task.
  - Contaminated or damaged gloves are replaced

TSCA Section 6(c)(A)(i) requires the Risk Mitigation Rule to take into account the magnitude of exposure. The Risk Evaluation overestimates dermal exposure.

Risk Mitigation Rule Summary

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1. CTC is the building block for the next-generation low GWP alternatives.
   A. Environmental Benefits
   B. Economic Benefits

2. The Risk Mitigation Rule should recognize, but not unnecessarily duplicate, federal controls:
   A. NESHAPs established by EPA to reduce CTC and other HAP emissions to levels that present an acceptable level of risk and protect public health with an ample margin of safety.
   B. Workplace limits enforced by OSHA
   C. OSHA's Process Safety Mgmt (PSM) and EPA's Risk Mgmt Program (RMP) performance-based requirements, including facility specific:
      1. Operating instructions (SOPs)
      2. Emission control instructions
      3. PPE requirements
      4. Mechanical Integrity
      5. Mgmt of Change
      6. Pre-Startup Safety Review (PSSR)

Questions from EPA

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1. The SOP states that goggles and work gloves are required anytime valves are operated and Figure 2 mentions nitrile gloves, which is consistent with some of the information provided during the risk evaluation process. Some work gloves do not offer chemical protection or offer limited protection. Are nitrile gloves the only gloves used?
    - Is there a specific standard (e.g. ASTM) that is used or the manufacturer uses to determine the type of gloves?
2. How are the PPE selections modified when the chemical hazard involves a mixture of chemicals (compared to a single individual chlorinated solvent hazard)?
3. The document states that gloves are donned before sampling and loading/unloading activities. In addition, we understand tasks take 5-30 mins. How many times are gloves reused and how is the number of re-uses calculated based on breakthrough time and other workplace factors? How are employees trained to recognize when a glove can no longer be reused?

Questions from EPA…

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4. If concentrations and amounts of accidental contact are minimal, how does the facility determine if the gloves should be replaced? Is it simply based on employee inspection of evidence? Have you considered using charcoal patch testing?
5. Could you clarify what is entailed in the step “Extra PPE can be removed if conditions permit”?
6. Do you use any tools in addition to gloves, such as glove bags, tongs, funnels, SafeTainersTM, etc. for any of the tasks that may lead to contact with CTC? If not, have you considered these tools? If these tools are not helpful or feasible, could you explain why not?
7. What circumstances trigger the need for the lower and the higher range of PPE when documentation suggests a range?

Questions from EPA…

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8. The Waste Packaging SOP has a step for cleaning: “If the exterior of the drum is contaminated, clean the exterior of the drum.” Could you clarify how the drum is cleaned and what PPE is used during this step?
9. We understand that the NESHAPs require management practices consisting of quarterly inspections for leaks. Are there any other additional inspections, for examples due to process changes or equipment updates, and, if so, how often do they occur?
10. Upon entering the production area or designated process area, at what point do respirator use requirements take effect?
11. What administrative controls (e.g. training, signs designating process areas, etc.) are in place to ensure SOP requirements are followed?

BACKUP INFORMATION

- The next few slides were also shown in today's meeting

Layers of Protection
CTC Manufacturing or Processing

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FACILITY DESIGN

ENGINEERING CONTROLS (e.g., NESHAP requirements)

- Closed Vent System – hard piping into control devices or recycled
- Emission controls such as scrubbers, thermal oxidizers or flares with a required destruction efficiency
- Vapor recovery units, vapor balancing to a control device
- Caps and/or double valves so no single layer to a potential open line
- Closed loop sampling
- Welding fittings

ADMINISTRATIVE CONTROLS (e.g., SOPs)

- Employee Training and Qualification
- Standard Operating Procedure
- Permitting Requirements
- Access Controls
- Leak Detection and Repair
- Distributive Control Systems

PERSONAL PROTECTIVE EQUIPMENT (PPE)

- Standard Plant PPE is typically hard hat, safety glasses, steel-toed shoes, earplugs (as required by signage).
- Chemical gloves, chemical resistant suit and respirator use is required based upon task.
- Full shift and task-based sampling confirms engineering controls and administrative controls are protective
- Monitored by Specific Exposure Groups

IH Monitoring Confirms Control and SOP Effectiveness. (Measured Outside of PPE.)

Layers of Protection Loading/Unloading

Engineering Controls: NESHAP Controls for loading/unloading, transfer racks (40 CFR 63.126-130, 2475, 2525) *e.g.*, vapor recovery units, vapor balancing, incineration with a required destruction efficiency.

Administrative Controls: Standard Operating Procedures includes the procedures to use the engineering controls and the necessary PPE for the task.

PPE: chemical resistant gloves, clothing and footwear; air supplied respirator.

Rail Loading SOP Example

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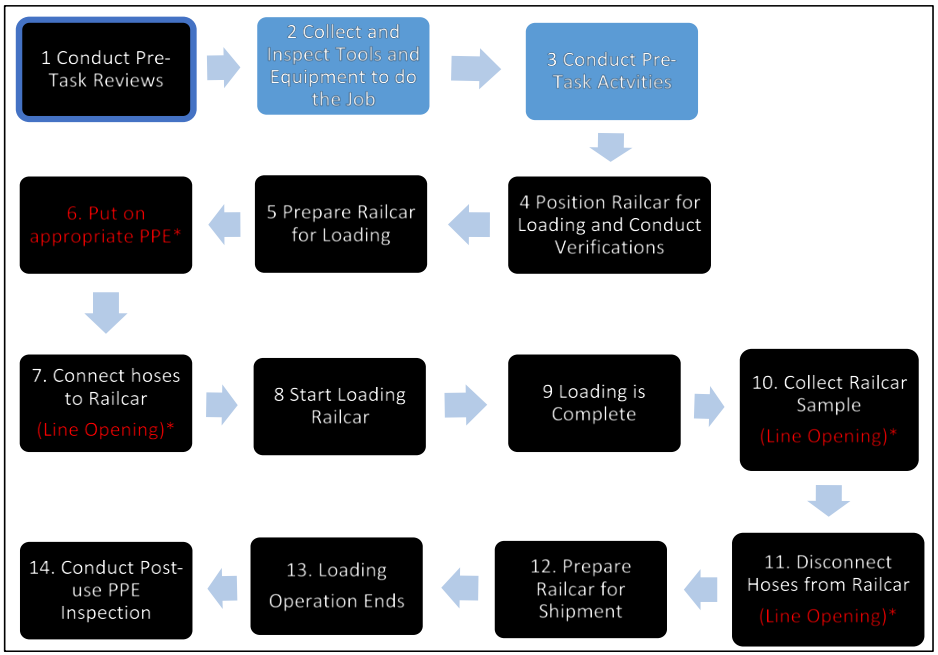
1. **SOP Flow Chart**

Color Key:

- **Occur in office / control room**
- **Occur in field**



*At a minimum, Line and Equipment Opening Activities require additional PPE: Full or Half Face Air Purifying Respirator and Chemical Resistant Gloves. Some LEO tasks with higher risk of exposure require Chemical Suit and Supplied Air Respirator

Layers of Protection Sampling

Engineering Controls: Process sampling systems for CTC prevents releases or potential personnel exposure.

Administrative Controls: Standard Operating Procedure (SOP) includes the procedures to use the engineering controls and the necessary PPE for the task.

PPE requirements: Goggles, hand protection and air purifying respirator

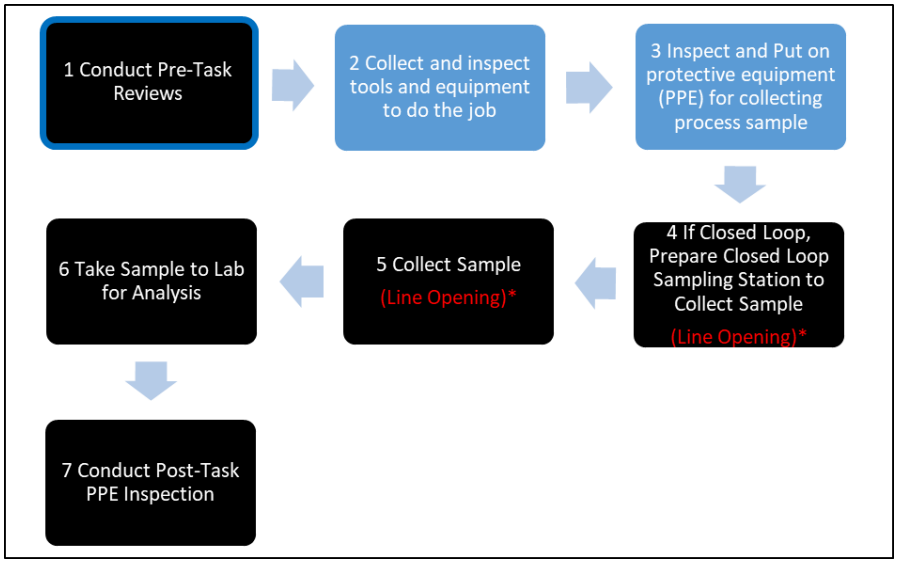
Process Sampling SOP Example

halogenated solvents industry alliance, inc.

1. **SOP Flow Chart**

Color Key:

- **Occur in office / control room**
- **Occur in field**



*At a minimum, Line and Equipment Opening Activities require additional PPE: Full or Half Face Air Purifying Respirator and Chemical Resistant Gloves. Some LEO tasks with higher risk of exposure require Chemical Suit and Supplied Air Respirator

Layers of Protection Line Opening

HSIA halogenated solvents industry alliance, inc.

Administrative Controls: Standard Operating Procedure and Permitting requirements before each task:

- Required hazard analysis
- Communication tool between maintenance and operations
- Ensure that work hazards are identified and mitigated prior to the work beginning
- Barricade

Engineering Controls: two layers of protection for the duration of the task for example, for a line break:

- Line clearing
- multiple layers of isolation

PPE: chemical resistant gloves, clothing and footwear; air supplied respirator

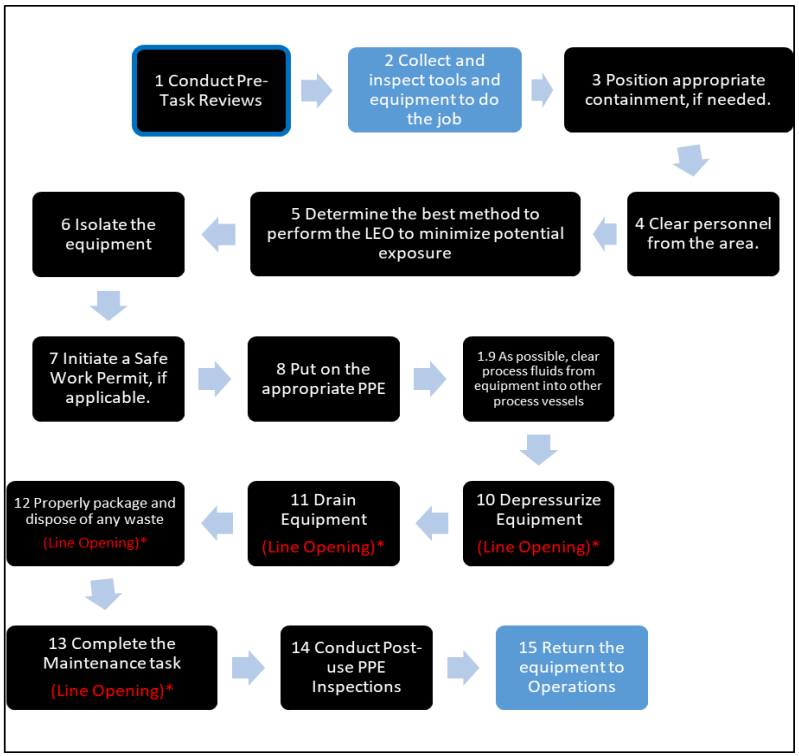
Line Opening SOP Example

halogenated solvents industry alliance, inc.

1. **SOP Flow Chart**

Color Key:

- **Occur in office / control room**
- **Occur in field**



*At a minimum, Line and Equipment Opening Activities require additional PPE: Full or Half Face Air Purifying Respirator and Chemical Resistant Gloves. Some LEO tasks with higher risk of exposure require Chemical Suit and Supplied Air Respirator

Dermal Modeling Overestimates Exposure

HSIA halogenated solvents industry alliance, inc.

Closed, hard-piped systems, engineering controls and procedures for manufacturing and processing prevent the type of dermal exposure scenarios modeled in the risk evaluations.

EPA Assumption in dermal model	Actual Potential Dermal Exposure for intermittent tasks such as loading, unloading, sampling and line openings
Undiluted, full hand CTC contact each shift.	Tasks are 15 min. Engineering controls and PPE protect from potential exposure. Rare, worst-case exposures are reduced to drops, not full hand contact.
Workers do not wash hands during a shift.	Any liquid prompts immediate glove removal and hand washing. Hands are washed after the task. (Not an infinite dose).
Workers wear the same gloves for 8 hours.	The integrity of gloves are inspected both before the task and when removed immediately after the task.

TSCA Section 6(c)(A)(i) requires the Risk Mitigation Rule to take into account the magnitude of exposure. The Risk Evaluation overestimates dermal exposure.

Mode of Action (MOA) Analysis Perchloroethylene induced Mouse Liver Tumors

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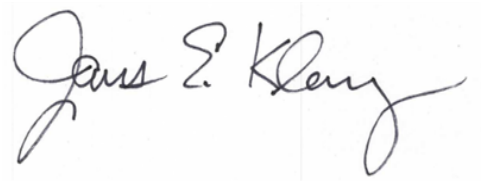

Signature

07/25/2022

Date

I have been asked on behalf of the Halogenated Solvents Industry Alliance, Inc. (HSIA) to comment on the mode of action (MOA) by which perchloroethylene induces liver tumors in mice following chronic exposure. I am a Professor Emeritus at Indiana University School of Public Health, Bloomington Indiana. I have been involved in liver toxicology and carcinogenesis research studies since 1976 and specifically on peroxisome-proliferator activated receptor alpha (PPAR alpha) research for over 35 years. I was involved in the generation and development of the MOA approach to human risk and chaired the initial MOA panel that put forth the analysis of PPAR alpha MOA activating compounds.

This document has two sections. The first section provides a summary of a MOA analysis of the mouse liver tumors by perchloroethylene, which concludes that perchloroethylene is a mouse liver tumorigen that functions through a PPAR alpha MOA (manuscript in preparation). The second section addresses some of the concerns and misconceptions that the USEPA TSCA Risk Evaluation for perchloroethylene puts forth in its analysis of the mouse liver tumor MOA.

Section 1: MOA Analysis of PCE-Induced Mouse Liver Tumors

Background

Perchloroethylene is a solvent used in dry cleaning operations and industrial applications such as metal degreasing. The results of two chronic inhalation studies (NTP, 1986; JISA, 1993) showed an increase in the incidence of hepatic neoplasia in male and female mice but not in similarly treated rats. Understanding the MOA (USEPA, 2005, Sonich-Mullin *et al.*, 2001) by which perchloroethylene selectively induces the mouse liver tumors is important in developing meaningful, scientifically based risk assessment. In performing MOA analysis, one identifies Key Events which are empirically observable causal steps needed to form a neoplasm. The Key Event is itself is a necessary step but not sufficient by itself to produce a neoplasm in the absence of other Key Events. An Associative Event in the MOA framework is a biological endpoint or process that while not causal for the formation of a neoplasm can be used as an indicator or biomarker for a Key Event. Modulating Factors include external or internal (host factors) that can modulate the dose–response relationship of one or more of the Key Events thereby changing the probability and/or magnitude of the end result. The following proposed MOA is supported by a preponderance of experimental evidence from multiple laboratories. The MOA for the perchloroethylene induced mouse liver tumors is through PPAR alpha activation. The PPAR alpha MOA has been extensively studied and involves the activation of the nuclear receptor PPAR alpha which results in subsequent changes in selective cell proliferation and formation of liver neoplasia (Klaunig *et al.*, 2003; Corton *et al.*, 2014; Corton *et al.*, 2018; Felter *et al.*, 2018). The following MOA involves five steps. Literature support for each of the Key events is provided below.

MOA of Perchloroethylene induced mouse liver tumors

Key Events

1 Perchloroethylene metabolism to trichloroacetic acid (TCA)
2 Activation of PPAR alpha by TCA
3. Activation PPAR alpha results in alteration in hepatic cell growth genes and pathways
   Increase in cell proliferation and/or Inhibition of apoptosis
4. Selective clonal expansion of hepatic preneoplastic foci cells
5. Formation of hepatic neoplasms

Key Event 1. Perchloroethylene metabolism to TCA

In the first Key Event of this MOA, perchloroethylene is metabolized to trichloroacetic acid (TCA) via oxidation by CYP enzymes (most likely CYP2E1). It is well established that perchloroethylene is metabolize to TCA in the mouse liver which results in the accumulation of TCA in the mouse liver. CYP2E1 is a major contributor to oxidation of chlorinated solvents including perchloroethylene in the liver (Hanioka *et al.*, 1995; Kim and Ghanayem, 2006). The preponderance of evidence has shown that perchloroethylene is metabolized to TCA primarily by CYP2E1 in the mouse liver.

Key Event 2. Activation of PPARα by TCA

TCA has been demonstrated by multiple laboratories to activate PPAR alpha as measured by peroxisome proliferation. The Associate Events for the PPAR alpha MOA: Cyp4a1 induction and the induction of palmitoyl CoA oxidase (PCO) enzyme activity and/or protein have been reported *in vivo* in the mouse following TCA treatment (De Angelo *et al.*, 1989; Elcombe *et al.*, 1985; Goldsworthy and Popp, 1987). A study by Laughter *et al.* 2004 used a PPARα-null mouse protocol to examine the activation of PPAR alpha by TCA. They showed that PPAR alpha was needed to produce the downstream PPAR alpha effects by TCA. In addition, a recent review by Corton concluded that TCA-induced liver tumors in the mouse arise by a PPARα-dependent MOA (Corton, 2008).

Perchloroethylene treated mice *in vivo* showed an increase in the number of peroxisomes and palmitoyl CoA activity (Goldsworthy and Popp, 1987, Odum *et al.*, 1988) indicative of PPAR alpha activation. In summary both TCA and perchloroethylene have consistently been shown to induce PPAR alpha in the mouse liver supporting the second Key event of this MOA.

Key Event 3. Activation PPAR alpha results in alteration in hepatic cell growth genes and pathways

For perchloroethylene, a dose-related increase in DNA synthesis was observed in treated B6C3F1 mice, but not in Sprague-Dawley rats treated for up to 16 days (Schumann *et al.*, 1980). TCA treatment of mice in drinking water also produced a dose dependent increase in

DNA synthesis up to 14 days of continual treatment (Sanchez and Bull, 1990). Ge *et al.* (2001) noted an increase in c-myc expression in liver from female B6C3F1 mice given a single oral dose of 500 mg/kg TCA. This correlated with earlier reports by (Tao *et al.*, 2000; Tao *et al.*, 1999) that showed a linkage between hypomethylation of DNA and induction of c-myc, in mouse liver after TCA treatment. In summary both perchloroethylene and TCA have been reported to increase DNA synthesis in the mouse liver, fulfilling this third Key Event.

Key Event 4. Selective clonal expansion of hepatic preneoplastic foci cells

In the rodent liver, increased cell proliferation and/or decreased apoptosis ultimately leads to selective clonal expansion of altered hepatocytes and tumors (Klaunig and Wang, 2018). This reflects the promotion stage of the tumorigenesis process. Multiple studies have shown that TCA treatment functions at the promotion stage of tumor development in the mouse liver (Herren-Freund *et al.*, 1987; Bull, 2000). Stauber and Bull (1998) treated male B6C3F1 mice with 2 g/L TCA in the drinking for up to 52 weeks. After 52 weeks of continuous TCA treatment, the rates of cell division in altered preneoplastic hepatic foci were significantly increased over surrounding normal hepatocytes. Thus, TCA is acting primarily through non-genotoxic mechanisms by selectively increasing cell division in the preneoplastic cells in the liver of the B6C3F1 mouse. In an initiation-promotion protocol, mice treated with 20 mmol/L TCA in drinking water for 52 weeks increased the yield of both hepatocellular adenomas and carcinomas in methylnitrosourea (MNU)- initiated mice over untreated control and TCA only treated mice (Pereira and Phelps, 1996).

Key Event 5. Formation of hepatic neoplasms

Perchloroethylene and its oxidative metabolite TCA produce liver neoplasms specifically in the mouse after chronic treatment. (Bull *et al.*, 1990; DeAngelo *et al.*, 1997; NTP, 1986; JISA, 1993) These results fulfill this key event.

Other Modes of Action for perchloroethylene induced mouse liver tumors

Alternate modes of action were considered, including mutagenicity/ genotoxicity, other nuclear receptors, and cytotoxicity.

Mutagenicity/ Genotoxicity

Multiple mutagenic and genotoxicity assays have examined both TCA and perchloroethylene for activity. The results have been consistently negative for mutagenicity and genotoxicity and do not support a mutagenic/ genotoxic MOA. A detailed review of the mutagenicity of perchloroethylene has also been performed by Gollapudi (2020) who concluded that the support for a mutagenic MOA for the perchloroethylene induced mouse liver tumors is weak. Therefore, mutagenesis or genotoxicity as an alternate MOA is not supported.

Other nuclear receptors

No studies that specifically examined the other prominent liver receptors (CAR, PXR, AHR, and Estrogen) associated with rodent liver tumorigenesis. While the contribution of receptor in addition to the PPAR alpha cannot be completely ruled out, the overwhelming data show that for both perchloroethylene and its metabolite TCA the activation of PPAR alpha is the major response.

Cytotoxicity

The cytotoxicity MOA is demonstrated by model rodent liver carcinogenic compounds such as chloroform and carbon tetrachloride where continuous exposure produces a chronic hepatocyte necrosis followed by compensatory hyperplasia. The hyperplasia results in the formation and/or promotion of preneoplastic cells that can progress to neoplasms. It is important to note that the cytotoxicity and resulting necrosis produced must be sufficient to involve a strong proliferative response in the liver. For TCA and perchloroethylene, while slight increases in liver serum enzymes and hepatocyte injury have been reported, these findings are not sufficient to produce the central lobular necrosis and compensatory hyperplasia required for the cytotoxicity MOA. When cell injury has been reported, it is directly related to high dose treatment in strains of mice that do not correlate with the tumorigenicity studies.

<u>PPARα-dependent rodent liver tumor response is **not** relevant to humans</u>

The PPAR alpha MOA has been accepted by the liver carcinogenesis scientific community to not be of human relevance (Klaunig *et al.*, 2003; Corton, 2010; Corton *et al.*, 2014; Corton *et al.*, 2018; Felter *et al.*, 2018). Extensive reviews of the mechanisms supporting the PPAR alpha MOA have shown that in the rodent (rat and mice), a three-tier response is seen following activation of PPAR alpha including: (1) peroxisome proliferation, (2) cell growth modification (cell proliferation), and (3) lipid metabolism gene expression. In humans, only one tier of the three has been demonstrated – the lipid metabolism gene expression which accounts for the hypolipidemic effects of PPAR alpha drugs. The cell growth modification, required for tumor growth, is not seen in humans with PPAR alpha activation (Klaunig *et al.*, 2003; Corton, 2010; Corton *et al.*, 2014; Corton *et al.*, 2018; Felter *et al.*, 2018). In further support, there have been several large retrospective epidemiological studies that have examined the chronic treatment with the PPAR alpha activating hypolipidemic drugs gemfibrozil and clofibrate (reviewed in Klaunig *et al.*, 2003 and Corton *et al.*, 2018). These studies have shown no elevated risk of mortality from liver cancer associated with over a decade of chronic use of these hypolipidemic pharmaceuticals.

Conclusions

Perchloroethylene is a mouse liver tumorigen that functions through a PPAR alpha MOA. TCA, the oxidative metabolite of perchloroethylene, appears to be the metabolite responsible for the observed PPAR alpha activation. The data supporting this MOA are extensive and have been generated independently in a number of laboratories. Given that the PPAR alpha MOA has been accepted not to be of human relevance, perchloroethylene is not a human risk for liver cancer.

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Section 2: Specific Comments on EPA's Assessment of the Mouse Liver Tumor Mode of Action (MOA) in the Final TSCA Risk Evaluation for Perchloroethylene

In the final TSCA Risk Evaluation for perchloroethylene, the review of the MOA of perchloroethylene induced mouse liver tumors concluded:

> "in summary, PCE likely induces liver tumors in mice through multiple modes of action mediated largely by metabolites. TCA appears to be an important hepatic metabolite but is probably not the only metabolite involved in hepatic effects of PCE." "Based on limited data on PCE and studies of the related compound, trichloroethylene, PPARα activation is not the primary MOA for PCE-induced liver tumors but may influence both the metabolism and the nature of the hepatic effects induced. In addition to PPARα activation, PCE exposure also upregulates genes involved in ABC transporters, and downregulates nucleotide metabolism and mitochondrial-related genes. In summary, the MOA by which PCE induces liver tumors is not known"

Unfortunately, this evaluation of the perchloroethylene mouse liver tumor MOA was poorly performed. Selective data were cherry picked to support the conclusion of the document and ignored the extensive data base supporting a PPAR alpha MOA for perchloroethylene and TCA. An overriding concern of this document was the lack of understanding of the carcinogenesis process overall and the rodent liver cancer process specifically. Along these lines, there was a lack of appreciation for the mouse strain variability specifically regarding the liver carcinogenesis process.

Specific comments

1. EPA considered methylation status or more specifically DNA hypomethylation in the liver tumor MOA for perchloroethylene. The comment "Notably, c-myc DNA hypomethylation occurred earlier than increases in liver cell proliferation (Ge et al., 2001)" is misleading because the authors of the paper stated:

> "DCA and TCA have been shown to induce DNA replication after exposure of five or more days. In the present study, we demonstrated that increased cell proliferation by DCA and TCA did not occur until 72 hours after the first dose of the chlorinated acetic acids. Furthermore, decrease in the methylation of the c-myc gene also did not occur prior to 72 hours and was further decreased at 96 hours. Thus, the decrease in the methylation of the c-myc gene corresponded with the occurrence of the hypomethylated sites in newly replicated DNA"

2. The document also points to an alternate MOA-based almost solely on a paper by Philip *et al.* (2007):

> "Studies in mice and rats exposed for at least 4 weeks provide clear evidence for the hepatotoxic effects of PCE (see Section 3.2.3.1.4), and demonstrate that mice are more

> sensitive to these effects than are rats. In mice, oral exposure to PCE has resulted in increased serum alanine aminotransferase (ALT) levels, increased liver weight, hepatocellular hypertrophy, fatty degeneration and necrosis, and regenerative cell proliferation/increased DNA synthesis (Philip et al., 2007)"

The two highest doses used in the Philip study produced cytotoxicity and necrosis. This may be reflective of the mouse strain used (Swiss mouse) as well as the dose used since other studies with other mouse strains did not produce a necrotic response. In the chronic bioassay little necrosis or cytotoxicity was noted. It is apparent that the Swiss mouse responds to the treatment in a different manner than the bioassay strains. The document should note this discrepancy in summarizing the results of studies with the Swiss mouse and the lack of concordance with other studies employing the B6C3F1 mouse (in which the liver tumors were detected with perchloroethylene and TCA). An additional comment is made in the MOA review based on the Philip paper:

> "The earliest time point measured, and histopathologic evidence of regenerative repair was seen after 30 days of exposure to the two higher doses (Philip et al., 2007) as cited in (U.S. EPA, 2012c), demonstrating that hepatocyte injury occurred early and may have preceded cell proliferation"

The statement that the injury may have proceeded cell proliferation is perplexing. In the case of compounds that induce hepatocyte injury and necrosis (acetaminophen for example) the injury occurs first, then necrosis is seen followed by the compensatory hyperplasia. Cell proliferation always follows the injury and resulting necrosis.

3. Citing other studies in mice and rats, the liver tumor MOA review in the TSCA Risk Evaluation noted that perchloroethylene "induces a modest peroxisome proliferating response in both species, but only mice develop liver tumors, indicating a lack of concordance between peroxisome proliferation and occurrence of liver tumors across species." This statement is misleading. In the Odum *et al.* (1988) paper, "Peroxisome proliferation was not observed in rat liver" and "Trichloroacetic acid (TCA), a known carcinogen and hepatic peroxisome proliferating agent, was found to be a major metabolite of [perchloroethylene]. Blood levels of this metabolite measured in mice and rats during and for 48 hr after a single 6-hr exposure to 400 ppm [perchloroethylene] showed that peak blood levels in mice were 13 times higher than those seen in rats." Their conclusion was that the difference in metabolism of perchloroethylene to TCA in mice and rats leads to the species difference in hepatic peroxisome proliferation which is believed to be the basis of the species difference in hepatocarcinogenicity. Elcombe *et al.* (1985) concluded "that the species difference in the hepatocarcinogenicity of [trichloroethylene] seen between rats and mice was due to a species difference in peroxisomal proliferation and cell proliferation". In the Goldsworthy and Popp (1987) paper the results are "[trichloroethylene] and [perchloroethylene] elevated PCO activity in mouse liver whereas only [trichloroethylene] elevated rat liver."