PEER REVIEW DRAFT. DO NOT CITE OR QUOTE

United States
Environmental Protection Agency

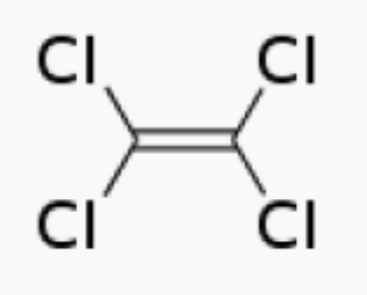
Office of Chemical Safety and
Pollution Prevention

Draft Risk Evaluation for Perchloroethylene (Ethene, 1,1,2,2-Tetrachloro)

CASRN: 127-18-4

Systematic Review Supplemental File:

Data Quality Evaluation of Human Health Hazard Studies – Animal Studies



April 2020

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1. Acute Toxicity Studies

1.1. Animal toxicity evaluation results of Beliles et al 1980 for acute inhalation studies on genotoxicity in vivo outcomes

Study reference:	Beliles, R. P.,Brusick, D. J.,Mecler, F. J. (1980). Teratogenic-mutagenic risk of workplace contaminants: trichloroethylene, perchloroethylene, and carbon disulfide HERO ID: 58331					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
Test Substance	1. Test Substance Identity	Identified by chemical name and synonym	High	1	2	2
	2. Test Substance Source	Manufacturer and lot number given.	High	1	1	1
	3. Test Substance Purity	91% pure, impurities were not characterized	Medium	2	1	2
Test Design	4. Negative and Vehicle Controls	Filtered air controls; control animals exposed in a different room.	High	1	2	2
	5. Positive Controls	Positive controls (reference mutagens) were used for all studies.	High	1	1	1
	6. Randomized Allocation	randomly assigned to groups	High	1	1	1
Exposure Characterization	7. Preparation and Storage of Test Substance	Method and equipment used to generate the test substance as a vapor were reported and appropriate.	High	1	1	1
	8. Consistency of Exposure Administration	See footnote at end of page.[1]	High	1	1	1
	9. Reporting of Doses/Concentrations	Target and analytical concentrations were provided. Range of measure concentration did not deviate more than 10%.	High	1	2	2
	10. Exposure Frequency and Duration	Acute duration appropriate for dominant lethal and spermhead abnormality.	High	1	1	1

[1] Metrics that received a "High" rating met the criteria as discussed in the Applications of Systematic Review for TSCA Risk Evaluation.

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Study reference:	**Beliles, R. P.,Brusick, D. J.,Mecler, F. J. (1980). Teratogenic-mutagenic risk of workplace contaminants: trichloroethylene, perchloroethylene, and carbon disulfide** **HERO ID: 58331**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	11. Number of Exposure Groups and Dose Spacing	2 exposure concentrations (100 and 500ppm)	Medium	2	1	2
	12. Exposure Route and Method	Dynamic chamber , whole body, assumed that Perc does not condense.	High	1	1	1
Test Organism	13. Test Animal Characteristics	Species, strain and source were reported; starting age and bw not given.	Medium	2	2	4
	14. Adequacy and Consistency of Animal Husbandry Conditions	well reported	High	1	1	1
	15. Number per Group	6-10/group	High	1	1	1
Outcome Assessment	16. Outcome Assessment Methodology	Dominant lethal assay, spermhead abnormality, chromosomal aberration in rat bone marrow,	High	1	2	2
	17. Consistency of Outcome Assessment	See footnote at end of page.[1]	High	1	1	1
	18. Sampling Adequacy	See footnote at end of page.[1]	High	1	1	1
	19. Blinding of Assessors	Blinding was not reported, but most outcomes were not subjective.	Medium	2	1	2
	20. Negative Control Response	See footnote at end of page.[1]	High	1	1	1
Confounding / Variable Control	21. Confounding Variables in Test Design and Procedures	None related to genotoxicity	High	1	2	2
	22. Health Outcomes Unrelated to Exposure	None related to genotoxicity	High	1	1	1

[1] Metrics that received a “High” rating met the criteria as discussed in the Applications of Systematic Review for TSCA Risk Evaluation.

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Study reference:	**Beliles, R. P.,Brusick, D. J.,Mecler, F. J. (1980). Teratogenic-mutagenic risk of workplace contaminants: trichloroethylene, perchloroethylene, and carbon disulfide** **HERO ID: 58331**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
Data Presentation and Analysis	23. Statistical Methods	Statistics were well described and appropriate	High	1	1	1
	24. Reporting of Data	All outcomes were reported.	High	1	2	2
High: >=1 and <1.7 **Medium: >=1.7 and <2.3** **Low: >=2.3 and <=3**		**Sum of scores:**			**31**	**36**
		Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factors:		**1.1613**	**Overall Score: Nearest *:**	**1.2**
		Overall Quality Level:		**High**		

1.2. Animal toxicity evaluation results of Dow et al 1950 for an acute and repeat inhalation exposures study on mortality, body weight, respiratory, cardiovascular, hepatic, renal, hematological and immune, reproductive, neurological/behavior, endocrine, gastrointestinal, musculoskeletal, ocular and sensory outcomes

Study reference:	**Dow Chem, Co (1950). Vapor toxicity of tetrachloroethylene for laboratory animals and human subjects** **HERO ID: 4214242**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
Test Substance	1. Test Substance Identity	Tetrachoroethylene identified by name and structure.	High	1	2	2
	2. Test Substance Source	"* samples of commercial product" - manufacturer not identified. Confirmed identity in lab.	Medium	2	1	2
	3. Test Substance Purity	99.9%C	High	1	1	1
Test Design	4. Negative and Vehicle Controls	No controls reported for acute studies. In repeat-exposure study, authors indicated untreated and air-exposed controls were used "for each experiment". It is not clear if they were all concurrent because exposure duration varied drastically in different exposure groups within the same species.	Unacceptable	4	2	8
	5. Positive Controls		Not Rated	NA	NA	NA
	6. Randomized Allocation	Animals were "carefully selected on the basis of general appearance, body weight, and growth during a preliminary period of observation".	Low	3	1	3
Exposure Characterization	7. Preparation and Storage of Test Substance	Vaporization method reported with limited details. Storage not reported.	Medium	2	1	2

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Study reference:	Dow Chem, Co (1950). Vapor toxicity of tetrachloroethylene for laboratory animals and human subjects HERO ID: 4214242					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	8. Consistency of Exposure Administration	Exposure durations varied widely between exposure groups within the same species (unclear if each duration had a concurrent control group). Only guinea pigs had two exposure groups (and presumably a control group) with the same duration (exposed 14 days over an 18 day period) for meaningful dose-response analysis (but data reporting inadequate for analysis). Different chambers were used for different concentrations in repeat-exposure studies.	Unacceptable	4	1	4
	9. Reporting of Doses/Concentrations	Only target levels were reported. Air concentrations were monitored, and reportedly within 10% of target	Medium	2	2	4
	10. Exposure Frequency and Duration	Exposure at different concentrations in acute studies ranged from minutes to 14 hours. Exposure at different concentrations in repeat exposure studies (7 hr/d, 5 d/wk) ranged from 18-236d for various species.	Low	3	1	3

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Study reference:	Dow Chem, Co (1950). Vapor toxicity of tetrachloroethylene for laboratory animals and human subjects HERO ID: 4214242					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	11. Number of Exposure Groups and Dose Spacing	Acute exposure:: 4 exposure levels, no control. (lack of control addressed in prior Metric 4, not here) Repeated exposure: All exposure groups except Monkeys had at lease 2 exposure groups plus control. With the exception of 2 (of 4) guinea pig groups, exposure groups were not directly comparable due to different exposure durations.	Low	3	1	3
	12. Exposure Route and Method	Acute: glass, 160L, air rate of 15-30 L/min (which equates 6-12 air changes per hour).. Animals in groups of 5-12. Repeat: Metal chamber about 450L for 100 ppm, metal chamber of 1700 L for 200 and 400 ppm, glass chamber of 160L for 1600 and 2500 ppm. Air flow rate not reported.	Unacceptable	4	1	4

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Study reference:	Dow Chem, Co (1950). Vapor toxicity of tetrachloroethylene for laboratory animals and human subjects HERO ID: 4214242					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
Test Organism	13. Test Animal Characteristics	Rat: Internal albino colony originally obtained from Wistar Institute of Anatomy and Biology in 1938 Gn Pig: Heterogeneous stock purchased from "commercial breeder" Rabbit: Albino, internal heterogeneous colony (no further details) Monkey: Rhesus - "newly imported", no further details. No ages reported for any species. Initial BW data only available graphically for a couple exposure groups.	Low	3	2	6
	14. Adequacy and Consistency of Animal Husbandry Conditions	Diet for each species reported. No other husbandry conditions reported.	Low	3	1	3
	15. Number per Group	Acute: 5-30 per dose per duration Repeat: Rat: 5-22/sex per group Rabbit: 2/sex per group Guinea Pig: 5-15/sex per group Monkey - 2 M/group Number varied widely between exposure groups.	Medium	2	1	2
Outcome Assessment	16. Outcome Assessment Methodology	Acute: Mortality, clinical signs, hepatic injury Repeat: Mortalty, clinical signs, BW, select organ weight and histology, hematology in some animals	High	1	2	2

Study reference:	Dow Chem, Co (1950). Vapor toxicity of tetrachloroethylene for laboratory animals and human subjects HERO ID: 4214242					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	17. Consistency of Outcome Assessment	Acute: Timing different across exposure groups. Unclear for repeat exposure - all animals were evaluated for mortality, CS, BW, OW, and "organic injury" - assuming gross necropsy; periodic hematology was performed on "several groups of animals", not further defined; clinical chemistry was evaluated in "many cases"; in "many instances" organs were examined histologically. Depending on which groups were evaluated, timing was different due to different exposure durations between exposure levels.	Unacceptable	4	1	4
	18. Sampling Adequacy	Unclear how many animals were evaluated for several of the metrics (see Metric 17)	Low	3	1	3
	19. Blinding of Assessors		Not Rated	NA	NA	NA
	20. Negative Control Response	Data reporting limited. Where exposure group data were reported quantitatively, control data were included. Remaining data reported qualitatively (change or no change from control).	Low	3	1	3

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Study reference:	Dow Chem, Co (1950). Vapor toxicity of tetrachloroethylene for laboratory animals and human subjects HERO ID: 4214242					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
Confounding / Variable Control	21. Confounding Variables in Test Design and Procedures	Acute: Anaesthetic effects with unconsciousness and failure of respiration in acute study at all exposures except the lowest (2000 ppm) Repeat: CNS depression also reported at highest concentration (2500 ppm) in rat, mice, GP (no mention of respiratory depression)	Low	3	2	6
	22. Health Outcomes Unrelated to Exposure	data on attrition and/or health outcomes unrelated to exposure for each study group were not reported because only substantial differences among groups were noted	Medium	2	1	2
Data Presentation and Analysis	23. Statistical Methods	Acute- no statistics, data for mortality adequate for independent analsysi Repeat: t-test was reported used "wherever possible"" Reported only for guinea pig group exposed to 0 or 200 ppm for "as many as 158 Seven-hour Exposures in 220 days"	Low	3	1	3
	24. Reporting of Data	Only limited data sets were reported quantitatively, the majority were reported qualitatively only (even with exposure-related effects)	Low	3	2	6
High: >=1 and <1.7 Medium: >=1.7 and <2.3 Low: >=2.3 and <=3		**Sum of scores:**			**29**	**76**
		Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factors:		**2.6207**	**Overall Score: Nearest *:**	**2.6[1]**

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Study reference:	Dow Chem, Co (1950). Vapor toxicity of tetrachloroethylene for laboratory animals and human subjects HERO ID: 4214242					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
		Overall Quality Level:		**Unacceptable[1]**		
Study Quality Comment:	**Footnote 1: Consistent with our *Application of A Systematic Review in TSCA Risk Evaluations* document, if a metric for a data source receives a score of Unacceptable (score = 4), EPA will determine the study to be unacceptable. In this case, four of the metrics were rated as unacceptable. As such, the study is considered unacceptable and the score is presented solely to increase transparency.**					

1.3. Animal toxicity evaluation results of Dow et al 1983 for an acute eye irritation study in rabbits on irritation outcomes

Study reference:	**Dow Chem, Co (1983). Initial submission: perchloroethylene solvent formulation: acute toxicological properties & industrial handling hazards, with cover letter dated 102591 (sanitized)** **HERO ID: 4214440**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
Test Substance	1. Test Substance Identity	Test substance identity was reported by unambiguous name, and reference was made to an appendix containing the composition, but the table was blanked out in the appendix in the pdf.	Low	3	2	6
	2. Test Substance Source	Test substance source was reported, but without certification or analytical verification of identity.	Medium	2	1	2
	3. Test Substance Purity	Purity was not reported; reference was made to an appendix containing the composition, but the table was blanked out in the appendix in the pdf.	Low	3	1	3
Test Design	4. Negative and Vehicle Controls	Negative control group not required for eye irritation tests; untreated eye serves as control	Not Rated	NA	NA	NA
	5. Positive Controls	Positive controls not typical for this study type.	Not Rated	NA	NA	NA
	6. Randomized Allocation	Animal allocation to study groups was not described.	Low	3	1	3
Exposure Characterization	7. Preparation and Storage of Test Substance	No information on preparation or storage of test material was provided.	Unacceptable	4	1	4

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Study reference:	**Dow Chem, Co (1983). Initial submission: perchloroethylene solvent formulation: acute toxicological properties & industrial handling hazards, with cover letter dated 102591 (sanitized)** **HERO ID: 4214440**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	8. Consistency of Exposure Administration	Study does not clearly state that undiluted test material was used, but based on the language and approach to other experiments in the paper, it is likely that this is the case.	Medium	2	1	2
	9. Reporting of Doses/Concentrations	Exposure reported as volume of test material; concentration/purity of of Perc in test material was not reported.	Medium	2	2	4
	10. Exposure Frequency and Duration	Dermal patches were left in place for 24 hours which is adequate.	High	1	1	1
	11. Number of Exposure Groups and Dose Spacing	Single exposure level is acceptable for eye irritation testing.	High	1	1	1
	12. Exposure Route and Method	Route and method are typical for this study type.	High	1	1	1
Test Organism	13. Test Animal Characteristics	Test animal source, species, strain, and sex were reported; age and initial body weight were not.	Medium	2	2	4
	14. Adequacy and Consistency of Animal Husbandry Conditions	Housing conditions, acclimation, and photoperiod were reported, but temperature and humidity were not.	Medium	2	1	2
	15. Number per Group	9 rabbits were used; this is more than required for testing.	High	1	1	1
Outcome Assessment	16. Outcome Assessment Methodology	Outcome assessment methodology was adequately reported; Draize scoring method was cited but scoring details not provided.	Medium	2	2	4

Study reference:	**Dow Chem, Co (1983). Initial submission: perchloroethylene solvent formulation: acute toxicological properties & industrial handling hazards, with cover letter dated 102591 (sanitized)** **HERO ID: 4214440**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	17. Consistency of Outcome Assessment	Two exposure groups were used (one with eyes rinsed after 30 sec and one with no rinsing)	Medium	2	1	2
	18. Sampling Adequacy	All exposed animals were evaluated for all outcomes.	High	1	1	1
	19. Blinding of Assessors	As there was no control group blinding was not possible/necessary.	Not Rated	NA	NA	NA
	20. Negative Control Response	There was no negative control group.	Not Rated	NA	NA	NA
Confounding / Variable Control	21. Confounding Variables in Test Design and Procedures	No potentially confounding factors were identified. Eye condition was examined and determined to be healthy before testing.	High	1	2	2
	22. Health Outcomes Unrelated to Exposure	No health outcomes unrelated to exposure were reported.	High	1	1	1
Data Presentation and Analysis	23. Statistical Methods	Statistical analysis is not typical for eye irritation tests.	Not Rated	NA	NA	NA
	24. Reporting of Data	Individual and group irritation scores for each time point were reported.	High	1	2	2
High: >=1 and <1.7 Medium: >=1.7 and <2.3 Low: >=2.3 and <=3		**Sum of scores:**			**24**	**44**
		Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factors:		**NA**	**Overall Score: Nearest *:**	**NA**
		Overall Quality Level:		**Low**		
Study Quality Comment:	**The reviewer upgraded this study's overall quality rating, changing its status from unacceptable to acceptable. They noted: The only metric that was unacceptable was test storage and preparation which is of low concern in a single exposure eye irritation test. Note: The study was initially assigned a rating of unacceptable (score = 4) with a calculated score of 1.9 (shown solely for transparency). No calculated score is identified for the current rating in the table above because the study was upgraded to low.**					

1.4. Animal toxicity evaluation results of Dow et al 1983 for an acute dermal lethality study in rabbits on mortality and irritation outcomes

Study reference:	Dow Chem, Co (1983). Initial submission: perchloroethylene solvent formulation: acute toxicological properties & industrial handling hazards, with cover letter dated 102591 (sanitized) HERO ID: 4214440					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
Test Substance	1. Test Substance Identity	Test substance identity was reported by unambiguous name, and reference was made to an appendix containing the composition, but the table was blanked out in the appendix in the pdf.	Low	3	2	6
	2. Test Substance Source	Test substance source was reported, but without certification or analytical verification of identity.	Medium	2	1	2
	3. Test Substance Purity	Purity was not reported; reference was made to an appendix containing the composition, but the table was blanked out in the appendix in the pdf.	Low	3	1	3
Test Design	4. Negative and Vehicle Controls	Negative controls not common in lethality studies	Not Rated	NA	NA	NA
	5. Positive Controls	Positive controls not typical for this study type.	Not Rated	NA	NA	NA
	6. Randomized Allocation	There was only one group	Not Rated	NA	NA	NA
Exposure Characterization	7. Preparation and Storage of Test Substance	No information on preparation or storage of test material was provided.	Unacceptable	4	1	4
	8. Consistency of Exposure Administration	Volume and skin surface area of application were not reported.	Medium	2	1	2
	9. Reporting of Doses/Concentrations	Exposure reported as mg/kg. Initial body weights were not reported.	Medium	2	2	4

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Study reference:	**Dow Chem, Co (1983). Initial submission: perchloroethylene solvent formulation: acute toxicological properties & industrial handling hazards, with cover letter dated 102591 (sanitized)** **HERO ID: 4214440**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	10. Exposure Frequency and Duration	Exposure was for 24 hours which is adequate.	High	1	1	1
	11. Number of Exposure Groups and Dose Spacing	Only one dose (200 mg/kg) was tested, and it was well below the recommended dose for a limit test (2000 mg/kg). An attempt was made to test 2000 mg/kg but this dose resulted in significant animal pain.	Low	3	1	3
	12. Exposure Route and Method	Acute Percutaneous Absorption	High	1	1	1
Test Organism	13. Test Animal Characteristics	Test animal source, species, strain, and sex were reported; age and initial body weight were not.	Medium	2	2	4
	14. Adequacy and Consistency of Animal Husbandry Conditions	Housing conditions, acclimation, and photoperiod were reported, but temperature and humidity were not.	Medium	2	1	2
	15. Number per Group	5 male rabbits were used; this number is consistent with guidelines.	High	1	1	1
Outcome Assessment	16. Outcome Assessment Methodology	Outcome assessment methodologies for mortality, body weight, and necropsy were reported. Irritation responses were described, but a scoring system was not applied.	Low	3	2	6
	17. Consistency of Outcome Assessment	Only a single group was used.	Not Rated	NA	NA	NA

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Study reference:	**Dow Chem, Co (1983). Initial submission: perchloroethylene solvent formulation: acute toxicological properties & industrial handling hazards, with cover letter dated 102591 (sanitized)** **HERO ID: 4214440**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	18. Sampling Adequacy	Although the protocol called for only surviving animals to be necropsied, all exposed animals survived, so all were necropsied.	High	1	1	1
	19. Blinding of Assessors	As there was only one group blinding was not possible/necessary.	Not Rated	NA	NA	NA
	20. Negative Control Response	Negative controls not required for acute lethality test	Not Rated	NA	NA	NA
Confounding / Variable Control	21. Confounding Variables in Test Design and Procedures	No potentially confounding factors were identified, but initial health conditions were not reported.	Medium	2	2	4
	22. Health Outcomes Unrelated to Exposure	No health outcomes unrelated to exposure were reported.	High	1	1	1
Data Presentation and Analysis	23. Statistical Methods	Statistical analysis is not possible on a single exposure group.	Not Rated	NA	NA	NA
	24. Reporting of Data	Data reporting was adequate for the type of study.	Medium	2	2	4
High: >=1 and <1.7 Medium: >=1.7 and <2.3 Low: >=2.3 and <=3		**Sum of scores:**			**22**	**45**
		Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factors:		**NA**	**Overall Score: Nearest *:**	**NA**
		Overall Quality Level:		**Low**		
Study Quality Comment:	**The reviewer upgraded this study's overall quality rating, changing its status from unacceptable to acceptable. They noted: The only metric that was unacceptable was test substance preparation and storage, which is of low concern for single dose dermal administration. Note: The study was initially assigned a rating of unacceptable (score = 4) with a calculated score of 2.2 (shown solely for transparency). No calculated score is identified for the current rating in the table above because the study was upgraded to low.**					

1.5. Animal toxicity evaluation results of Dow et al 1983 for an acute dermal irritation study on irritation outcomes

Study reference:	Dow Chem, Co (1983). Initial submission: perchloroethylene solvent formulation: acute toxicological properties & industrial handling hazards, with cover letter dated 102591 (sanitized) #journal#, #volume#(#issue#), #Pages# HERO ID: 4214440					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
Test Substance	1. Test Substance Identity	Test substance identity was reported by unambiguous name, and reference was made to an appendix containing the composition, but the table was blanked out in the appendix in the pdf.	Low	3	2	6
	2. Test Substance Source	Test substance source was reported, but without certification or analytical verification of identity.	Medium	2	1	2
	3. Test Substance Purity	Purity was not reported; reference was made to an appendix containing the composition, but the table was blanked out in the appendix in the pdf.	Low	3	1	3
Test Design	4. Negative and Vehicle Controls	Negative control groups not required for dermal irritation test	Not Rated	NA	NA	NA
	5. Positive Controls	Positive controls not typical for this study type.	Not Rated	NA	NA	NA
	6. Randomized Allocation	There was only one group	Not Rated	NA	NA	NA
Exposure Characterization	7. Preparation and Storage of Test Substance	No information on preparation or storage of test material was provided.	Unacceptable	4	1	4
	8. Consistency of Exposure Administration	Skin surface area tested was not reported.	Low	3	1	3
	9. Reporting of Doses/Concentrations	See footnote at end of page.[1]	High	1	2	2

[1] Metrics that received a "High" rating met the criteria as discussed in the Applications of Systematic Review for TSCA Risk Evaluation.

PEER REVIEW DRAFT. DO NOT CITE OR QUOTE

Study reference:	**Dow Chem, Co (1983). Initial submission: perchloroethylene solvent formulation: acute toxicological properties & industrial handling hazards, with cover letter dated 102591 (sanitized) #journal#, #volume#(#issue#), #Pages#** **HERO ID: 4214440**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	10. Exposure Frequency and Duration	Dermal patches were left in place for 24 hours which is adequate.	High	1	1	1
	11. Number of Exposure Groups and Dose Spacing	Only one exposure level was tested, but it reflected the highest concentration (undiluted) possible.	Medium	2	1	2
	12. Exposure Route and Method	See footnote at end of page.[1]	High	1	1	1
Test Organism	13. Test Animal Characteristics	Test animal source, species, strain, and sex were reported; age and initial body weight were not.	Medium	2	2	4
	14. Adequacy and Consistency of Animal Husbandry Conditions	Housing conditions, acclimation, and photoperiod were reported, but temperature and humidity were not.	Medium	2	1	2
	15. Number per Group	6 rabbits were used; this is more than required for testing.	High	1	1	1
Outcome Assessment	16. Outcome Assessment Methodology	Outcome assessment methodology was inadequately reported (lacking irritation scoring details)	Unacceptable	4	2	8
	17. Consistency of Outcome Assessment	Only a single group was used.	Not Rated	NA	NA	NA
	18. Sampling Adequacy	All exposed animals were evaluated for all outcomes.	High	1	1	1
	19. Blinding of Assessors	As there was only one group blinding was not possible/necessary.	Not Rated	NA	NA	NA
	20. Negative Control Response	There was no negative control group.	Not Rated	NA	NA	NA

PEER REVIEW DRAFT. DO NOT CITE OR QUOTE

Study reference:	**Dow Chem, Co (1983). Initial submission: perchloroethylene solvent formulation: acute toxicological properties & industrial handling hazards, with cover letter dated 102591 (sanitized) #journal#, #volume#(#issue#), #Pages#** **HERO ID: 4214440**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
Confounding / Variable Control	21. Confounding Variables in Test Design and Procedures	No potentially confounding factors were identified, but initial health conditions were not reported.	Medium	2	2	4
	22. Health Outcomes Unrelated to Exposure	No health outcomes unrelated to exposure were reported.	High	1	1	1
Data Presentation and Analysis	23. Statistical Methods	Statistical analysis is not typical for this study type.	Not Rated	NA	NA	NA
	24. Reporting of Data	Individual skin irritation scores were not reported.	Unacceptable	4	2	8
High: >=1 and <1.7 Medium: >=1.7 and <2.3 Low: >=2.3 and <=3		**Sum of scores:**			**23**	**53**
		Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factors:		**2.3043**	**Overall Score: Nearest *:**	**2.3[1]**
		Overall Quality Level:		**Unacceptable[1]**		
Study Quality Comment:	**Footnote 1: Consistent with our *Application of A Systematic Review in TSCA Risk Evaluations* document, if a metric for a data source receives a score of Unacceptable (score = 4), EPA will determine the study to be unacceptable. In this case, three of the metrics were rated as unacceptable. As such, the study is considered unacceptable and the score is presented solely to increase transparency.**					

1.6. Animal toxicity evaluation results of Dow et al 1983 for an acute oral toxicity study in rats on mortality and acute toxicity/poisoning outcomes

Study reference:	**Dow Chem, Co (1983). Initial submission: perchloroethylene solvent formulation: acute toxicological properties & industrial handling hazards, with cover letter dated 102591 (sanitized)** **HERO ID: 4214440**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
Test Substance	1. Test Substance Identity	Test substance identity was reported by unambiguous name, and reference was made to an appendix containing the composition, but the table was blanked out in the appendix in the pdf.	Low	3	2	6
	2. Test Substance Source	Test substance source was reported, but without certification or analytical verification of identity.	Medium	2	1	2
	3. Test Substance Purity	Purity was not reported; reference was made to an appendix containing the composition, but the table was blanked out in the appendix in the pdf.	Low	3	1	3
Test Design	4. Negative and Vehicle Controls	Negative controls not required for lethality studies.	Not Rated	NA	NA	NA
	5. Positive Controls	Positive controls not typical for this study type.	Not Rated	NA	NA	NA
	6. Randomized Allocation	Study did not report how animals were allocated to groups.	Low	3	1	3
Exposure Characterization	7. Preparation and Storage of Test Substance	No information on preparation or storage of test material was provided.	Unacceptable	4	1	4
	8. Consistency of Exposure Administration	Some details of exposure administration were not reported (e.g., gavage volume) but these are unlikely to affect the results.	Low	3	1	3
	9. Reporting of Doses/Concentrations	Doses were reported unambiguously as mg/kg bw	High	1	2	2

PEER REVIEW DRAFT. DO NOT CITE OR QUOTE

Study reference:	**Dow Chem, Co (1983). Initial submission: perchloroethylene solvent formulation: acute toxicological properties & industrial handling hazards, with cover letter dated 102591 (sanitized)** **HERO ID: 4214440**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	10. Exposure Frequency and Duration	Single exposure is typical for this study type.	High	1	1	1
	11. Number of Exposure Groups and Dose Spacing	There were 5 nonzero exposure groups, and the maximum dose administered (5000 mg/kg) is commonly used in limit tests. Dose range and spacing were adequate to enable calculation of LD50 values with reasonable confidence limits.	High	1	1	1
	12. Exposure Route and Method	Acute oral/gavage	High	1	1	1
Test Organism	13. Test Animal Characteristics	Test animal source, species, strain, and sex were reported; age and initial body weight were not.	Medium	2	2	4
	14. Adequacy and Consistency of Animal Husbandry Conditions	Housing conditions, acclimation, and photoperiod were reported, but temperature and humidity were not.	Medium	2	1	2
	15. Number per Group	6 rats/sex/dose were used.	Medium	2	1	2
Outcome Assessment	16. Outcome Assessment Methodology	Outcome assessment methodology was reported, but outcomes were limited to mortality, clinical signs, body weight, and gross necrospsy.	Medium	2	2	4
	17. Consistency of Outcome Assessment	There were no reported inconsistencies in outcome assessment.	High	1	1	1
	18. Sampling Adequacy	All exposed animals were evaluated for all outcomes.	High	1	1	1

PEER REVIEW DRAFT. DO NOT CITE OR QUOTE

Study reference:	**Dow Chem, Co (1983). Initial submission: perchloroethylene solvent formulation: acute toxicological properties & industrial handling hazards, with cover letter dated 102591 (sanitized)** **HERO ID: 4214440**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	19. Blinding of Assessors	Most outcomes (apart from clinical signs) were not subjective.	Not Rated	NA	NA	NA
	20. Negative Control Response	There was no negative control group.	Not Rated	NA	NA	NA
Confounding / Variable Control	21. Confounding Variables in Test Design and Procedures	No potentially confounding factors were identified, but food intake was not measured and could have affected body weights.	Medium	2	2	4
	22. Health Outcomes Unrelated to Exposure	No health outcomes unrelated to exposure were reported.	High	1	1	1
Data Presentation and Analysis	23. Statistical Methods	Statistical analysis of lethality data was conducted, and data enabling independent analysis were reported.	Medium	2	1	2
	24. Reporting of Data	Mortality and clinical signs were reported in detail, including time of death/onset of symptoms, but body weights were not reported.	Medium	2	2	4
High: >=1 and <1.7 Medium: >=1.7 and <2.3 Low: >=2.3 and <=3		**Sum of scores:**			**25**	**49**
		Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factors:		**NA**	**Overall Score: Nearest *:**	**NA**
		Overall Quality Level:		**Low**		
Study Quality Comment:	**The reviewer upgraded this study's overall quality rating, changing its status from unacceptable to acceptable. They noted: The only metric that was unacceptable was test substance preparation and storage, which is of low concern for single dose gavage administration. The study was initially assigned a rating of unacceptable (score = 4) with a calculated score of 2.0 (shown solely for transparency). No calculated score is identified for the current rating in the table above because the study was upgraded to low.**					

2. Short – Term Toxicity Studies

2.1. Animal toxicity evaluation results of Beliles et al 1980 for 3-week gestational inhalation studies on genotoxicity in vivo (mechanistic) outcomes

Study reference:	**Beliles, R. P.,Brusick, D. J.,Mecler, F. J. (1980). Teratogenic-mutagenic risk of workplace contaminants: trichloroethylene, perchloroethylene, and carbon disulfide** **HERO ID: 58331**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
Test Substance	1. Test Substance Identity	Identified by chemical name and synonym	High	1	2	2
	2. Test Substance Source	Manufacturer and lot number given.	High	1	1	1
	3. Test Substance Purity	91% pure, impurities were not characterized	Medium	2	1	2
Test Design	4. Negative and Vehicle Controls	Filtered air controls; "To avoid exposure of control animals to test materials, all control chambers were in a different chamber room than the exposure chambers. No test materials were taken into the control rooms."	High	1	2	2
	5. Positive Controls	Positive controls (reference mutagens) were used for all studies. "However, the contractor did not attempt to verify the purity of these commercially available samples."	High	1	1	1
	6. Randomized Allocation	"The animals were randomly assigned to experimental groups."	High	1	1	1
Exposure Characterization	7. Preparation and Storage of Test Substance	Method and equipment used to generate the test substance as a vapor were reported and appropriate.	High	1	1	1
	8. Consistency of Exposure Administration	Details of exposure administration were reported.	High	1	1	1

Study reference:	**Beliles, R. P.,Brusick, D. J.,Mecler, F. J. (1980). Teratogenic-mutagenic risk of workplace contaminants: trichloroethylene, perchloroethylene, and carbon disulfide** **HERO ID: 58331**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	9. Reporting of Doses/Concentrations	Target and analytical concentrations were provided. Range of measure concentration did not deviate more than 10% target concentration.	High	1	2	2
	10. Exposure Frequency and Duration	The exposure frequency and duration were reported and appropriate for this study.	High	1	1	1
	11. Number of Exposure Groups and Dose Spacing	2 exposure concentrations (100 and 500ppm)	Medium	2	1	2
	12. Exposure Route and Method	Dynamic chamber , whole body, assumed that Perc does not condense.	High	1	1	1
Test Organism	13. Test Animal Characteristics	Species, strain and source were reported; starting age and body weight not given.	Medium	2	2	4
	14. Adequacy and Consistency of Animal Husbandry Conditions	well reported	High	1	1	1
	15. Number per Group	6-10/group	High	1	1	1
Outcome Assessment	16. Outcome Assessment Methodology	Dominant lethal assay, spermhead abnormality, chromosomal aberration in rat bone marrow, rat dominant lethal test conducted.	High	1	2	2
	17. Consistency of Outcome Assessment	See footnote at end of page.[1]	High	1	1	1

[1] Metrics that received a “High” rating met the criteria as discussed in the Applications of Systematic Review for TSCA Risk Evaluation.

PEER REVIEW DRAFT. DO NOT CITE OR QUOTE

Study reference:	**Beliles, R. P.,Brusick, D. J.,Mecler, F. J. (1980). Teratogenic-mutagenic risk of workplace contaminants: trichloroethylene, perchloroethylene, and carbon disulfide** **HERO ID: 58331**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	18. Sampling Adequacy	See footnote at end of page.[1]	High	1	1	1
	19. Blinding of Assessors	Blinding was not reported, but most outcomes were not subjective.	Medium	2	1	2
	20. Negative Control Response		High	1	1	1
Confounding / Variable Control	21. Confounding Variables in Test Design and Procedures	None related to genotoxicity	High	1	2	2
	22. Health Outcomes Unrelated to Exposure	None related to genotoxicity	High	1	1	1
Data Presentation and Analysis	23. Statistical Methods	Statistics were well described and appropriate	High	1	1	1
	24. Reporting of Data	All outcomes were reported.	High	1	2	2
High: >=1 and <1.7 Medium: >=1.7 and <2.3 Low: >=2.3 and <=3		**Sum of scores:**			**31**	**36**
		Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factors:		**1.1613**	**Overall Score: Nearest *:**	**1.2**
		Overall Quality Level:		**High**		

2.2. Animal toxicity evaluation results of Boverhof et al 2013 for a 4-week inhalation (perc) study on mortality, nutrition and metabolic/adult exposure body weight, hematological and immune, hepatic, renal, and respiratory outcomes

Study reference:	**Boverhof, D. R.,Krieger, S. M.,Hotchkiss, J.,Stebbins, K. E.,Thomas, J.,Woolhiser, M. R. (2013). Assessment of the immunotoxic potential of trichloroethylene and perchloroethylene in rats following inhalation exposure Journal of Immunotoxicology, 10(3), 311-320** **HERO ID: 2127872**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
Test Substance	1. Test Substance Identity	The test substance was identified definitively.	High	1	2	2
	2. Test Substance Source	The source of the test substance was reported incompletely (a batch/lot number was not reported).	Medium	2	1	2
	3. Test Substance Purity	The test substance purity was acceptable (reported to be 99.98% pure).	High	1	1	1
Test Design	4. Negative and Vehicle Controls	A concurrent negative control group (filtered air only) was used and was appropriate.	High	1	2	2
	5. Positive Controls	A positive control group (injected with cyclophosphamide) was included in the antibody response test and was appropriate. A similar positive control was not included in the test for evaluating organ weights, histopathology, hematology, and bronchoalveolar lavage (not applicable).	High	1	1	1
	6. Randomized Allocation	The study authors did not report how animals were allocated to study groups.	Low	3	1	3

PEER REVIEW DRAFT. DO NOT CITE OR QUOTE

Study reference:	**Boverhof, D. R.,Krieger, S. M.,Hotchkiss, J.,Stebbins, K. E.,Thomas, J.,Woolhiser, M. R. (2013). Assessment of the immunotoxic potential of trichloroethylene and perchloroethylene in rats following inhalation exposure Journal of Immunotoxicology, 10(3), 311-320** **HERO ID: 2127872**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
Exposure Characterization	7. Preparation and Storage of Test Substance	The test substance preparation and method and equipment used to generate the test substance as a vapor were reported and appropriate. The study authors did not report how the test substance was stored	Medium	2	1	2
	8. Consistency of Exposure Administration	Details of the exposure administration were reported and exposures were administered consistently across study groups.	High	1	1	1
	9. Reporting of Doses/Concentrations	Concentrations were reported without ambiguity. Test concentrations in the chambers were analytically determined at least once per hour during the exposures and mean analytical concentrations were reported. The analytical method used to measure chamber concentrations was reported and appropriate.	High	1	2	2
	10. Exposure Frequency and Duration	The exposure frequency and duration of exposure were reported and appropriate for the study and outcomes of interest.	High	1	1	1

PEER REVIEW DRAFT. DO NOT CITE OR QUOTE

Study reference:	**Boverhof, D. R.,Krieger, S. M.,Hotchkiss, J.,Stebbins, K. E.,Thomas, J.,Woolhiser, M. R. (2013). Assessment of the immunotoxic potential of trichloroethylene and perchloroethylene in rats following inhalation exposure Journal of Immunotoxicology, 10(3), 311-320** **HERO ID: 2127872**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	11. Number of Exposure Groups and Dose Spacing	The number of exposure groups and concentration spacing were justified by the study authors (based on previous studies/animal data) and considered adequate to address the purpose of the study.	High	1	1	1
	12. Exposure Route and Method	The route and method of exposure were reported and were suited to the test substance. A dynamic whole body chamber was used and acceptable for the test substance vapor.	High	1	1	1
Test Organism	13. Test Animal Characteristics	The test animal species, strain, sex, and age were reported and the test animals were obtained from a commercial source. Initial body weights and health status at the start of the study were not reported although the animals were certified Virus Antibody Free by the source.	Medium	2	2	4
	14. Adequacy and Consistency of Animal Husbandry Conditions	Husbandry conditions were not sufficiently reported to evaluate if husbandry was adequate and if differences occurred between control and exposed groups.	Low	3	1	3

Study reference:	**Boverhof, D. R.,Krieger, S. M.,Hotchkiss, J.,Stebbins, K. E.,Thomas, J.,Woolhiser, M. R. (2013). Assessment of the immunotoxic potential of trichloroethylene and perchloroethylene in rats following inhalation exposure Journal of Immunotoxicology, 10(3), 311-320** **HERO ID: 2127872**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	15. Number per Group	The number of animals per group (8 females/dose group) was less than the typical number used in studies of the same or similar type (e.g., subchronic toxicity study).	Medium	2	1	2
Outcome Assessment	16. Outcome Assessment Methodology	The outcome assessment methodology addressed or reported the intended outcomes of interest and was sensitive for the outcomes of interest.	High	1	2	2
	17. Consistency of Outcome Assessment	Details of the outcome assessment protocol were reported and outcomes were assessed consistently across study groups.	High	1	1	1
	18. Sampling Adequacy	Details regarding sampling for the outcomes of interest were reported and the study used adequate sampling for the outcomes of interest.	High	1	1	1
	19. Blinding of Assessors	No subjective outcomes were reported.	Not Rated	NA	NA	NA
	20. Negative Control Response	The biological response of the negative control group was reported and acceptable.	High	1	1	1
Confounding / Variable Control	21. Confounding Variables in Test Design and Procedures	Respiratory rate was not reported to have been evaluated in this inhalation study; however, Perc is a potential respiratory irritant	Low	3	2	6

PEER REVIEW DRAFT. DO NOT CITE OR QUOTE

Study reference:	**Boverhof, D. R.,Krieger, S. M.,Hotchkiss, J.,Stebbins, K. E.,Thomas, J.,Woolhiser, M. R. (2013). Assessment of the immunotoxic potential of trichloroethylene and perchloroethylene in rats following inhalation exposure Journal of Immunotoxicology, 10(3), 311-320** **HERO ID: 2127872**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	22. Health Outcomes Unrelated to Exposure	Data on attrition and/or health outcomes unrelated to exposure for each study group were not reported because only substantial differences among groups were noted.	Medium	2	1	2
Data Presentation and Analysis	23. Statistical Methods	Statistical methods were clearly described and appropriate for the datasets.	High	1	1	1
	24. Reporting of Data	Data for most exposure-related findings were reported for most, but not all, outcomes by exposure group. However, some exposure-related data were not reported quantitatively (e.g., reduced body weights) and incidence data for histopathological findings were reported incompletely (only the mid- and high-concentrations; unclear if any animals were affected in the control or low-concentration groups).	Medium	2	2	4
High: >=1 and <1.7 Medium: >=1.7 and <2.3 Low: >=2.3 and <=3		**Sum of scores:**			**30**	**46**
		Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factors:		**1.5333**	**Overall Score: Nearest *:**	**1.5**
		Overall Quality Level:		**High**		

2.3. Animal toxicity evaluation results of Carney et al 2006 for a gestational exposure study on reproductive, growth (early life) and development, nutrition and metabolic/adult exposure body weight, mortality outcomes

Study reference:	**Carney, E. W.,Thorsrud, B. A.,Dugard, P. H.,Zablotny, C. L. (2006). Developmental toxicity studies in Crl:CD (SD) rats following inhalation exposure to trichloroethylene and perchloroethylene Birth Defects Research, Part B: Developmental and Reproductive Toxicology, 77(5), 405-412** **HERO ID: 630415**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
Test Substance	1. Test Substance Identity	tetrachloroethylene (PERC)	High	1	2	2
	2. Test Substance Source	INEOS CHlor Ltd, no batch number	Medium	2	1	2
	3. Test Substance Purity	>99%	High	1	1	1
Test Design	4. Negative and Vehicle Controls	See footnote at end of page.[1]	High	1	2	2
	5. Positive Controls	Not required by cited guidelines (OPPTS 870.370 and OECD 414)	Not Rated	NA	NA	NA
	6. Randomized Allocation	Animals were randomly assigned to four groups	High	1	1	1
Exposure Characterization	7. Preparation and Storage of Test Substance	The method and equipment used to generate the test substance as a gas, vapor, or aerosol were NOT reported. It is not clear if the vapor generation method reported for TCE was also used for PERC (different laboratories, different chambers, different flow rates, etc). However, since analytical concentrations were reported, omission of vapor generation details is unlikely to have a substantial impact on results	Medium	2	1	2

[1] Metrics that received a "High" rating met the criteria as discussed in the Applications of Systematic Review for TSCA Risk Evaluation.

Study reference:	**Carney, E. W.,Thorsrud, B. A.,Dugard, P. H.,Zablotny, C. L. (2006). Developmental toxicity studies in Crl:CD (SD) rats following inhalation exposure to trichloroethylene and perchloroethylene Birth Defects Research, Part B: Developmental and Reproductive Toxicology, 77(5), 405-412** **HERO ID: 630415**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	8. Consistency of Exposure Administration	The concentrations of PERC were measured multiple times each exposure day using GC analysis. Exposure administration consistent across groups. (already downgraded metric 7 to unacceptable based on lack of methods for generating atmospheres, so that was not used to grade for this metric).	High	1	1	1
	9. Reporting of Doses/Concentrations	Target and analytical exposure levels were reported..	High	1	2	2
	10. Exposure Frequency and Duration	GD 6-19, 6 hr/d, 7 d/wk; Both guidelines cited indicate that animals should be dosed until the day prior to C-section and sacrifice, which was reported as GD 20.	High	1	1	1
	11. Number of Exposure Groups and Dose Spacing	3 exposure and 1 control. These test concentrations were based on the results from the previously discussed developmental toxicity studies. The highest exposure level of 600ppm (equivalent to 4.1mg PERC/L) exceeds the limit concentration of 2 mg/L specified in the EPA prenatal developmental toxicity test guideline (OPPTS 870.3700).	High	1	1	1

PEER REVIEW DRAFT. DO NOT CITE OR QUOTE

Study reference:	**Carney, E. W.,Thorsrud, B. A.,Dugard, P. H.,Zablotny, C. L. (2006). Developmental toxicity studies in Crl:CD (SD) rats following inhalation exposure to trichloroethylene and perchloroethylene Birth Defects Research, Part B: Developmental and Reproductive Toxicology, 77(5), 405-412** **HERO ID: 630415**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	12. Exposure Route and Method	Animals were whole body exposed in 0.75-cubic-meter exposure chambers. Chamber airflow was maintained at approximately 150 L/min. This resulted in approximately 12 air changes per hour.	High	1	1	1
Test Organism	13. Test Animal Characteristics	Crl:CD (SD) rats (Charles River). Virgin female rats. Initial BW not reported (body weights reported fro GD 3, 6, 9, 13, 17, and 20).	Medium	2	2	4
	14. Adequacy and Consistency of Animal Husbandry Conditions	Housing adequately described. Room temperature and humidity were maintained within laboratory specific ranges (19–231C and 40–70% relative humidity). A 12-hr photoperiod was maintained for all animals. Food an water available ad libitum except during exposure periods.	High	1	1	1
	15. Number per Group	22 dams/group; in accordance with guidelines	High	1	1	1

PEER REVIEW DRAFT. DO NOT CITE OR QUOTE

Study reference:	**Carney, E. W.,Thorsrud, B. A.,Dugard, P. H.,Zablotny, C. L. (2006). Developmental toxicity studies in Crl:CD (SD) rats following inhalation exposure to trichloroethylene and perchloroethylene Birth Defects Research, Part B: Developmental and Reproductive Toxicology, 77(5), 405-412** **HERO ID: 630415**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
Outcome Assessment	16. Outcome Assessment Methodology	Maternal toxicity - clinical signs, BW, feed consumption, mortality Reproductive/Devt - gravid uterine weights, placenta weight, # corpora lutea, uterine implants, resorptions, live/dead fetuses, fetal weight, external, skeletal, and visceral malformations/variations Although the current OECD test guideline 414 (updated in 2018) indicates that AGD should be measured in all live fetuses, the OECD TG 414 version available at the time of publication of this study was from 2001 and did not require measurement of AGD and the cited OPPTS guideline does not have that requirement.	Medium	2	2	4
	17. Consistency of Outcome Assessment	Consistent evaluation across groups	High	1	1	1
	18. Sampling Adequacy	17-22 pregnant dams	High	1	1	1
	19. Blinding of Assessors	Blinding not done for PERC and not required by cited guidelines.	Not Rated	NA	NA	NA
	20. Negative Control Response	Control data reported. Historical control data discussed when needed to assess results.	High	1	1	1

PEER REVIEW DRAFT. DO NOT CITE OR QUOTE

Study reference:	**Carney, E. W.,Thorsrud, B. A.,Dugard, P. H.,Zablotny, C. L. (2006). Developmental toxicity studies in Crl:CD (SD) rats following inhalation exposure to trichloroethylene and perchloroethylene Birth Defects Research, Part B: Developmental and Reproductive Toxicology, 77(5), 405-412** **HERO ID: 630415**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
Confounding / Variable Control	21. Confounding Variables in Test Design and Procedures	Initial BW not reported; no statistically significant changes in BW during study. Only change in food consumption was 7% decrease in high-exposure group from GD 6-8. Respiratory rate not specifically mentioned, but no exposure-related clinical signs reported in dams, so bradyapnea unlikely. Downgraded to medium since PERC is a respiratory irritant (HSDB)	Medium	2	2	4
	22. Health Outcomes Unrelated to Exposure	No mortalities, no clinical signs. Only attrition was time-mated females that were not pregnant (in all groups) that were not included in analysis.	High	1	1	1

PEER REVIEW DRAFT. DO NOT CITE OR QUOTE

Study reference:	Carney, E. W.,Thorsrud, B. A.,Dugard, P. H.,Zablotny, C. L. (2006). Developmental toxicity studies in Crl:CD (SD) rats following inhalation exposure to trichloroethylene and perchloroethylene Birth Defects Research, Part B: Developmental and Reproductive Toxicology, 77(5), 405-412 HERO ID: 630415					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
Data Presentation and Analysis	23. Statistical Methods	Litter is statistical unit. Continuous data were tested in both studies for homogeneity of variance using Bartlett's test. The raw, log-transformed and square root–transformed data were tested. Based on results, data were analyzed using either parametric or nonparametric tests. If 75% of the data (across all groups) were the same value, then a frequency analysis was performed. Treatment groups were compared using a Mantel test for a trend in proportions and also pairwise Fisher's Exact tests were used for each dose group against the control. Skeletal variants were analyzed by a generalized mixed linear model with a logit link function and used litter as a random effect/ Each treated group was compared to the control group using a Wald chi-square test.	High	1	1	1

PEER REVIEW DRAFT. DO NOT CITE OR QUOTE

Study reference:	**Carney, E. W.,Thorsrud, B. A.,Dugard, P. H.,Zablotny, C. L. (2006). Developmental toxicity studies in Crl:CD (SD) rats following inhalation exposure to trichloroethylene and perchloroethylene Birth Defects Research, Part B: Developmental and Reproductive Toxicology, 77(5), 405-412** **HERO ID: 630415**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	24. Reporting of Data	All reproductive and developmental findings were reported quantitatively in tabular or graphical format. maternal body weights and food consumption reported in tables. Mortality and clinical signs reported qualitatively (no exposure-related findings)	High	1	2	2
High: >=1 and <1.7 Medium: >=1.7 and <2.3 Low: >=2.3 and <=3		**Sum of scores:**			**29**	**37**
		Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factors:		**1.2759**	**Overall Score: Nearest *:**	**1.3**
		Overall Quality Level:		**High**		

2.4. Animal toxicity evaluation results of Nelson et al 1979 for a neurodevelopmental inhalation study (gd 7-13) study on growth (early life) and development outcomes

Study reference:	Nelson, B. K.,Taylor, B. J.,Setzer, J. V.,Hornung, R. W. (1979). Behavioral teratology of perchloroethylene in rats Journal of Environmental Pathology, Toxicology and Oncology, 3(1-2), 233-250 HERO ID: 58224					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
Test Substance	1. Test Substance Identity	TG-PERC	High	1	2	2
	2. Test Substance Source	TG-PERC obtained from Fisher Scientific; batch no. not reported, no independent analysis	Medium	2	1	2
	3. Test Substance Purity	98.5% pure	High	1	1	1
Test Design	4. Negative and Vehicle Controls	sham exposed group	High	1	2	2
	5. Positive Controls	OECD guideline 426 (developmental neurotoxicity) states "To guard against possible false-negative findings and the inherent difficulties in “proving a negative,” available positive and historical control data should be discussed, especially when there are no treatment-related effects". However, positive control is not a requirement - especially since exposure-related effects were observed. Therefore, N/A was selected.	Not Rated	NA	NA	NA
	6. Randomized Allocation	The study did not report how animals were allocated to study groups	Low	3	1	3

PEER REVIEW DRAFT. DO NOT CITE OR QUOTE

Study reference:	Nelson, B. K.,Taylor, B. J.,Setzer, J. V.,Hornung, R. W. (1979). Behavioral teratology of perchloroethylene in rats Journal of Environmental Pathology, Toxicology and Oncology, 3(1-2), 233-250 HERO ID: 58224					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
Exposure Characterization	7. Preparation and Storage of Test Substance	Storage not reported. PERC was vaporized using heated flask, mixed with filtered room air and introduced into exposure chamber (airflow change rate 4x/min).	Medium	2	1	2
	8. Consistency of Exposure Administration	Exposure conditions were identical for sham-exposed controls and exposure group.	High	1	1	1
	9. Reporting of Doses/Concentrations	Only target exposure levels were reported. PERC levels in exposure chambers were continuously monitored by a Miran infrared analyzer and a charcoal tube sample was taken from the chamber air (generally one per day) and sent to an independent laboratory for gas chromatographic analysis. But results of analyses were not reported.	Low	3	2	6
	10. Exposure Frequency and Duration	GD 7-13; 7 hr/d	High	1	1	1
	11. Number of Exposure Groups and Dose Spacing	Only exposure group plus control (unacceptable based on PECO statement), but the use of two separate exposure durations (GD 7-13, GD 14-20) mitigates this concern; exposure level selected based on dose-finding study.	Low	3	1	3

PEER REVIEW DRAFT. DO NOT CITE OR QUOTE

Study reference:	Nelson, B. K.,Taylor, B. J.,Setzer, J. V.,Hornung, R. W. (1979). Behavioral teratology of perchloroethylene in rats Journal of Environmental Pathology, Toxicology and Oncology, 3(1-2), 233-250 HERO ID: 58224					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	12. Exposure Route and Method	Whole-body, dynamic chamber (0.41 cu m). Air flow 4 changes/min. Unclear how many animals per exposure chamber?	Medium	2	1	2
Test Organism	13. Test Animal Characteristics	Virgin male and female SD rats obtained from Harlan Industries and mated. Sperm-positive females used in study.	High	1	2	2
	14. Adequacy and Consistency of Animal Husbandry Conditions	Husbandry conditions were consistent; pregnant females housed alone.	High	1	1	1
	15. Number per Group	13-19 dams/group; litters culled to 4/sex within 16 hrs of delivery	High	1	1	1
Outcome Assessment	16. Outcome Assessment Methodology	Comprehensive neurobehavioral testing, neurochemical analysis, and neurohistopathology was conducted on PND 4-46, using 1/sex per litter; pup body weights were also monitored. However, confidence downgraded to medium because maternal toxicity was not evaluated in this study (only pilot study).	Medium	2	2	4
	17. Consistency of Outcome Assessment	Consistent evaluation between groups.	High	1	1	1
	18. Sampling Adequacy	1/sex per litter in neurobehavioral testing (so litter is statistical unit)	High	1	1	1

PEER REVIEW DRAFT. DO NOT CITE OR QUOTE

Study reference:	Nelson, B. K.,Taylor, B. J.,Setzer, J. V.,Hornung, R. W. (1979). Behavioral teratology of perchloroethylene in rats Journal of Environmental Pathology, Toxicology and Oncology, 3(1-2), 233-250 HERO ID: 58224					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	19. Blinding of Assessors	The study authors did not indicate whether or not assessors of neurobehavior were blinded. Certain tests contain subjective endpoints, which could have introduced bias. Pup body weight and histopathology do not require blinding.	Low	3	1	3
	20. Negative Control Response	Control data reported. Study authors noted that offspring of animals sham-exposed from 7-13 (this study) and 14-20 (additional study) differed. Study authors indicated that this stressed importance of appropriate controls; however, it could also indicate variation in control replicates.	Low	3	1	3
Confounding / Variable Control	21. Confounding Variables in Test Design and Procedures	All females weighed 200-300 g at study initiation. Dam BW and food consumption were not reported for this study, but in the pilot study (which used the same exposure level), no significant change in BW or food consumption was observed in exposed dams. Study authors did not indicate whether respiratory rate was measured. Since PERC is a respiratory irritant, confidence downgraded to low.	Low	3	2	6

PEER REVIEW DRAFT. DO NOT CITE OR QUOTE

Study reference:	**Nelson, B. K.,Taylor, B. J.,Setzer, J. V.,Hornung, R. W. (1979). Behavioral teratology of perchloroethylene in rats Journal of Environmental Pathology, Toxicology and Oncology, 3(1-2), 233-250** **HERO ID: 58224**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	22. Health Outcomes Unrelated to Exposure	data on attrition and/or health outcomes unrelated to exposure for each study group were not reported because only substantial differences among groups were noted	Medium	2	1	2
Data Presentation and Analysis	23. Statistical Methods	Multivariate ANOVA for most, open field and ascent tests analyzed with contingency tables; neurochemical data analyzed with 2-tailed students t-test	High	1	1	1
	24. Reporting of Data	Graphical presentation of control and exposure group data was provided for some exposure-related endpoints; others were reported qualitatively as significant findings. Non-significant findings reported qualitatively.	Medium	2	2	4
High: >=1 and <1.7 Medium: >=1.7 and <2.3 Low: >=2.3 and <=3		**Sum of scores:**			**30**	**54**
		Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factors:		**NA**	**Overall Score: Nearest *:**	**NA**
		Overall Quality Level:		**Low**		
Study Quality Comment:	**The reviewer downgraded this study's overall quality rating. They noted: Study was downgraded for the following reasons: 1) lack of blinding in neurobehavioral assessment (which was primary focus of study), 2) variation in control replicates, 3) lack of evaluation of maternal effects in main study (only pilot study), and 4) only one exposure level Note: The original calculated score for this study was 1.8. This value is not presented above because the final rating was changed based on professional judgement.**					

2.5. Animal toxicity evaluation results of Nelson et al 1979 for a neurodevelopmental inhalation study (gd 14-20) on growth (early life) and development and neurological/behavior outcomes

Study reference:	Nelson, B. K.,Taylor, B. J.,Setzer, J. V.,Hornung, R. W. (1979). Behavioral teratology of perchloroethylene in rats Journal of Environmental Pathology, Toxicology and Oncology, 3(1-2), 233-250 HERO ID: 58224					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
Test Substance	1. Test Substance Identity	Technical Grade-PCE;	High	1	2	2
	2. Test Substance Source	TG-PERC obtained from Fisher Scientific; batch no. not reported, no independent analysis	Medium	2	1	2
	3. Test Substance Purity	98.5% pure	High	1	1	1
Test Design	4. Negative and Vehicle Controls	sham exposed group	High	1	2	2
	5. Positive Controls	OECD guideline 426 (developmental neurotoxicity) states "To guard against possible false-negative findings and the inherent difficulties in “proving a negative,” available positive and historical control data should be discussed, especially when there are no treatment-related effects". However, positive control is not a requirement - especially since exposure-related effects were observed. Therefore, N/A was selected.	Not Rated	NA	NA	NA
	6. Randomized Allocation	The study did not report how animals were allocated to study groups	Low	3	1	3

Study reference:	Nelson, B. K.,Taylor, B. J.,Setzer, J. V.,Hornung, R. W. (1979). Behavioral teratology of perchloroethylene in rats Journal of Environmental Pathology, Toxicology and Oncology, 3(1-2), 233-250 HERO ID: 58224					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
Exposure Characterization	7. Preparation and Storage of Test Substance	Storage not reported. PERC was vaporized using heated flask, mixed with filtered room air and introduced into exposure chamber (airflow change rate 4x/min).	Medium	2	1	2
	8. Consistency of Exposure Administration	Exposure conditions were identical for sham-exposed controls and exposure groups.	High	1	1	1
	9. Reporting of Doses/Concentrations	Only target exposure levels were reported. PERC levels in exposure chambers were continuously monitored by a Miran infrared analyzer and a charcoal tube sample was taken from the chamber air (generally one per day) and sent to an independent laboratory for gas chromatographic analysis. But results of analyses were not reported.	Low	3	2	6
	10. Exposure Frequency and Duration	GD 14-20; 7 hr/d	High	1	1	1
	11. Number of Exposure Groups and Dose Spacing	2 exposure groups plus control; exposure levels selected based on dose-finding study	High	1	1	1
	12. Exposure Route and Method	Whole-body, dynamic chamber (0.41 cu m). Air flow 4 changes/min. Unclear how many animals per exposure chamber?	Medium	2	1	2

PEER REVIEW DRAFT. DO NOT CITE OR QUOTE

Study reference:	**Nelson, B. K.,Taylor, B. J.,Setzer, J. V.,Hornung, R. W. (1979). Behavioral teratology of perchloroethylene in rats Journal of Environmental Pathology, Toxicology and Oncology, 3(1-2), 233-250** **HERO ID: 58224**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
Test Organism	13. Test Animal Characteristics	Virgin male and female SD rats obtained from Harlan Industries and mated. Sperm-positive females used in study.	High	1	2	2
	14. Adequacy and Consistency of Animal Husbandry Conditions	Husbandry conditions were consistent; pregnant females housed alone.	High	1	1	1
	15. Number per Group	15-21 dams/group; litters culled to 4/sex within 16 hrs of delivery	High	1	1	1
Outcome Assessment	16. Outcome Assessment Methodology	Comprehensive neurobehavioral testing, neurochemical analysis, and neurohistopathology was conducted on PND 4-46, using 1/sex per litter; pup body weights were also monitored. However, confidence downgraded to medium because maternal toxicity was not evaluated in this study (only pilot study).	Medium	2	2	4
	17. Consistency of Outcome Assessment	Consistent evaluation between groups.	High	1	1	1
	18. Sampling Adequacy	1/sex per litter in neurobehavioral testing (so litter is statistical unit)	High	1	1	1
	19. Blinding of Assessors	The study authors did not indicate whether or not assessors of neurobehavior were blinded. Certain tests contain subjective endpoints, which could have introduced bias. Pup body weight and histopathology do not require blinding.	Low	3	1	3

PEER REVIEW DRAFT. DO NOT CITE OR QUOTE

Study reference:	Nelson, B. K.,Taylor, B. J.,Setzer, J. V.,Hornung, R. W. (1979). Behavioral teratology of perchloroethylene in rats Journal of Environmental Pathology, Toxicology and Oncology, 3(1-2), 233-250 HERO ID: 58224					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	20. Negative Control Response	Control data reported. Study authors noted that offspring of animals sham-exposed from 7-13 (different study) and 14-20 (this study) differed. Study authors indicated that this stressed importance of appropriate controls; however, it could also indicate variation in control replicates.	Low	3	1	3
Confounding / Variable Control	21. Confounding Variables in Test Design and Procedures	All females weighed 200-300 g at study initiation. Dam BW and food consumption were not reported for this study, but in the pilot study (which used high exposure level), no significant change in BW or food consumption was observed in exposed dams. Study authors did not indicate whether respiratory rate was measured. Since PERC is a respiratory irritant, confidence downgraded to low.	Low	3	2	6
	22. Health Outcomes Unrelated to Exposure	data on attrition and/or health outcomes unrelated to exposure for each study group were not reported because only substantial differences among groups were noted	Medium	2	1	2

PEER REVIEW DRAFT. DO NOT CITE OR QUOTE

Study reference:	**Nelson, B. K.,Taylor, B. J.,Setzer, J. V.,Hornung, R. W. (1979). Behavioral teratology of perchloroethylene in rats Journal of Environmental Pathology, Toxicology and Oncology, 3(1-2), 233-250** **HERO ID: 58224**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
Data Presentation and Analysis	23. Statistical Methods	Multivariate ANOVA for most, open field and ascent tests analyzed with contingency tables; neurochemical data analyzed with 2-tailed students t-test	High	1	1	1
	24. Reporting of Data	Control and high-exposure level data reported Graphical presentation of control and high-exposure level data was provided for some exposure-related endpoints; others were reported qualitatively as significant findings. Non-significant findings reported qualitatively. All low-exposure group data reported qualitatively (no exposure-related findings)	Medium	2	2	4
High: >=1 and <1.7 Medium: >=1.7 and <2.3 Low: >=2.3 and <=3		**Sum of scores:**			**30**	**52**
		Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factors:		**NA**	**Overall Score: Nearest *:**	**NA**
		Overall Quality Level:		**Low**		
Study Quality Comment:	**The reviewer downgraded this study's overall quality rating. They noted: Study was downgraded for the following reasons: 1) lack of blinding in neurobehavioral assessment (which was primary focus of study), 2) variation in control replicates, and 3) lack of evaluation of maternal effects in main study (only pilot study). Note: The original calculated score for this study was 1.7. This value is not presented above because the final rating was changed based on professional judgement.**					

2.6. Animal toxicity evaluation results of NTP 1986 for 1-day inhalation studies in rats and mice on acute toxicity, neurological/behavioral, mortality, nutrition and metabolic/adult exposure body weight outcomes

Study reference:	Ntp, (1986). Toxicology and carcinogenesis studies of tetrachloroethylene (perchloroethylene) (CAS no. 127-18-4) in F344/N rats and B6C3F1 mice (inhalation studies) HERO ID: 632655					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
Test Substance	1. Test Substance Identity	high-purity tetrachloroethylene, Dowper stabilized	High	1	2	2
	2. Test Substance Source	Dow Chemical, lot TA03116F-01. Purity and identity analyses conducted.	High	1	1	1
	3. Test Substance Purity	Confirmed analytically - approximately 99.9%	High	1	1	1
Test Design	4. Negative and Vehicle Controls	Chamber controls were used.	High	1	2	2
	5. Positive Controls	Not needed for study type.	Not Rated	NA	NA	NA
	6. Randomized Allocation	stratified by weight then assigned to groups according to a table of random numbers (weight is a nonrandom component)	Medium	2	1	2
Exposure Characterization	7. Preparation and Storage of Test Substance	Tetrachloroethylene was found to be stable for 2 weeks at 60" C (Appendix H). Tetrachloroethylene was stored at 0" C Tetrachloroethylene was vaporized at 100"-110" C, diluted with air, and. introduced into the chambers. Detailed descriptions in Table 2 and in Appendix I.	High	1	1	1
	8. Consistency of Exposure Administration	Concentrations in the exposure chambers were monitored 8-12 times per exposure period by a Hewlett-Packard 5840A Gas Chromatograph. No deviations from protocol noted.	High	1	1	1

Study reference:	Ntp, (1986). Toxicology and carcinogenesis studies of tetrachloroethylene (perchloroethylene) (CAS no. 127-18-4) in F344/N rats and B6C3F1 mice (inhalation studies) HERO ID: 632655					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	9. Reporting of Doses/Concentrations	Only target concentrations reported for non-chronic studies., but actual exposures expected to be close to target based on 2-yr analytical values.	Medium	2	2	4
	10. Exposure Frequency and Duration	1-d, 4 hr	Medium	2	1	2
	11. Number of Exposure Groups and Dose Spacing	5 dose groups plus control	High	1	1	1
	12. Exposure Route and Method	Inhalation, dynamic whole-body chamber. Flow rate not reported	Low	3	1	3
Test Organism	13. Test Animal Characteristics	F344/N rats and B6C3F1 mice, Frederick Cancer Research Center. 5-7 wks at study initiation. Initial body weights reported in Tables 6 and 17.	High	1	2	2
	14. Adequacy and Consistency of Animal Husbandry Conditions	Some details of husbandry in Table 5; Room conditions not reported	Medium	2	1	2
	15. Number per Group	5/sex/group	High	1	1	1
Outcome Assessment	16. Outcome Assessment Methodology	Mortality, clinical signs, body weight, necropsy	High	1	2	2
	17. Consistency of Outcome Assessment	Consistent evaluation in all study groups	High	1	1	1
	18. Sampling Adequacy	5/sex/group	High	1	1	1
	19. Blinding of Assessors	Evaluated endpoints did not require blinding	Not Rated	NA	NA	NA
	20. Negative Control Response	Control responses reported.	High	1	1	1

Study reference:	Ntp, (1986). Toxicology and carcinogenesis studies of tetrachloroethylene (perchloroethylene) (CAS no. 127-18-4) in F344/N rats and B6C3F1 mice (inhalation studies) HERO ID: 632655					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
Confounding / Variable Control	21. Confounding Variables in Test Design and Procedures	There were no reported differences among the study groups in initial body weight. Food and water intake were not reported. Respiratory rate not reported, but severe clinical signs included anesthesia were reported in exposed animals. Unclear if bradypnea was present.	Low	3	2	6
	22. Health Outcomes Unrelated to Exposure	data on attrition and/or health outcomes unrelated to exposure for each study group were not reported because only substantial differences among groups were noted	Medium	2	1	2
Data Presentation and Analysis	23. Statistical Methods	No statsitics Data for mortality and terminal BW were reported adequately for independent analysis. Clinical signs data inadequate for independent analysis.	Medium	2	1	2
	24. Reporting of Data	Quantitative mortality and body weight data. Exposure-related clinical signs reported qualitatively.	Medium	2	2	4
High: >=1 and <1.7 Medium: >=1.7 and <2.3 Low: >=2.3 and <=3		**Sum of scores:**			**29**	**44**
		Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factors:		**1.5172**	**Overall Score: Nearest *:**	**1.5**
		Overall Quality Level:		**High**		

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2.7. Animal toxicity evaluation results of NTP 1986 for 14-day inhalation studies in rats and mice on neurological/behavioral, mortality, nutrition and metabolic/adult exposure body weight outcomes

Study reference:	Ntp, (1986). Toxicology and carcinogenesis studies of tetrachloroethylene (perchloroethylene) (CAS no. 127-18-4) in F344/N rats and B6C3F1 mice (inhalation studies) HERO ID: 632655					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
Test Substance	1. Test Substance Identity	high-purity tetrachloroethylene, Dowper stabilized	High	1	2	2
	2. Test Substance Source	Dow Chemical, lot TA03116F-01. Purity and identity analyses conducted.	High	1	1	1
	3. Test Substance Purity	Confirmed analytically - approximately 99.9%	High	1	1	1
Test Design	4. Negative and Vehicle Controls	Chamber controls were used.	High	1	2	2
	5. Positive Controls	Not needed for study type.	Not Rated	NA	NA	NA
	6. Randomized Allocation	stratified by weight then assigned to groups according to a table of random numbers (weight is a nonrandom component)	Medium	2	1	2
Exposure Characterization	7. Preparation and Storage of Test Substance	Tetrachloroethylene was found to be stable for 2 weeks at 60" C (Appendix H). Tetrachloroethylene was stored at 0" C Tetrachloroethylene was vaporized at 100"-110" C, diluted with air, and. introduced into the chambers. Detailed descriptions in Table 2 and in Appendix I.	High	1	1	1

Study reference:	Ntp, (1986). Toxicology and carcinogenesis studies of tetrachloroethylene (perchloroethylene) (CAS no. 127-18-4) in F344/N rats and B6C3F1 mice (inhalation studies) HERO ID: 632655					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	8. Consistency of Exposure Administration	Concentrations in the exposure chambers were monitored 8-12 times per exposure period by a Hewlett-Packard 5840A Gas Chromatograph. No deviations from protocol noted.	High	1	1	1
	9. Reporting of Doses/Concentrations	Only target concentrations reported for non-chronic studies., but actual exposures expected to be close to target based on 2-yr analytical values.	Medium	2	2	4
	10. Exposure Frequency and Duration	14-d, 6 hr/d, 5 d/wk.	High	1	1	1
	11. Number of Exposure Groups and Dose Spacing	5 dose groups plus control	High	1	1	1
	12. Exposure Route and Method	Inhalation, dynamic whole-body chamber. Flow rate not reported	Low	3	1	3
Test Organism	13. Test Animal Characteristics	F344/N rats and B6C3F1 mice, Charles River Breeding. 6-8 wks at study initiation. Initial body weights reported in Tables 7 and 18.	High	1	2	2
	14. Adequacy and Consistency of Animal Husbandry Conditions	Some details of husbandry in Table 5; room conditions not reported.	Medium	2	1	2
	15. Number per Group	5/sex/group	High	1	1	1
Outcome Assessment	16. Outcome Assessment Methodology	Mortality, clinical signs, body weight	High	1	2	2
	17. Consistency of Outcome Assessment	Consistent evaluation in all study groups for 14-d study.	High	1	1	1

Study reference:	Ntp, (1986). Toxicology and carcinogenesis studies of tetrachloroethylene (perchloroethylene) (CAS no. 127-18-4) in F344/N rats and B6C3F1 mice (inhalation studies) HERO ID: 632655					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	18. Sampling Adequacy	5/sex/group	High	1	1	1
	19. Blinding of Assessors	Evaluated endpoints did not require blinding	Not Rated	NA	NA	NA
	20. Negative Control Response	Control responses reported.	High	1	1	1
Confounding / Variable Control	21. Confounding Variables in Test Design and Procedures	There were no reported differences among the study groups in initial body weight. Food and water intake were not reported. Respiratory rate not reported, but dyspnea was reported at highest exposure in both rats and mice.	Low	3	2	6
	22. Health Outcomes Unrelated to Exposure	data on attrition and/or health outcomes unrelated to exposure for each study group were not reported because only substantial differences among groups were noted	Medium	2	1	2
Data Presentation and Analysis	23. Statistical Methods	Detailed statistical tests reported for survival and tumor analysis of 2-yr study, unclear if any statistics were conducted on shorter-duration studies.. Data for mortality and terminal BW were reported adequately for independent analysis. Clinical signs data inadequate for independent analysis.	Medium	2	1	2
	24. Reporting of Data	Quantitative mortality and body weight data. Exposure-related clinical signs reported qualitatively.	Medium	2	2	4

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Study reference:	Ntp, (1986). Toxicology and carcinogenesis studies of tetrachloroethylene (perchloroethylene) (CAS no. 127-18-4) in F344/N rats and B6C3F1 mice (inhalation studies) HERO ID: 632655					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
High: >=1 and <1.7 Medium: >=1.7 and <2.3 Low: >=2.3 and <=3		Sum of scores:			29	43
		Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factors:		1.4828	Overall Score: Nearest *:	1.5
		Overall Quality Level:		High		

2.8. Animal toxicity evaluation results of NTP 1986 for 14-day inhalation studies in rats and mice (histology) on reproductive, hematological and immune, renal, hepatic, cardiovascular, endocrine, gastrointestinal, respiratory, skin and connective tissue, thyroid outcomes

Study reference:	**Ntp, (1986). Toxicology and carcinogenesis studies of tetrachloroethylene (perchloroethylene) (CAS no. 127-18-4) in F344/N rats and B6C3F1 mice (inhalation studies)** **HERO ID: 632655**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
Test Substance	1. Test Substance Identity	high-purity tetrachloroethylene, Dowper stabilized	High	1	2	2
	2. Test Substance Source	Dow Chemical, lot TA03116F-01. Purity and identity analyses conducted.	High	1	1	1
	3. Test Substance Purity	Confirmed analytically - approximately 99.9%	High	1	1	1
Test Design	4. Negative and Vehicle Controls	Chamber controls were used.	High	1	2	2
	5. Positive Controls	Not needed for study type.	Not Rated	NA	NA	NA
	6. Randomized Allocation	stratified by weight then assigned to groups according to a table of random numbers (weight is a nonrandom component)	Medium	2	1	2
Exposure Characterization	7. Preparation and Storage of Test Substance	Tetrachloroethylene was found to be stable for 2 weeks at 60" C (Appendix H). Tetrachloroethylene was stored at 0" C Tetrachloroethylene was vaporized at 100"-110" C, diluted with air, and. introduced into the chambers. Detailed descriptions in Table 2 and in Appendix I.	High	1	1	1

Study reference:	Ntp, (1986). Toxicology and carcinogenesis studies of tetrachloroethylene (perchloroethylene) (CAS no. 127-18-4) in F344/N rats and B6C3F1 mice (inhalation studies) HERO ID: 632655					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	8. Consistency of Exposure Administration	Concentrations in the exposure chambers were monitored 8-12 times per exposure period by a Hewlett-Packard 5840A Gas Chromatograph. No deviations from protocol noted.	High	1	1	1
	9. Reporting of Doses/Concentrations	Only target concentrations reported for non-chronic studies., but actual exposures expected to be close to target based on 2-yr analytical values.	Medium	2	2	4
	10. Exposure Frequency and Duration	14-d, 6 hr/d, 5 d/wk.	High	1	1	1
	11. Number of Exposure Groups and Dose Spacing	5 dose groups plus control	High	1	1	1
	12. Exposure Route and Method	Inhalation, dynamic whole-body chamber. Flow rate not reported	Low	3	1	3
Test Organism	13. Test Animal Characteristics	F344/N rats and B6C3F1 mice, Charles River Breeding. 6-8 wks at study initiation. Initial body weights reported in Tables 7 and 18.	High	1	2	2
	14. Adequacy and Consistency of Animal Husbandry Conditions	Some details of husbandry in Table 5; room conditions not reported.	Medium	2	1	2
	15. Number per Group	5/sex/group	High	1	1	1
Outcome Assessment	16. Outcome Assessment Methodology	comprehensive histopathology	High	1	2	2
	17. Consistency of Outcome Assessment	Consistent evaluation in all study groups for 14-d study.	High	1	1	1

Study reference:	Ntp, (1986). Toxicology and carcinogenesis studies of tetrachloroethylene (perchloroethylene) (CAS no. 127-18-4) in F344/N rats and B6C3F1 mice (inhalation studies) HERO ID: 632655					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	18. Sampling Adequacy	5/sex/group	High	1	1	1
	19. Blinding of Assessors	Evaluated endpoints did not require blinding	Not Rated	NA	NA	NA
	20. Negative Control Response	Control responses reported.	High	1	1	1
Confounding / Variable Control	21. Confounding Variables in Test Design and Procedures	There were no reported differences among the study groups in initial body weight. Food and water intake were not reported. Respiratory rate not reported, but dyspnea was reported at highest exposure in both rats and mice.	Low	3	2	6
	22. Health Outcomes Unrelated to Exposure	data on attrition and/or health outcomes unrelated to exposure for each study group were not reported because only substantial differences among groups were noted	Medium	2	1	2
Data Presentation and Analysis	23. Statistical Methods	Detailed statistical tests reported for survival and tumor analysis of 2-yr study, unclear if any statistics were conducted on shorter-duration studies. Histo data not reported.	Unacceptable	4	1	4
	24. Reporting of Data	Histological results not reported; no statement regarding lack of exposure-related findings.	Unacceptable	4	2	8
High: >=1 and <1.7 Medium: >=1.7 and <2.3 Low: >=2.3 and <=3		**Sum of scores:**			**26**	**49**
		Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factors:		**1.8846**	**Overall Score: Nearest *:**	**1.8[1]**

PEER REVIEW DRAFT. DO NOT CITE OR QUOTE

Study reference:	Ntp, (1986). Toxicology and carcinogenesis studies of tetrachloroethylene (perchloroethylene) (CAS no. 127-18-4) in F344/N rats and B6C3F1 mice (inhalation studies) HERO ID: 632655					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
		Overall Quality Level:		**Unacceptable[1]**		
Study Quality Comment:	**Footnote 1: Consistent with our *Application of A Systematic Review in TSCA Risk Evaluations* document, if a metric for a data source receives a score of Unacceptable (score = 4), EPA will determine the study to be unacceptable. In this case, two of the metrics were rated as unacceptable. As such, the study is considered unacceptable and the score is presented solely to increase transparency.**					

2.9. Animal toxicity evaluation results of Seo et al 2012

Study reference:	**Seo, M.,Kobayashi, R. yo,Okamura, T.,Ikeda, K.,Satoh, M.,Inagaki, N.,Nagai, H.,Nagase, H. (2012). Enhancing effects of trichloroethylene and tetrachloroethylene on type I allergic responses in mice Journal of Toxicological Sciences, 37(2), 439-445** **HERO ID: 2128339**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
Test Substance	1. Test Substance Identity	See footnote at end of page.[1]	High	1	2	2
	2. Test Substance Source	See footnote at end of page.[1]	High	1	1	1
	3. Test Substance Purity	See footnote at end of page.[1]	High	1	1	1
Test Design	4. Negative and Vehicle Controls	Concurrent control did not receive vehicle (DMSO) but author states that this concentration of DMSO did not have effects in preliminary experiments.	Medium	2	2	4
	5. Positive Controls	Positive control is not required.	Not Rated	NA	NA	NA
	6. Randomized Allocation	The study did not report how animals were allocated to study groups. Some experiments were done on cells isolated from animals.	Low	3	1	3
Exposure Characterization	7. Preparation and Storage of Test Substance	The storage of perchloroethylene was not stated, but it is not known to be unstable (WI).	Medium	2	1	2
	8. Consistency of Exposure Administration	The drinking water dosing was changed every other day, not every day. The concentration was below the solubility, but the test compound is slightly volatile.	Medium	2	1	2

[1] Metrics that received a "High" rating met the criteria as discussed in the Applications of Systematic Review for TSCA Risk Evaluation.

PEER REVIEW DRAFT. DO NOT CITE OR QUOTE

Study reference:	**Seo, M.,Kobayashi, R. yo,Okamura, T.,Ikeda, K.,Satoh, M.,Inagaki, N.,Nagai, H.,Nagase, H. (2012). Enhancing effects of trichloroethylene and tetrachloroethylene on type I allergic responses in mice Journal of Toxicological Sciences, 37(2), 439-445** **HERO ID: 2128339**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	9. Reporting of Doses/Concentrations	Nominal drinking water concentrations are provided and doses are presented as mean ug ingested per day by each group of 8 mice (not adjusted for body weight). Also, it is unclear if water intake varied among treatment groups. The IP dose injections and the in vitro doses were defined.	Medium	2	2	4
	10. Exposure Frequency and Duration	The dosing was in drinking water ad libitum, but the duration was defined.	High	1	1	1
	11. Number of Exposure Groups and Dose Spacing	Dose spacing was 10-100 fold.	High	1	1	1
	12. Exposure Route and Method	Test substance if volatile, but drinking water was changed every other day.	Medium	2	1	2
Test Organism	13. Test Animal Characteristics	Mouse strains were identified. Body weight and health status were not reported.	Medium	2	2	4
	14. Adequacy and Consistency of Animal Husbandry Conditions	Minimal details on husbandry conditions were provided. The dietary mix was not identified.	Low	3	1	3
	15. Number per Group	The number of animals per study group was not reported.	Unacceptable	4	1	4

Study reference:	**Seo, M.,Kobayashi, R. yo,Okamura, T.,Ikeda, K.,Satoh, M.,Inagaki, N.,Nagai, H.,Nagase, H. (2012). Enhancing effects of trichloroethylene and tetrachloroethylene on type I allergic responses in mice Journal of Toxicological Sciences, 37(2), 439-445** **HERO ID: 2128339**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
Outcome Assessment	16. Outcome Assessment Methodology	See footnote at end of page.[1]	High	1	2	2
	17. Consistency of Outcome Assessment	The outcomes were consistent across experiments.	High	1	1	1
	18. Sampling Adequacy	It is not clear what the experimental unit was (i.e., whether the outcome was measured separately for each individual animal).	Low	3	1	3
	19. Blinding of Assessors	Outcome was not subjective. The measurements used analytical devices.	Not Rated	NA	NA	NA
	20. Negative Control Response	See footnote at end of page.[1]	High	1	1	1
Confounding / Variable Control	21. Confounding Variables in Test Design and Procedures	Water intake was not reported separately for each dose group, so it is unclear whether there were differences in water intake among doses. The in vitro study and the IP study designs were better controlled.	Low	3	2	6
	22. Health Outcomes Unrelated to Exposure	Heath outcomes unrelated to exposure were not reported; however, no differences in health among study groups were reported.	Medium	2	1	2
Data Presentation and Analysis	23. Statistical Methods	Limited details regarding statistics were provided. Graphs were plotted for the results, but the numerical raw data was not provided.	Medium	2	1	2

[1] Metrics that received a "High" rating met the criteria as discussed in the Applications of Systematic Review for TSCA Risk Evaluation.

PEER REVIEW DRAFT. DO NOT CITE OR QUOTE

Study reference:	**Seo, M.,Kobayashi, R. yo,Okamura, T.,Ikeda, K.,Satoh, M.,Inagaki, N.,Nagai, H.,Nagase, H. (2012). Enhancing effects of trichloroethylene and tetrachloroethylene on type I allergic responses in mice Journal of Toxicological Sciences, 37(2), 439-445** **HERO ID: 2128339**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	24. Reporting of Data	See footnote at end of page.[1]	High	1	2	2
High: >=1 and <1.7 Medium: >=1.7 and <2.3 Low: >=2.3 and <=3		**Sum of scores:**			**28**	**53**
		Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factors:		**1.8929**	**Overall Score: Nearest *:**	**1.9[1]**
		Overall Quality Level:		**Unacceptable[1]**		
Study Quality Comment:	**Footnote 1: Consistent with our *Application of A Systematic Review in TSCA Risk Evaluations* document, if a metric for a data source receives a score of Unacceptable (score = 4), EPA will determine the study to be unacceptable. In this case, one of the metrics were rated as unacceptable. As such, the study is considered unacceptable and the score is presented solely to increase transparency.**					

PEER REVIEW DRAFT. DO NOT CITE OR QUOTE

3. Subchronic Toxicity Studies

3.1. Animal toxicity evaluation results of Buben et al 1985 for a 6 week gavage study of perc in mice study on hepatic outcomes

Study reference:	**Buben, J. A.,O'Flaherty, E. J. (1985). Delineation of the role of metabolism in the hepatotoxicity of trichloroethylene and perchloroethylene: A dose-effect study Toxicology and Applied Pharmacology, 78(1), 105-122** **HERO ID: 65239**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
Test Substance	1. Test Substance Identity	Test substance identified by unambiguous name	High	1	2	2
	2. Test Substance Source	Test substance obtained commercially	High	1	1	1
	3. Test Substance Purity	Perc reported to have purity >99%.	High	1	1	1
Test Design	4. Negative and Vehicle Controls	Sham-treated controls received corn oil vehicle.	High	1	2	2
	5. Positive Controls		Not Rated	NA	NA	NA
	6. Randomized Allocation	Study reports random allocation to study groups.	High	1	1	1
Exposure Characterization	7. Preparation and Storage of Test Substance	Preparation method was reported and appropriate (prepared fresh 2-3x/wk); stability of test material in vehicle was either not evaluated or not reported,. but not expected to be of concern given the frequency of preparation.	Medium	2	1	2
	8. Consistency of Exposure Administration	Details of administration (e.g., time of day) were not reported; no dosing errors were noted.	Medium	2	1	2
	9. Reporting of Doses/Concentrations	Dose volumes were adjusted based on individual animal body weights obtained 3x/week.	High	1	2	2

PEER REVIEW DRAFT. DO NOT CITE OR QUOTE

Study reference:	**Buben, J. A.,O'Flaherty, E. J. (1985). Delineation of the role of metabolism in the hepatotoxicity of trichloroethylene and perchloroethylene: A dose-effect study Toxicology and Applied Pharmacology, 78(1), 105-122** **HERO ID: 65239**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	10. Exposure Frequency and Duration	Animals were dosed 5 days/week for 6 weeks. The duration was sufficient to induce the effects of interest (hepatotoxicity).	High	1	1	1
	11. Number of Exposure Groups and Dose Spacing	Study used 7 exposure groups plus control; overall range of doses was 100-fold; high dose was adequate to identify effect. The lowest Perc dose of 20 mg/kg may be a NOAEL, but histopathology was only evaluated at 200mg/kg and 1000 mg/kg (effects seen at both) so it is difficult to determine the NOAEL.	High	1	1	1
	12. Exposure Route and Method	Exposure route and method were appropriate for the study type and test material.	High	1	1	1
Test Organism	13. Test Animal Characteristics	Test animal source, strain, sex, and age were reported. The ages of mice at study initiation varied between 3 and 5 months; however, as mice are adult at these ages, the age range is not expected to influence hepatotoxicity.	Medium	2	2	4
	14. Adequacy and Consistency of Animal Husbandry Conditions	Temperature and light-dark cycle, and housing conditions were reported and appropriate, but humidity was not reported.	Medium	2	1	2

PEER REVIEW DRAFT. DO NOT CITE OR QUOTE

Study reference:	**Buben, J. A.,O'Flaherty, E. J. (1985). Delineation of the role of metabolism in the hepatotoxicity of trichloroethylene and perchloroethylene: A dose-effect study Toxicology and Applied Pharmacology, 78(1), 105-122** **HERO ID: 65239**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	15. Number per Group	Test animal source, strain, sex, and age were reported. The ages of mice at study initiation varied between 3 and 5 months; however, as mice are adult at these ages, the age range is not expected to influence hepatotoxicity. A two-month spread in ages is not a concern, especially since animals were randomly allocated.	High	1	1	1
Outcome Assessment	16. Outcome Assessment Methodology	Study focused on hepatotoxicity based on organ weight, liver G6P activity and triglycerides, serum ALT, and histopathology.	High	1	2	2
	17. Consistency of Outcome Assessment	Study did not report any inconsistencies in execution of outcome assessments. Histopathy was only reported in two dose groups.	Medium	2	1	2
	18. Sampling Adequacy	Incomplete information was provided on sampling adequacy across endpoints. HIstopathology examinations were performed on controls, high dose animals, and on animals of one intermediate dose group.	Medium	2	1	2
	19. Blinding of Assessors		Not Rated	NA	NA	NA
	20. Negative Control Response	Responses of negative control group were adequate.	High	1	1	1

PEER REVIEW DRAFT. DO NOT CITE OR QUOTE

Study reference:	**Buben, J. A.,O'Flaherty, E. J. (1985). Delineation of the role of metabolism in the hepatotoxicity of trichloroethylene and perchloroethylene: A dose-effect study Toxicology and Applied Pharmacology, 78(1), 105-122** **HERO ID: 65239**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
Confounding / Variable Control	21. Confounding Variables in Test Design and Procedures	Study did not report any potential differences among study groups that might influence the assessment.	High	1	2	2
	22. Health Outcomes Unrelated to Exposure	There were no reported differences among groups unrelated to exposure	High	1	1	1
Data Presentation and Analysis	23. Statistical Methods	Statistical methods were reported and appeared to be appropriate.	High	1	1	1
	24. Reporting of Data	Histopathology results were reported semiquantitatively (incidences not reported); no statistical analysis of incidences was performed, and the available data are not adequate to perform independent statistical analysis. Data was quantitatively reported for all outcomes other than histopathy at all dose groups.	Medium	2	2	4
High: >=1 and <1.7 Medium: >=1.7 and <2.3 Low: >=2.3 and <=3		**Sum of scores:**			**29**	**38**
		Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factors:		**NA**	**Overall Score: Nearest *:**	**NA**
		Overall Quality Level:		**Medium**		
Study Quality Comment:	**The reviewer downgraded this study's overall quality rating. They noted: HIstopathology examinations were performed in control, 200 and 1000 mg/kg dose groups, and lesions were seen in both exposed groups. Although there were lower dose groups in which no changes in other parameters were observed, it would be difficult to identify a NOAEL in the absence of confirmatory histopathology results for the lower dose groups. Note: The original calculated score for this study was 1.4. This value is not presented above because the final rating was changed based on professional judgement.**					

3.2. Animal toxicity evaluation results of E. I. Dupont De Nemours 1941 for a 10 week inhalation study in dogs on neurological/behavior, cardiovascular, hematological and immune outcomes

Study reference:	**E. I. Dupont Denemours,Co, Inc (1941). Initial submission: the toxicity of perchloroethylene with cover letter dated 10/15/92** **HERO ID: 4214432**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
Test Substance	1. Test Substance Identity	Test substance identified by unambiguous name and molecular formula, but without certification or validation of identity.	Medium	2	2	4
	2. Test Substance Source	Test substance source was not reported, and given the age of the study, it was probably not obtained from a manufacturer.	Low	3	1	3
	3. Test Substance Purity	Test substance purity/grade not reported.	Low	3	1	3
Test Design	4. Negative and Vehicle Controls	A concurrent negative control group was not included; animals served as their own controls.	Unacceptable	4	2	8
	5. Positive Controls	positive control not typical for this study type.	Not Rated	NA	NA	NA
	6. Randomized Allocation	Animals were not allocated to groups; rather, health outcomes assessed before and after exposure in all animals	Unacceptable	4	1	4
Exposure Characterization	7. Preparation and Storage of Test Substance	No information on test substance preparation or storage, or methods for atmosphere generation, was presented.	Unacceptable	4	1	4
	8. Consistency of Exposure Administration	There were no details provided to enable assessment of consistency, except that exposure concentrations were increased over the course of the exposure period.	Unacceptable	4	1	4

Study reference:	**E. I. Dupont Denemours,Co, Inc (1941). Initial submission: the toxicity of perchloroethylene with cover letter dated 10/15/92** **HERO ID: 4214432**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	9. Reporting of Doses/Concentrations	Exposure concentrations were reported inconsistently within the study; the methods section reports concentrations that differ from those in the results sections.. Study reported exposure concentrations without any indication of how these were estimated or measured. There is no indication that exposure concentrations were verified analytically.	Unacceptable	4	2	8
	10. Exposure Frequency and Duration	Dogs were exposed 6 hr/d, 5 d/wk for 10 weeks and Guinea Pigs were exposed for two weeks (No exposure detail reported)	Medium	2	1	2
	11. Number of Exposure Groups and Dose Spacing	Only one group of animals was included; these animals were exposed to increasing concentrations over time, and effects compared with pre-exposure conditions.	Unacceptable	4	1	4
	12. Exposure Route and Method	There is no description of the inhalation chamber used	Unacceptable	4	1	4
Test Organism	13. Test Animal Characteristics	Test animal source, strain, and sex were not reported.	Low	3	2	6
	14. Adequacy and Consistency of Animal Husbandry Conditions	No information on animal husbandry was provided.	Low	3	1	3
	15. Number per Group	Four animals were exposed, and served as their own controls.	Low	3	1	3

PEER REVIEW DRAFT. DO NOT CITE OR QUOTE

Study reference:	**E. I. Dupont Denemours,Co, Inc (1941). Initial submission: the toxicity of perchloroethylene with cover letter dated 10/15/92** **HERO ID: 4214432**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
Outcome Assessment	16. Outcome Assessment Methodology	The outcome assessment methodologies were not reported, and the outcomes assessed were not sensitive (oxygen content of blood, electrocardiography, some hematology endpoints, and gross pathology)	Unacceptable	4	2	8
	17. Consistency of Outcome Assessment	Outcome assessments were not adequately reported for meaningful interpretation of results.	Unacceptable	4	1	4
	18. Sampling Adequacy	Information was not adequate to evaluate sampling adequacy, but it appears that all animals were evaluated for all endpoints.	Low	3	1	3
	19. Blinding of Assessors	Most outcomes were not subjective.	Not Rated	NA	NA	NA
	20. Negative Control Response	There was no control group; dogs served as their own controls.	Unacceptable	4	1	4
Confounding / Variable Control	21. Confounding Variables in Test Design and Procedures	No information on potential confounding factors was reported. Initial body weight and food and water intake were not reported.	Low	3	2	6
	22. Health Outcomes Unrelated to Exposure	Data on attrition or health outcomes unrelated to exposure were not reported.	Low	3	1	3
Data Presentation and Analysis	23. Statistical Methods	Statistical analysis was not performed, and reported data were not adequate to enable independent statistical analysis.	Unacceptable	4	1	4

PEER REVIEW DRAFT. DO NOT CITE OR QUOTE

Study reference:	**E. I. Dupont Denemours,Co, Inc (1941). Initial submission: the toxicity of perchloroethylene with cover letter dated 10/15/92** **HERO ID: 4214432**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	24. Reporting of Data	Most data were reported qualitatively and without clear reference to the pre-exposure response.	Unacceptable	4	2	8
High: >=1 and <1.7 **Medium: >=1.7 and <2.3** **Low: >=2.3 and <=3**		**Sum of scores:**			**29**	**100**
		Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factors:		**3.4483**	**Overall Score: Nearest *:**	**3.4[1]**
		Overall Quality Level:		**Unacceptable[1]**		
Study Quality Comment:	**Footnote 1: Consistent with our *Application of A Systematic Review in TSCA Risk Evaluations* document, if a metric for a data source receives a score of Unacceptable (score = 4), EPA will determine the study to be unacceptable. In this case, twelve of the metrics were rated as unacceptable. As such, the study is considered unacceptable and the score is presented solely to increase transparency.**					

3.3. Animal toxicity evaluation results of Natl Institute of Health 1977 for a 6-week oral (rats and mice) study on mortality and metabolic/adult exposure body weight outcomes

Study reference:	Natl Inst Of, Health (1977). Bioassay of tetrachloroethylene for possible carcinogenicity HERO ID: 4214470					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
Test Substance	1. Test Substance Identity	The test substance was identified definitively.	High	1	2	2
	2. Test Substance Source	The source of the test substance was reported, including manufacturer. A lot/batch number was not reported.	Medium	2	1	2
	3. Test Substance Purity	The purity was reported by the manufacturer (at least 99%). The study report also stated that gas-liquid chromatography showed the major component consisting of over 99% of the total peak area, with a minor impurity present, which was not identified.	Medium	2	1	2
Test Design	4. Negative and Vehicle Controls	The study authors reported using an appropriate concurrent control group (vehicle control administered corn oil only).	High	1	2	2
	5. Positive Controls	Positive control is not indicated for the study type.	Not Rated	NA	NA	NA
	6. Randomized Allocation	The study did not report how animals were allocated to study groups.	Low	3	1	3

PEER REVIEW DRAFT. DO NOT CITE OR QUOTE

Study reference:	Natl Inst Of, Health (1977). Bioassay of tetrachloroethylene for possible carcinogenicity HERO ID: 4214470					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
Exposure Characterization	7. Preparation and Storage of Test Substance	The test substance preparation and storage conditions were reported but there were minor limitations in the test substance preparation. The test substance was prepared weekly, sealed, and stored at 34 degrees F, which the study authors noted were considered conditions that would allow test substance to remain stable for 10 days. However, no report of stability in the vehicle (corn oil), or of PERC in the prepared solutions, was reported.	Medium	2	1	2
	8. Consistency of Exposure Administration	Details of exposure administration were not fully reported (volume administered by gavage was not reported). However, reported information indicated that exposures were administered consistently across study groups.	Medium	2	1	2

PEER REVIEW DRAFT. DO NOT CITE OR QUOTE

Study reference:	Natl Inst Of, Health (1977). Bioassay of tetrachloroethylene for possible carcinogenicity HERO ID: 4214470					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	9. Reporting of Doses/Concentrations	Initial administered doses were reported; however, dose levels were raised and/or lowered during the study in both rats and mice based on clinical signs and there is some ambiguity in the actual dose levels after adjustment and the exact days during the study when doses were raised and/or lowered (only reported in weeks). For example, for rats, the study authors stated that the low doses were adjusted accordingly, so that they consistently remained one-half of the high dose but actual adjusted dose levels were not reported.	Medium	2	2	4
	10. Exposure Frequency and Duration	Exposure frequency (5 consecutive d/wk) was reported and acceptable. However, the exposure duration was shorter than studies of similar type (i.e., 2 years for carcinogenicity studies is typical for rodents) and was not justified by the study authors. In this study, animals were dosed for 78 weeks followed by an observation period of 32 weeks in rats and 12 weeks in mice.	Medium	2	1	2

Study reference:	Natl Inst Of, Health (1977). Bioassay of tetrachloroethylene for possible carcinogenicity HERO ID: 4214470					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	11. Number of Exposure Groups and Dose Spacing	The number of exposure groups and spacing were considered adequate to address the purpose of the study. However, the highest doses produced a high rate of early mortality in both rats and mice, which the study authors noted may indicate that the optimum dose was exceeded in both species.	Medium	2	1	2
	12. Exposure Route and Method	The route and method of exposure were reported and were suited to the test substance.	High	1	1	1
Test Organism	13. Test Animal Characteristics	The test animal source, species, strain, sex, age, and starting body weight were reported. The test animal (species, strain, sex, life-stage, source) was appropriate for the evaluation of the specific outcome(s) of interest.	Medium	2	2	4
	14. Adequacy and Consistency of Animal Husbandry Conditions	Due to starting the vehicle control rats and mice earlier than animals of other groups, and housing of vehicle control rats and a different room than other rats, there may have been some differences in husbandry / exposure conditions.	Low	3	1	3
	15. Number per Group	The number per group was acceptable (5/sex/group) for the 6-week, range-finding study	High	1	1	1

Study reference:	Natl Inst Of, Health (1977). Bioassay of tetrachloroethylene for possible carcinogenicity HERO ID: 4214470					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
Outcome Assessment	16. Outcome Assessment Methodology	The outcome assessment methodology was only briefly reported. For example, it was not reported how often body weights were determined during the 6-week dosing period and 2-week observation period. Additionally, the only endpoints evaluated were grossly observable endpoints, including clinical signs and mortality.	Low	3	2	6
	17. Consistency of Outcome Assessment	Details of the outcome assessment protocol were not reported and these deficiencies are likely to have a substantial impact on results.	Low	3	1	3
	18. Sampling Adequacy	Details regarding sampling of outcomes were not reported and this deficiency is likely to have a substantial impact on results.	Low	3	1	3
	19. Blinding of Assessors	No subjective outcomes were reported.	Not Rated	NA	NA	NA
	20. Negative Control Response	The biological responses of the negative control group were adequate.	High	1	1	1
Confounding / Variable Control	21. Confounding Variables in Test Design and Procedures	No confounding variables in test design or procedures were reported.	High	1	2	2
	22. Health Outcomes Unrelated to Exposure	Data on attrition and/or health outcomes unrelated to exposure for each study group were not reported because only substantial differences among groups were noted.	Medium	2	1	2

PEER REVIEW DRAFT. DO NOT CITE OR QUOTE

Study reference:	Natl Inst Of, Health (1977). Bioassay of tetrachloroethylene for possible carcinogenicity HERO ID: 4214470					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
Data Presentation and Analysis	23. Statistical Methods	The statistical methods were clearly described by the study authors and were appropriate for datasets.	High	1	1	1
	24. Reporting of Data	Data were reported incompletely. Body weights were reported in figures and changes in body weight gain were reported in percentages in the text.	Low	3	2	6
High: >=1 and <1.7 Medium: >=1.7 and <2.3 Low: >=2.3 and <=3		**Sum of scores:**			**29**	**56**
		Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factors:		**NA**	**Overall Score: Nearest *:**	**NA**
		Overall Quality Level:		**Low**		
Study Quality Comment:	**The reviewer downgraded this study's overall quality rating based on limited reporting of outcome assessment methodology and protocol and limited reporting of data. Note: The original calculated score for this study was 1.9. This value is not presented above because the final rating was changed based on professional judgement.**					

PEER REVIEW DRAFT. DO NOT CITE OR QUOTE

4. Chronic Toxicity Studies

4.1. Animal toxicity evaluation results of Dow et al 1978 for a 12 month inhalation study in rats, with lifetime observation on renal, hepatic, nutrition and metabolic/adult exposure body weight, hematological and immune outcomes

Study reference:	Dow Chem, Co (1978). Results of a long-term inhalation toxicity study on rats of a perchloroethylene (tetrachloroethylene) formulation #journal#, #volume#(#issue#), #Pages# HERO ID: 4214237					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
Test Substance	1. Test Substance Identity	Test substance identified by name and CASRN	High	1	2	2
	2. Test Substance Source	Test substance was identified by lot number and verified analytically, with results presented.	High	1	1	1
	3. Test Substance Purity	Purity was not reported explicitly, but based on GC results and reported percentages of contaminants, test substance was >99% (vol%) perc (impurities comprised 63 ppm vol %)	Medium	2	1	2
Test Design	4. Negative and Vehicle Controls	Negative controls were not sham-exposed, but rather held in the room where exposed animals were housed when not in exposure chambers.	Low	3	2	6
	5. Positive Controls	Positive controls not typical for this study type	Not Rated	NA	NA	NA
	6. Randomized Allocation	Study reported random allocation	High	1	1	1
Exposure Characterization	7. Preparation and Storage of Test Substance	Method of vapor generation was described in detail and appropriate (dynamic airflow); however, there was no diagram of the chamber, so it is unclear whether vertical mixing was adequate (Perc vapor is much heavier than air) and/or whether analytical measurements were in the animals' breathing zones.	Medium	2	1	2

Study reference:	**Dow Chem, Co (1978). Results of a long-term inhalation toxicity study on rats of a perchloroethylene (tetrachloroethylene) formulation #journal#, #volume#(#issue#), #Pages#** **HERO ID: 4214237**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	8. Consistency of Exposure Administration	Control animals were not sham-exposed. Authors report that exposures during first 5 months ran at the same time in both exposed groups, but thereafter they ran at different times of day (low dose in morning and high dose in evening) using the same exposure chamber. Finally, the high dose group was accidentally exposed to concentrations of 1500 ppm for 3 days during the first week.	Low	3	1	3
	9. Reporting of Doses/Concentrations	Concentrations were measured using infrared spectrophotometry and analytical results were reported. Mean analytical values were within 10% of nominal. Analytical method was less than ideal, and it is unclear whether the measurements were in the animals' breathing zones. Time to achieve desired exposure concentration in the chambers was not reported,.	Low	3	2	6
	10. Exposure Frequency and Duration	Frequency (6 hr/d, 5 d/wk) and duration (12 mo) of exposure were reported and appropriate for noncancer endpoints.	High	1	1	1

PEER REVIEW DRAFT. DO NOT CITE OR QUOTE

Study reference:	**Dow Chem, Co (1978). Results of a long-term inhalation toxicity study on rats of a perchloroethylene (tetrachloroethylene) formulation #journal#, #volume#(#issue#), #Pages#** **HERO ID: 4214237**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	11. Number of Exposure Groups and Dose Spacing	Two exposure concentrations differing 2-fold were tested; these were selected based on multiples of the maximum permissible excursion concentration from ACGIH. Little to no toxicity was reported, suggesting that the high concentration may not have been high enough.	Low	3	1	3
	12. Exposure Route and Method	Route and method were reported and appropriate (dynamic whole body chamber was used for vapor that may condense.)	Medium	2	1	2
Test Organism	13. Test Animal Characteristics	Test animal species, strain, sex, age, source, and body weight were reported; however, authors did not report acclimation or pathogen testing/health status prior to study initiation.	Medium	2	2	4
	14. Adequacy and Consistency of Animal Husbandry Conditions	Animal husbandry conditions (temperature, humidity, light-dark cycle, housing) were not reported.	Low	3	1	3
	15. Number per Group	Exposed groups consisted of 96/sex and controls consisted of 192/sex.	High	1	1	1

PEER REVIEW DRAFT. DO NOT CITE OR QUOTE

Study reference:	**Dow Chem, Co (1978). Results of a long-term inhalation toxicity study on rats of a perchloroethylene (tetrachloroethylene) formulation #journal#, #volume#(#issue#), #Pages#** **HERO ID: 4214237**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
Outcome Assessment	16. Outcome Assessment Methodology	Nearly all evaluations took place 12 to 19 months after the end of exposure. Hematology (with the exception of a small number of animals evaluated earlier), clinical chemistry, and urinalysis evaluations were performed 12 months after exposure ended or at terminal necropsy up to 19 months after the end of exposure. Except for groups of 3 rats/sex/exposure, organ weight and pathology assessments occurred at death/moribund sacrifice or at study termination 19 months after exposure ended. Hematology and clinical chemistry methods were not reported.	Unacceptable	4	2	8
	17. Consistency of Outcome Assessment	Outcome assessment was performed consistently across groups. Apart from the unexplained loss of a few rats per group, which was evaluated under health outcomes unrelated to exposure, no inconsistencies in the execution were noted.	Medium	2	1	2

PEER REVIEW DRAFT. DO NOT CITE OR QUOTE

Study reference:	**Dow Chem, Co (1978). Results of a long-term inhalation toxicity study on rats of a perchloroethylene (tetrachloroethylene) formulation #journal#, #volume#(#issue#), #Pages#** **HERO ID: 4214237**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	18. Sampling Adequacy	Sampling of endpoints at the end of exposure was not adequate; only 3/sex/group were sacrificed for organ weights and histopathology at the end of the 12 month exposure. This number is too small to discern subtle differences.	Unacceptable	4	1	4
	19. Blinding of Assessors	Blinding was not reported for subjective outcomes consisting of cageside observations. Other endpoints were not subjective and/or blinding is not typical.	Not Rated	NA	NA	NA
	20. Negative Control Response	Control responses were reported and appeared to be adequate and without excessive variability.	High	1	1	1
Confounding / Variable Control	21. Confounding Variables in Test Design and Procedures	No information on respiratory rates or indications of reflex bradypnea was reported. Food and water intake during the study were not reported.	Low	3	2	6

Study reference:	**Dow Chem, Co (1978). Results of a long-term inhalation toxicity study on rats of a perchloroethylene (tetrachloroethylene) formulation #journal#, #volume#(#issue#), #Pages#** **HERO ID: 4214237**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	22. Health Outcomes Unrelated to Exposure	Study authors reported unexplained discrepancies between initial animal numbers and final animal numbers (instead of 96/sex/exposure group and 192/sex controls, 91 to 94/sex/exposure group and 189/sex controls were accounted for). However, the remaining numbers were sufficient to observe an effect and the attrition appeared to be essentially consistent across groups so this discrepancy was not considered unacceptable.	Low	3	1	3
Data Presentation and Analysis	23. Statistical Methods	Statistical analyses were performed and described, and appropriate to the endpoints.	High	1	1	1
	24. Reporting of Data	All data were reported with measures of variability and numbers evaluated.	High	1	2	2
High: >=1 and <1.7 Medium: >=1.7 and <2.3 Low: >=2.3 and <=3		**Sum of scores:**			**29**	**70**
		Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factors:		**2.4138**	**Overall Score: Nearest *:**	**2.4[1]**
		Overall Quality Level:		**Unacceptable[1]**		
Study Quality Comment:	**Footnote 1: Consistent with our *Application of A Systematic Review in TSCA Risk Evaluations* document, if a metric for a data source receives a score of Unacceptable (score = 4), EPA will determine the study to be unacceptable. In this case, two of the metrics were rated as unacceptable. As such, the study is considered unacceptable and the score is presented solely to increase transparency.**					

4.2. Animal toxicity evaluation results of Halogenated Solvents, Indust for a multigen inhalation study in rats on reproductive, renal, hepatic, growth (early life) and development, neurological/behavior, nutrition and metabolic/adult exposure body weight outcomes

Study reference:	**Halogenated Solvents, Indus (1995). Perchloroethylene: multigeneration inhalation study in the rat, with cover letter dated 07/06/95 #journal#, #volume#(#issue#), #Pages#** **HERO ID: 4214380**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
Test Substance	1. Test Substance Identity	Test substance identified by unambiguous name	High	1	2	2
	2. Test Substance Source	Test substance source and lot number was identified and certificate of analysis provided.	High	1	1	1
	3. Test Substance Purity	Test substance purity reported to be 99.9% (w/w).	High	1	1	1
Test Design	4. Negative and Vehicle Controls	Study does not explicitly state that controls were sham-treated, but descriptions of exposure imply sham-treatment: "the females in the control, 300, and 1000 ppm groups were exposed"	Medium	2	2	4
	5. Positive Controls	Positive controls not typical for this study type	Not Rated	NA	NA	NA
	6. Randomized Allocation	Study reports allocation method, which was semi random while preventing sibling matings.	Medium	2	1	2
Exposure Characterization	7. Preparation and Storage of Test Substance	Preparation and storage conditions were reported, and stability was satisfactory. Methods for test atmosphere generation were reported and appropriate. Air changes per hour were appropriate (>10 based on chamber volume of 3400 L and air flow rate of 700 L/min).	High	1	1	1

PEER REVIEW DRAFT. DO NOT CITE OR QUOTE

Study reference:	**Halogenated Solvents, Indus (1995). Perchloroethylene: multigeneration inhalation study in the rat, with cover letter dated 07/06/95 #journal#, #volume#(#issue#), #Pages#** **HERO ID: 4214380**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	8. Consistency of Exposure Administration	Animals were exposed in cages arranged vertically in the exposure chamber, which could allow for some inconsistencies in breathing zone concentrations if vertical mixing was inadequate (Perc is much more dense than air). In addition, the exposure frequency varied between 5 and 7 days per week at different phases of the study, but the frequencies were the same across different exposure groups.	Medium	2	1	2
	9. Reporting of Doses/Concentrations	Analytical concentrations were reported and mean values were within 10% of nominal at all phases..	High	1	2	2
	10. Exposure Frequency and Duration	Exposure frequency and duration were typical for this study type	High	1	1	1
	11. Number of Exposure Groups and Dose Spacing	Three nonzero exposure groups were used, with half log spacing. Exposure range was sufficient to enable identification of effect levels.	High	1	1	1
	12. Exposure Route and Method	Inhalation study, adequately described	High	1	1	1
Test Organism	13. Test Animal Characteristics	Species, strain, sex, health status, age, body weight, and source were reported and appropriate.	High	1	2	2

PEER REVIEW DRAFT. DO NOT CITE OR QUOTE

Study reference:	**Halogenated Solvents, Indus (1995). Perchloroethylene: multigeneration inhalation study in the rat, with cover letter dated 07/06/95 #journal#, #volume#(#issue#), #Pages#** **HERO ID: 4214380**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	14. Adequacy and Consistency of Animal Husbandry Conditions	Authors noted that faulty light switches altered the light cycle for F0 parents and this alteration may have been responsible for reduced pre-coital interval in exposed groups.	Low	3	1	3
	15. Number per Group	All groups consisted of 24/sex. EPA guidelines call for group size yielding 20 pregnant females so group size was appropriate.	High	1	1	1
Outcome Assessment	16. Outcome Assessment Methodology	Outcome assessment methodology was reported. Neither sperm parameters nor estrus cyclicity was evaluated; water intake was not measured. In addition, only testes, kidneys, and liver weights were obtained (EPA guidelines recommend several other organ weights), and histopathology did not include organs typically assessed in this study type (e.g., pituitary and adrenal glands). Ages at vaginal opening/preputial separation were not evaluated in F1 offspring.	Medium	2	2	4

Study reference:	**Halogenated Solvents, Indus (1995). Perchloroethylene: multigeneration inhalation study in the rat, with cover letter dated 07/06/95 #journal#, #volume#(#issue#), #Pages#** **HERO ID: 4214380**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	17. Consistency of Outcome Assessment	Histopathology examinations were not consistent across animals. Histopathology examinations were initially limited to liver and kidney of control and high dose animals, and reproductive organs of suspected infertile animals. Additional groups were evaluated for liver and kidney histopathology but the assessment was not consistent across groups. HIstologic examination of testes was extended to fertile F1 males, necessitating re-examination of infertile males for consistency.	Medium	2	1	2
	18. Sampling Adequacy	Sampling was reported and appropriate; endpoints evaluated in all exposed animals.	High	1	1	1
	19. Blinding of Assessors	Study did not report blinding for clinical observations, but the main outcomes assessed were not subjective.	Not Rated	NA	NA	NA
	20. Negative Control Response	Control responses were reported and appeared to be appropriate.	High	1	1	1
Confounding / Variable Control	21. Confounding Variables in Test Design and Procedures	No confounding factors apart from the lighting malfunction in the first generation were noted. Respiratory rate was not reported.	Medium	2	2	4

PEER REVIEW DRAFT. DO NOT CITE OR QUOTE

Study reference:	**Halogenated Solvents, Indus (1995). Perchloroethylene: multigeneration inhalation study in the rat, with cover letter dated 07/06/95 #journal#, #volume#(#issue#), #Pages#** **HERO ID: 4214380**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	22. Health Outcomes Unrelated to Exposure	Authors noted that there was no evidence of disease or infection that might have affected outcomes.	High	1	1	1
Data Presentation and Analysis	23. Statistical Methods	Statistical analysis was performed, described, and appropriate to the outcomes.	High	1	1	1
	24. Reporting of Data	All data were presented graphically or in tabular form, with measures of variability.	High	1	2	2
High: >=1 and <1.7 Medium: >=1.7 and <2.3 Low: >=2.3 and <=3		**Sum of scores:**			**29**	**40**
		Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factors:		**NA**	**Overall Score: Nearest *:**	**NA**
		Overall Quality Level:		**Medium**		
Study Quality Comment:	**The reviewer downgraded this study's overall quality rating. They noted: Study was generally well conducted but evaluations were limited and performed inconsistently Note: The original calculated score for this study was 1.3. This value is not presented above because the final rating was changed based on professional judgement.**					

4.3. Animal toxicity evaluation results of NTP 1986 for 13-week inhalation studies in rats and mice on reproductive, hematological and immune, neurological/behavior, renal, hepatic, cardiovascular, endocrine, gastrointestinal, mortality, nutrition and metabolic/adult exposure body weight, respiratory, skin and connective tissue, and thyroid outcomes

Study reference:	**Ntp, (1986). Toxicology and carcinogenesis studies of tetrachloroethylene (perchloroethylene) (CAS no. 127-18-4) in F344/N rats and B6C3F1 mice (inhalation studies)** **HERO ID: 632655**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
Test Substance	1. Test Substance Identity	high-purity tetrachloroethylene, Dowper stabilized	High	1	2	2
	2. Test Substance Source	Dow Chemical, lot TA03116F-01. Purity and identity analyses conducted.	High	1	1	1
	3. Test Substance Purity	Confirmed analytically - approximately 99.9%	High	1	1	1
Test Design	4. Negative and Vehicle Controls	Chamber controls were used.	High	1	2	2
	5. Positive Controls	Not needed for study type.	Not Rated	NA	NA	NA
	6. Randomized Allocation	computer generated tables of random numbers	High	1	1	1
Exposure Characterization	7. Preparation and Storage of Test Substance	Tetrachloroethylene was found to be stable for 2 weeks at 60" C (Appendix H). Tetrachloroethylene was stored at 0" C Tetrachloroethylene was vaporized at 100"-110" C, diluted with air, and. introduced into the chambers. Detailed descriptions in Table 2 and in Appendix I.	High	1	1	1
	8. Consistency of Exposure Administration	Concentrations in the exposure chambers were monitored 8-12 times per exposure period by a Hewlett-Packard 5840A Gas Chromatograph. No deviations from protocol noted.	High	1	1	1

PEER REVIEW DRAFT. DO NOT CITE OR QUOTE

Study reference:	Ntp, (1986). Toxicology and carcinogenesis studies of tetrachloroethylene (perchloroethylene) (CAS no. 127-18-4) in F344/N rats and B6C3F1 mice (inhalation studies) HERO ID: 632655					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	9. Reporting of Doses/Concentrations	Only target concentrations reported for non-chronic studies., but actual exposures expected to be close to target based on 2-yr analytical values.	Medium	2	2	4
	10. Exposure Frequency and Duration	13-wk, 6 hr/d, 5 d/wk.	High	1	1	1
	11. Number of Exposure Groups and Dose Spacing	5 dose groups plus control	High	1	1	1
	12. Exposure Route and Method	Inhalation, dynamic whole-body chamber. Flow rate not reported	Low	3	1	3
Test Organism	13. Test Animal Characteristics	F344/N rats and B6C3F1 mice, Charles River Breeding. 7-9 wks at study initiation. Initial body weights reported in Tables 8, and 19.	High	1	2	2
	14. Adequacy and Consistency of Animal Husbandry Conditions	Details of husbandry in Table 5	High	1	1	1
	15. Number per Group	10/sex/group	High	1	1	1
Outcome Assessment	16. Outcome Assessment Methodology	Mortality, clinical signs, body weight, comprehensive histopathology	High	1	2	2
	17. Consistency of Outcome Assessment	The majority of organs/tissues were only evaluated in control and high-dose groups. Organs with exposure-related findings were evaluated in lower-dose groups as needed.	High	1	1	1
	18. Sampling Adequacy	10/sex/group	High	1	1	1

Study reference:	Ntp, (1986). Toxicology and carcinogenesis studies of tetrachloroethylene (perchloroethylene) (CAS no. 127-18-4) in F344/N rats and B6C3F1 mice (inhalation studies) HERO ID: 632655					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	19. Blinding of Assessors	Evaluated endpoints did not require blinding	Not Rated	NA	NA	NA
	20. Negative Control Response	Control responses reported.	High	1	1	1
Confounding / Variable Control	21. Confounding Variables in Test Design and Procedures	There were no reported differences among the study groups in initial body weight. Food and water intake were not reported. Respiratory rate was not specifically mentioned, but no exposure-related clinical signs were reported. While there is no evidence of bradypnea. Animal temperature should be measured to rule out bradypnea.	Medium	2	2	4
	22. Health Outcomes Unrelated to Exposure	data on attrition and/or health outcomes unrelated to exposure for each study group were not reported because only substantial differences among groups were noted	Medium	2	1	2
Data Presentation and Analysis	23. Statistical Methods	Detailed statistical tests reported for survival and tumor analysis of 2-yr study, unclear if any statistics were conducted on shorter-duration studies.. Data for mortality, terminal BW, liver and lung histo findings (rat) and liver and kidney findings (mouse) were adequately reported for independent analysis.	Medium	2	1	2

PEER REVIEW DRAFT. DO NOT CITE OR QUOTE

Study reference:	**Ntp, (1986). Toxicology and carcinogenesis studies of tetrachloroethylene (perchloroethylene) (CAS no. 127-18-4) in F344/N rats and B6C3F1 mice (inhalation studies)** **HERO ID: 632655**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	24. Reporting of Data	Quantitative mortality, body weight, and exposure-related nonneoplastic findings (lung and liver in rats, liver and kidney in mice). Histological results from other organs not reported; assumed to be no exposure-related findings.. Exposure-related clinical signs reported qualitatively in mice.	Low	3	2	6
High: >=1 and <1.7 **Medium: >=1.7 and <2.3** **Low: >=2.3 and <=3**		**Sum of scores:**			**29**	**41**
		Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factors:		**1.4138**	**Overall Score: Nearest *:**	**1.4**
		Overall Quality Level:		**High**		

4.4. Animal toxicity evaluation results of Tinston et al 1994 for a multigeneration inhalation study on reproductive, growth (early life) and development, and renal outcomes

Study reference:	Tinston, D. J. (1994). Perchloroethylene: A multigeneration inhalation study in the rat HERO ID: 631041					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
Test Substance	1. Test Substance Identity	Idenitified by chemical name.	High	1	2	2
	2. Test Substance Source	Manufacturer and lot no. were given.	High	1	1	1
	3. Test Substance Purity	99.9% pure	High	1	1	1
Test Design	4. Negative and Vehicle Controls	filtered air	High	1	2	2
	5. Positive Controls	Positive controls are not used for multigeneration studies.	Not Rated	NA	NA	NA
	6. Randomized Allocation	The F0 parents were distributed amongst the four experimental groups after ensuring that any litters containing unhealthy individuals and litters at the extreme of the weight range were excluded from the randomization procedure. Allocation from within the litters was also at random. The F1, F1A and F2A litters and normal pups from each litter were randomly selected.	High	1	1	1
Exposure Characterization	7. Preparation and Storage of Test Substance	Preparation and storage were well described; analysis determined that stability was satisfactory.	High	1	1	1
	8. Consistency of Exposure Administration	Same exposure frequency, chamber design and animals per chamber.	High	1	1	1

Study reference:	Tinston, D. J. (1994). Perchloroethylene: A multigeneration inhalation study in the rat HERO ID: 631041					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	9. Reporting of Doses/Concentrations	The authors report that the daily mean analyzed concentrations of Perchloroethylene were close to target.	High	1	2	2
	10. Exposure Frequency and Duration	6h/day 5 day per week, except during mating and gestation (6h/day, 7 days/week)/	High	1	1	1
	11. Number of Exposure Groups and Dose Spacing	3 exposure groups plus a control, not justified by study suthors, but dose response relationships were apparent.	Medium	2	1	2
	12. Exposure Route and Method	Whole body chamber; unclear whether vapor would condense; 12 exchanges/hour were calculated from data provided.	Medium	2	1	2
Test Organism	13. Test Animal Characteristics	Species and source were reported.	High	1	2	2
	14. Adequacy and Consistency of Animal Husbandry Conditions	All husbandry conditions were reported.	High	1	1	1
	15. Number per Group	~25/sex/group	High	1	1	1
Outcome Assessment	16. Outcome Assessment Methodology	The outcome assessment methodology reported.	High	1	2	2
	17. Consistency of Outcome Assessment	See footnote at end of page.[1]	High	1	1	1
	18. Sampling Adequacy	F2C litter inlcuded control and high dose group only.	Medium	2	1	2
	19. Blinding of Assessors	Blinding not reported; however outcomes were objective.	Not Rated	NA	NA	NA

[1] Metrics that received a “High” rating met the criteria as discussed in the Applications of Systematic Review for TSCA Risk Evaluation.

PEER REVIEW DRAFT. DO NOT CITE OR QUOTE

Study reference:	Tinston, D. J. (1994). Perchloroethylene: A multigeneration inhalation study in the rat HERO ID: 631041					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	20. Negative Control Response	Some clinical signs and histopath. lesions in controls.	Medium	2	1	2
Confounding / Variable Control	21. Confounding Variables in Test Design and Procedures	Increased breathing rate was observed at 300 ppm; breathing irregulaties occurred at 1000 ppm;	Low	3	2	6
	22. Health Outcomes Unrelated to Exposure	Problems with the lighting in the early part of the mating period; changes in pre-coital interval resulted from alterations in the photoperiod.	Low	3	1	3
Data Presentation and Analysis	23. Statistical Methods	Statistical methods were clearly described.	High	1	1	1
	24. Reporting of Data	Data tables were provided for all outcomes.	High	1	2	2
High: >=1 and <1.7 Medium: >=1.7 and <2.3 Low: >=2.3 and <=3		**Sum of scores:**			**29**	**39**
		Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factors:		**1.3448**	**Overall Score: Nearest *:**	**1.3**
		Overall Quality Level:		**High**		

PEER REVIEW DRAFT. DO NOT CITE OR QUOTE

5. Cancer Studies

5.1. Animal toxicity evaluation results of Dow et al 1978 for a 12 month inhalation study in rats, with lifetime observation (cancer) on cancer outcomes

Study reference:	**Dow Chem, Co (1978). Results of a long-term inhalation toxicity study on rats of a perchloroethylene (tetrachloroethylene) formulation** **HERO ID: 4214237**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
Test Substance	1. Test Substance Identity	Test substance identified by name and CASRN	High	1	2	2
	2. Test Substance Source	Test substance was identified by lot number and verified analytically, with results presented.	High	1	1	1
	3. Test Substance Purity	Purity was not reported explicitly, but based on GC results and reported percentages of contaminants, test substance was >99% (vol%) perc (impurities comprised 63 ppm vol %)	Medium	2	1	2
Test Design	4. Negative and Vehicle Controls	Negative controls were not sham-exposed, but rather held in the room where exposed animals were housed when not in exposure chambers.	Low	3	2	6
	5. Positive Controls	Positive controls not typical for this study type	Not Rated	NA	NA	NA
	6. Randomized Allocation	Study reported random allocation	High	1	1	1
Exposure Characterization	7. Preparation and Storage of Test Substance	Method of vapor generation was described in detail and appropriate (dynamic airflow); however, there was no diagram of the chamber, so it is unclear whether vertical mixing was adequate (Perc vapor is much heavier than air) and/or whether analytical measurements were in the animals' breathing zones.	Medium	2	1	2

Study reference:	**Dow Chem, Co (1978). Results of a long-term inhalation toxicity study on rats of a perchloroethylene (tetrachloroethylene) formulation** **HERO ID: 4214237**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	8. Consistency of Exposure Administration	Control animals were not sham-exposed. Authors report that exposures during first 5 months ran at the same time in both exposed groups, but thereafter they ran at different times of day (low dose in morning and high dose in evening) using the same exposure chamber. Finally, the high dose group was accidentally exposed to concentrations of 1500 ppm for 3 days during the first week.	Low	3	1	3
	9. Reporting of Doses/Concentrations	Concentrations were measured using infrared spectrophotometry and analytical results were reported. Mean analytical values were within 10% of nominal. Analytical method was less than ideal, and it is unclear whether the measurements were in the animals' breathing zones. Time to achieve desired exposure concentration in the chambers was not reported,.	Low	3	2	6
	10. Exposure Frequency and Duration	Duration (12 mo) of exposure is not considered adequate for cancer endpoints.	Low	3	1	3

PEER REVIEW DRAFT. DO NOT CITE OR QUOTE

Study reference:	Dow Chem, Co (1978). Results of a long-term inhalation toxicity study on rats of a perchloroethylene (tetrachloroethylene) formulation HERO ID: 4214237					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	11. Number of Exposure Groups and Dose Spacing	Two exposure concentrations differing 2-fold were tested; these were selected based on multiples of the maximum permissible excursion concentration from ACGIH. Little to no toxicity was reported, suggesting that the high concentration may not have been high enough.	Low	3	1	3
	12. Exposure Route and Method	Route and method were reported and appropriate (dynamic whole body chamber was used for vapor that may condense.)	Medium	2	1	2
Test Organism	13. Test Animal Characteristics	Test animal species, strain, sex, age, source, and body weight were reported; however, authors did not report acclimation or pathogen testing/health status prior to study initiation.	Medium	2	2	4
	14. Adequacy and Consistency of Animal Husbandry Conditions	Animal husbandry conditions (temperature, humidity, light-dark cycle, housing) were not reported.	Low	3	1	3
	15. Number per Group	Exposed groups consisted of 96/sex and controls consisted of 192/sex.	High	1	1	1

PEER REVIEW DRAFT. DO NOT CITE OR QUOTE

Study reference:	**Dow Chem, Co (1978). Results of a long-term inhalation toxicity study on rats of a perchloroethylene (tetrachloroethylene) formulation** **HERO ID: 4214237**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
Outcome Assessment	16. Outcome Assessment Methodology	Except for groups of 3 rats/sex/exposure, histopathology assessments occurred at death/moribund sacrifice or at study termination 19 months after exposure ended. This very long postexposure observation period may have resulted in tumor regression.	Unacceptable	4	2	8
	17. Consistency of Outcome Assessment	Outcome assessment was performed consistently across groups. Apart from the unexplained loss of a few rats per group, which was evaluated under health outcomes unrelated to exposure, no inconsistencies in the execution were noted.	Medium	2	1	2
	18. Sampling Adequacy	Sampling of endpoints at the end of exposure was not adequate; only 3/sex/group were sacrificed for histopathology at the end of the 12 month exposure. This number is too small to discern differences in tumor incidences.	Unacceptable	4	1	4
	19. Blinding of Assessors	Blinding is not typical for initial histopathology review.	High	1	1	1
	20. Negative Control Response	Control responses were reported and appeared to be adequate and without excessive variability.	High	1	1	1

Study reference:	**Dow Chem, Co (1978). Results of a long-term inhalation toxicity study on rats of a perchloroethylene (tetrachloroethylene) formulation** **HERO ID: 4214237**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
Confounding / Variable Control	21. Confounding Variables in Test Design and Procedures	No information on respiratory rates or indications of reflex bradypnea was reported. Food and water intake during the study were not reported.	Low	3	2	6
	22. Health Outcomes Unrelated to Exposure	Study authors reported unexplained discrepancies between initial animal numbers and final animal numbers (instead of 96/sex/exposure group and 192/sex controls, 91 to 94/sex/exposure group and 189/sex controls were accounted for). However, the remaining numbers were sufficient to observe an effect and the attrition appeared to be essentially consistent across groups so this discrepancy was not considered unacceptable.	Low	3	1	3
Data Presentation and Analysis	23. Statistical Methods	Statistical analyses were performed and described, and appropriate to the endpoints.	High	1	1	1
	24. Reporting of Data	Tumor incidences were reported with numbers of animals evaluated for each organ and timepoint..	High	1	2	2
High: >=1 and <1.7 **Medium: >=1.7 and <2.3** **Low: >=2.3 and <=3**		**Sum of scores:**			**30**	**67**
		Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factors:		**2.2333**	**Overall Score: Nearest *:**	**2.2[1]**

Study reference:	**Dow Chem, Co (1978). Results of a long-term inhalation toxicity study on rats of a perchloroethylene (tetrachloroethylene) formulation** **HERO ID: 4214237**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
		Overall Quality Level:		**Unacceptable[1]**		
Study Quality Comment:	**Footnote 1: Consistent with our *Application of A Systematic Review in TSCA Risk Evaluations* document, if a metric for a data source receives a score of Unacceptable (score = 4), EPA will determine the study to be unacceptable. In this case, two of the metrics were rated as unacceptable. As such, the study is considered unacceptable and the score is presented solely to increase transparency.**					

5.2. Animal toxicity evaluation results of Jisa et al 1993 for a cancer bioassay study on cancer; nutrition and metabolic/adult exposure body weight outcomes

Study reference:	Jisa, (1993). Carcinogenicity study of tetrachloroethylene by inhalation in rats and mice HERO ID: 630653					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
Test Substance	1. Test Substance Identity	Structural formula, CASRN, physiochemical properties were provided	High	1	2	2
	2. Test Substance Source	Source and lot numbers provided; identity verified by mass spec and infrared absorption spectrum of each lot	High	1	1	1
	3. Test Substance Purity	Purity such that effects likely due to test subsstance	High	1	1	1
Test Design	4. Negative and Vehicle Controls	Concurrent negative controls were included	High	1	2	2
	5. Positive Controls	Positive control animals were not required for this study	Not Rated	NA	NA	NA
	6. Randomized Allocation	Animals assigned to each treatment group by grouping method (optimal stratification system).	Medium	2	1	2
Exposure Characterization	7. Preparation and Storage of Test Substance	Method of generating vapor and storage was described in detail and appropriate	High	1	1	1
	8. Consistency of Exposure Administration	Exposures were administered consistently	High	1	1	1
	9. Reporting of Doses/Concentrations	Nominal and analytical concentrations were reported, tetrachloroethylene concentration inside the inhalation chamber was determined before exposure started and then every 15 minutes until exposure was completed using GC.	High	1	2	2

PEER REVIEW DRAFT. DO NOT CITE OR QUOTE

Study reference:	Jisa, (1993). Carcinogenicity study of tetrachloroethylene by inhalation in rats and mice HERO ID: 630653					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	10. Exposure Frequency and Duration	The frequency and duration were reported and appropriate	High	1	1	1
	11. Number of Exposure Groups and Dose Spacing	The rationale for the exposure concentrations and number of groups were reported.	High	1	1	1
	12. Exposure Route and Method	The route and method of exposure were adequate.	High	1	1	1
Test Organism	13. Test Animal Characteristics	Species, age, health, sex, starting body weight provided for both rats and mice	High	1	2	2
	14. Adequacy and Consistency of Animal Husbandry Conditions	Conditions were reported and the same across groups.	High	1	1	1
	15. Number per Group	The number was reported and appropriate. 50/sex/group	High	1	1	1
Outcome Assessment	16. Outcome Assessment Methodology	The outcome assessment methodology addressed the intended outcomes of interest	High	1	2	2
	17. Consistency of Outcome Assessment	Outcomes assess consistently across groups	High	1	1	1
	18. Sampling Adequacy	Sampling was adequate for the outcomes	High	1	1	1
	19. Blinding of Assessors	Blinding not required	Not Rated	NA	NA	NA
	20. Negative Control Response	Negative responses were adequate	High	1	1	1
Confounding / Variable Control	21. Confounding Variables in Test Design and Procedures	No confounding variable reported	High	1	2	2
	22. Health Outcomes Unrelated to Exposure	No confounding variables reported	High	1	1	1

PEER REVIEW DRAFT. DO NOT CITE OR QUOTE

Study reference:	Jisa, (1993). Carcinogenicity study of tetrachloroethylene by inhalation in rats and mice HERO ID: 630653					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
Data Presentation and Analysis	23. Statistical Methods	Statistical methods were appropriate	High	1	1	1
	24. Reporting of Data	Data for non-cancer endpoints summarized in text, but specific details not provided.	Medium	2	2	4
High: >=1 and <1.7 Medium: >=1.7 and <2.3 Low: >=2.3 and <=3		**Sum of scores:**			**29**	**32**
		Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factors:		**1.1034**	**Overall Score: Nearest *:**	**1.1**
		Overall Quality Level:		**High**		

5.3. Animal toxicity evaluation results of Natl Institute of Health 1977 for a 78-week cancer bioassay (rats and mice) study on cancer, mortality, respiratory, hepatic, renal, thyroid, cardiovascular, neurological/behavior, nutrition and metabolic/adult exposure body weight, hematological and immune, skin and connective tissue, and gastrointestinal outcomes

Study reference:	**Natl Inst Of, Health (1977). Bioassay of tetrachloroethylene for possible carcinogenicity** **HERO ID: 4214470**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
Test Substance	1. Test Substance Identity	The test substance was identified definitively.	High	1	2	2
	2. Test Substance Source	The source of the test substance was reported, including manufacturer. A lot/batch number was not reported.	Medium	2	1	2
	3. Test Substance Purity	The purity was reported by the manufacturer (at least 99%). The study report also stated that gas-liquid chromatography showed the major component consisting of over 99% of the total peak area, with a minor impurity present, which was not identified.	Medium	2	1	2
Test Design	4. Negative and Vehicle Controls	The study authors reported using an appropriate concurrent control group (vehicle control and untreated control groups.)	High	1	2	2
	5. Positive Controls	Positive control is not indicated for the study type.	Not Rated	NA	NA	NA
	6. Randomized Allocation	The study did not report how animals were allocated to study groups.	Low	3	1	3

PEER REVIEW DRAFT. DO NOT CITE OR QUOTE

Study reference:	Natl Inst Of, Health (1977). Bioassay of tetrachloroethylene for possible carcinogenicity HERO ID: 4214470					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
Exposure Characterization	7. Preparation and Storage of Test Substance	The test substance preparation and storage conditions were reported but there were minor limitations in the test substance preparation. The test substance was prepared weekly, sealed, and stored at 34 degrees F, which the study authors noted were considered conditions that would allow test substance to remain stable for 10 days. However, no report of stability in the vehicle (corn oil), or of PERC in the prepared solutions, was reported.	Medium	2	1	2
	8. Consistency of Exposure Administration	Details of exposure administration were not fully reported (volume administered by gavage was not reported).	Low	3	1	3

PEER REVIEW DRAFT. DO NOT CITE OR QUOTE

Study reference:	Natl Inst Of, Health (1977). Bioassay of tetrachloroethylene for possible carcinogenicity HERO ID: 4214470					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	9. Reporting of Doses/Concentrations	Initial administered doses were reported; however, dose levels were raised and/or lowered during the study in both rats and mice based on clinical signs and there is some ambiguity in the actual dose levels after adjustment and the exact days during the study when doses were raised and/or lowered (only reported in weeks). For example, for rats, the study authors stated that the low doses were adjusted accordingly, so that they consistently remained one-half of the high dose but actual adjusted dose levels were not reported (p. 11 of the study report).	Low	3	2	6
	10. Exposure Frequency and Duration	Exposure frequency (5 consecutive d/wk) was reported and acceptable. However, the exposure duration was shorter than studies of similar type (i.e., 2 years for carcinogenicity studies is typical for rodents) and was not justified by the study authors. In this study, animals were dosed for 78 weeks followed by an observation period of 32 weeks in rats and 12 weeks in mice.	Medium	2	1	2

PEER REVIEW DRAFT. DO NOT CITE OR QUOTE

Study reference:	Natl Inst Of, Health (1977). Bioassay of tetrachloroethylene for possible carcinogenicity HERO ID: 4214470					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	11. Number of Exposure Groups and Dose Spacing	The number of exposure groups was considered adequate for the purpose of the study. However, the highest doses produced a high rate of early mortality in both rats and mice, which the study authors noted may indicate that the optimum dose was exceeded in both species.	Medium	2	1	2
	12. Exposure Route and Method	The route and method of exposure were reported and were suited to the test substance.	High	1	1	1
Test Organism	13. Test Animal Characteristics	The test animal source, species, strain, sex, age, and starting body weight were reported. However, health status at the beginning of the study was not reported.	Medium	2	2	4

	14. Adequacy and Consistency of Animal Husbandry Conditions	The study authors stated that housing rooms were maintained in a temperature range of 20 to 24 deg C, a relative humidity of 45 to 55%, with a 12-hour light cycle and 12 complete changes of room air per hour. However, some differences between PERC-treated / untreated control animals and the vehicle control animals were reported, which included that PERC-treated / untreated control rats were housed in one room while the vehicle control rats were housed in another room. The study authors also reported that the vehicle control rats were approximately 4 weeks older than rats in the PERC-treated and untreated control groups and, therefore, were started on the test 4 weeks earlier. Similarly, vehicle control mice were approximately 2 weeks older than mice in the other groups and, therefore, were started on the test earlier. Due to starting the vehicle control rats and mice earlier than animals of other groups, and housing of vehicle control rats and a different room than other rats, there may have been some differences in husbandry / exposure conditions.	Low	3	1	3
	15. Number per Group	The number of animals in the PERC-treated groups (50/sex/group) was reported, appropriate for the study type and outcome analysis, and consistent	Medium	2	1	2

Study reference:	Natl Inst Of, Health (1977). Bioassay of tetrachloroethylene for possible carcinogenicity HERO ID: 4214470					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
		with studies of the same or similar type; however, the number of animals in each of the two control groups (vehicle and untreated each had 20/sex/group) was lower than the typical number used in studies of the same or similar type.				
Outcome Assessment	16. Outcome Assessment Methodology	The outcome assessment methodology addressed or reported the intended outcomes of interest and was sensitive for the outcomes of interest.	High	1	2	2
	17. Consistency of Outcome Assessment	Details of the outcome assessment protocol were reported and outcomes were assessed consistently across study groups.	High	1	1	1
	18. Sampling Adequacy	Details regarding sampling for the outcomes of interest were reported and the study used adequate sampling for the outcomes of interest.	High	1	1	1
	19. Blinding of Assessors	No subjective outcomes were reported and histopathology examinations were not described as a re-evaluation	Not Rated	NA	NA	NA
	20. Negative Control Response	The biological responses of the negative control groups were adequate.	High	1	1	1

PEER REVIEW DRAFT. DO NOT CITE OR QUOTE

Study reference:	Natl Inst Of, Health (1977). Bioassay of tetrachloroethylene for possible carcinogenicity HERO ID: 4214470					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
Confounding / Variable Control	21. Confounding Variables in Test Design and Procedures	There were minor uncertainties regarding biological responses of the negative control. For example, in mice, while no appreciable differences in body weight gain were observed between PERC-treated and untreated mice, PERC-treated male mice gained less than vehicle control animals after the first three months and PERC-treated female mice gained less than vehicle control animals during the second year of the bioassay. These differences are unlikely to have a substantial impact on results.	Medium	2	2	4
	22. Health Outcomes Unrelated to Exposure	Data on attrition and/or health outcomes unrelated to exposure for each study group were not reported because only substantial differences among groups were noted.	Medium	2	1	2
Data Presentation and Analysis	23. Statistical Methods	The statistical methods were clearly described by the study authors and were appropriate for datasets.	High	1	1	1
	24. Reporting of Data	Some data are reported incompletely. For example, incidences for reported clinical signs were not reported. Severity scores were not reported for non-neoplastic data.	Low	3	2	6
		Sum of scores:			**29**	**54**

PEER REVIEW DRAFT. DO NOT CITE OR QUOTE

Study reference:	Natl Inst Of, Health (1977). Bioassay of tetrachloroethylene for possible carcinogenicity HERO ID: 4214470					
Domain	Metric	Eval Comment	Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]	Metric Score	Metric Weighting Factor	Weighted Score
High: >=1 and <1.7 Medium: >=1.7 and <2.3 Low: >=2.3 and <=3		Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factors:		1.8621	Overall Score: Nearest *:	1.9
		Overall Quality Level:		Medium		

5.4. Animal toxicity evaluation results of NTP 1986 for 2-year cancer biossay, inhalation studies in rats and mice on cancer, reproductive, hematological and immune, neurological/behavior, renal, hepatic, cardiovascular, endocrine, gastrointestinal, mortality, nutrition and metabolic/adult exposure body weight, respiratory, skin and connective tissues, thyroid outcomes

Study reference:	**NTP (1986). Toxicology and carcinogenesis studies of tetrachloroethylene (perchloroethylene) (CAS no. 127-18-4) in F344/N rats and B6C3F1 mice (inhalation studies)** **HERO ID: 632655**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
Test Substance	1. Test Substance Identity	high-purity tetrachloroethylene, Dowper stabilized	High	1	2	2
	2. Test Substance Source	Dow Chemical, lots TA03116F-01 and TA08190D. Purity and identity analyses conducted.	High	1	1	1
	3. Test Substance Purity	Confirmed analytically for both lots - approximately 99.9%	High	1	1	1
Test Design	4. Negative and Vehicle Controls	Chamber controls were used.	High	1	2	2
	5. Positive Controls	Not needed for study type.	Not Rated	NA	NA	NA
	6. Randomized Allocation	computer generated tables of random numbers.	High	1	1	1
Exposure Characterization	7. Preparation and Storage of Test Substance	Tetrachloroethylene was found to be stable for 2 weeks at 60" C (Appendix H). Tetrachloroethylene was stored at 0" C Tetrachloroethylene was vaporized at 100"-110" C, diluted with air, and. introduced into the chambers. Detailed descriptions in Table 2 and in Appendix I.	High	1	1	1

Study reference:	NTP (1986). Toxicology and carcinogenesis studies of tetrachloroethylene (perchloroethylene) (CAS no. 127-18-4) in F344/N rats and B6C3F1 mice (inhalation studies) HERO ID: 632655					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	8. Consistency of Exposure Administration	Concentrations in the exposure chambers were monitored 8-12 times per exposure period by a Hewlett-Packard 5840A Gas Chromatograph. On one occasion (September 13, 1982) in the 2-year studies, the concentration in the 400- ppm chamber was 800 ppm for 12 minutes and 2,400 ppm for 48 minutes. Animals were therefore not exposed at all on September 14, 1982	Medium	2	1	2
	9. Reporting of Doses/Concentrations	Target and analytical exposure levels reported for 2 yr study in rats and mice only. Mean analytical concentrations (99.5, 201, 403 ppm) very close to target (100, 200, 400 ppm).	High	1	2	2
	10. Exposure Frequency and Duration	2-yr, 6 hr/d, 5 d/wk.	High	1	1	1
	11. Number of Exposure Groups and Dose Spacing	2 dose groups plus control	High	1	1	1

PEER REVIEW DRAFT. DO NOT CITE OR QUOTE

Study reference:	NTP (1986). Toxicology and carcinogenesis studies of tetrachloroethylene (perchloroethylene) (CAS no. 127-18-4) in F344/N rats and B6C3F1 mice (inhalation studies) HERO ID: 632655					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	12. Exposure Route and Method	Inhalation, dynamic whole-body chamber. Flow rate not reported For the chemistry data, all of the available records concerning receipt, initial analysis, and stability testing by Midwest Research Instiitute (MRI) were examined. In addition, records pertaining to receipt, bulk chemical analysis, generation of chamber concentrations, exposure chamber monitoring, and gas chromatographic calibration by the study laboratory were examined.	Low	3	1	3
Test Organism	13. Test Animal Characteristics	F344/N rats and B6C3F1 mice, Charles River Breeding. 8-9 wks at study initiation. Initial BW reported in Tables 10 and 21, respectively.	High	1	2	2
	14. Adequacy and Consistency of Animal Husbandry Conditions	Details of husbandry in Table 5	High	1	1	1
	15. Number per Group	49-50/sex/group per species	High	1	1	1
Outcome Assessment	16. Outcome Assessment Methodology	Mortality, clinical signs, body weight, comprehensive histopathology	High	1	2	2
	17. Consistency of Outcome Assessment	Consistent evaluation in all study groups.	High	1	1	1
	18. Sampling Adequacy	49-50/sex/group	High	1	1	1

Study reference:	NTP (1986). Toxicology and carcinogenesis studies of tetrachloroethylene (perchloroethylene) (CAS no. 127-18-4) in F344/N rats and B6C3F1 mice (inhalation studies) HERO ID: 632655					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
	19. Blinding of Assessors	For histo - Slides/tissues are generally not evaluated in a blind fashion (i.e., without knowledge of dose group) unless the lesions in question are subtle or unless there is an inconsistent diagnosis of lesions by the laboratory pathologist and pathology work group. Evaluated endpoints did not require blinding.	Not Rated	NA	NA	NA
	20. Negative Control Response	Control responses reported. Historical incidences of tumors in control animals also reported.	High	1	1	1
Confounding / Variable Control	21. Confounding Variables in Test Design and Procedures	There were no reported differences among the study groups in initial body weight. Food and water intake were not reported. Respiratory rate was not specifically mentioned, but no exposure-related clinical signs were reported. While there is no evidence of bradypnea, animal temperature should be measured to rule out bradypnea.	Medium	2	2	4
	22. Health Outcomes Unrelated to Exposure	data on attrition and/or health outcomes unrelated to exposure for each study group were not reported because only substantial differences among groups were noted	Medium	2	1	2

Study reference:	**NTP (1986). Toxicology and carcinogenesis studies of tetrachloroethylene (perchloroethylene) (CAS no. 127-18-4) in F344/N rats and B6C3F1 mice (inhalation studies)** **HERO ID: 632655**					
Domain	**Metric**	**Eval Comment**	**Qualitative Determination [i.e.,High,Medium,Low,Unacceptable, or Not rated]**	**Metric Score**	**Metric Weighting Factor**	**Weighted Score**
Data Presentation and Analysis	23. Statistical Methods	Detailed statistical tests reported for survival and tumor analysis. Appendices C and D contain nonneoplastic data reporting sufficient for statistical analysis. Body weight data not adequate for independent analysis (no variance data)	Medium	2	1	2
	24. Reporting of Data	quantitative mortality, body weight, nonneoplastic, and neoplastic data. Clinical signs data not reported.	Medium	2	2	4
High: >=1 and <1.7 **Medium: >=1.7 and <2.3** **Low: >=2.3 and <=3**		**Sum of scores:**			**29**	**38**
		Overall Score = Sum of Weighted Scores/Sum of Metric Weighting Factors:		**1.3103**	**Overall Score: Nearest *:**	**1.3**
		Overall Quality Level:		**High**		