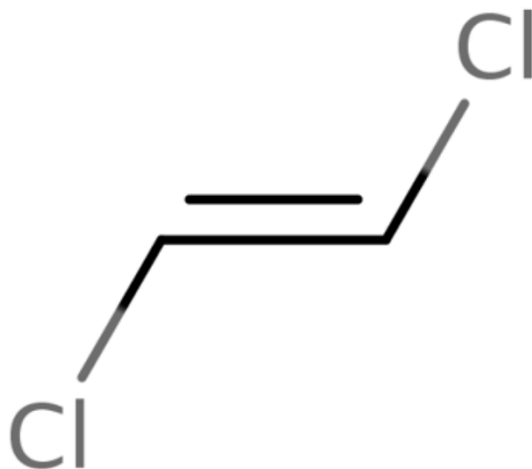

**Draft Data Quality Evaluation Information for
Human Health Hazard Animal Toxicology for
trans-1,2-Dichloroethylene**

Systematic Review Support Document for the Draft Risk Evaluation

CASRN: 156-60-5



June 2026

This supplemental file contains information regarding the data quality evaluation results for data sources that met the PECO screening criteria for the *Draft Risk Evaluation for trans-1,2-Dichloroethylene* and were used to characterize human health hazard in the *Draft Human Health and Environmental Hazard Assessment for trans-1,2-Dichloroethylene*. Due to data gaps identified for trans-1,2-dichloroethylene in the cancer analysis, analog data from cis-1,2-dichloroethylene were included for read-across in the *Draft Human Health and Environmental Hazard Assessment for trans-1,2-Dichloroethylene*. EPA conducted data quality evaluation based on author-reported descriptions and results; additional analyses (e.g., statistical analyses performed during data integration into the risk evaluation) potentially conducted by EPA are not contained in this supplemental file. For the data quality evaluation, EPA used the TSCA systematic review process described in the *Draft Systematic Review Protocol Supporting TSCA Risk Evaluations for Chemical Substances* (referred to hereafter as the '2021 Draft Systematic Review Protocol'). Any updated steps in the systematic review process since the publication of the 2021 Draft Systematic Review Protocol will be described in the *Draft Systematic Review Protocol for trans-1,2-Dichloroethylene*, to be released with the risk evaluation.

trans-1,2-Dichloroethylene

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HERO ID	Reference	Page
trans-1,2-Dichloroethylene		
Acute (less than or equal to 24 hr)		
8875453	[Redacted] (1999). [Redacted] Trans-1,2-dichloroethylene and cis-1,2-dichloroethylene: Inhalation median lethal concentration (LC50) study in rats.	6
200220	Barnes, D. W., Sanders, V. M., White, K. L., Jr, Shopp, G. M., Jr, Munson, A. E. (1985). Toxicology of trans-1,2-dichloroethylene in the mouse. Drug and Chemical Toxicology 8(5):373-392.	15
2310778	DuPont, (1988). Eye irritation test in rabbits of trans-1,2-dichloroethylene with cover letter dated 05/10/94 (sanitized).	19
2310779	DuPont, (1988). Skin irritation test in rabbits of trans-1,2-dichloroethylene with cover letter dated 05/10/94 (sanitized).	22
2310561	Eger, E. I., Halsey, M. J., Koblin, D. D., Laster, M. J., Ionescu, P., Königsberger, K., Fan, R., Nguyen, B. V., Hudlicky, T. (2001). The convulsant and anesthetic properties of cis-trans isomers of 1,2-dichlorohexafluorocyclobutane and 1,2-dichloroethylene. Anesthesia and Analgesia 93(4):922-927.	25
1740886	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.	27
1740814	Hayes, J. R., Condie Jr., L. W., Egle Jr., J. L., Borzelleca, J. F. (1987). The acute and subchronic toxicity in rats of trans-1,2-dichloroethylene in drinking water. Journal of the American College of Toxicology 6(4):471-478.	49
1748282	Jenkins, L. J., Trabulus, M. J., Murphy, S. D. (1972). Biochemical effects of 1,1-dichloroethylene in rats - Comparison with carbon-tetrachloride and 1,2-dichloroethylene. Toxicology and Applied Pharmacology 23(3):501-510.	53
62637	Munson, A. E., Sanders, V. M., Douglas, K. A., Sain, L. E., Kauffmann, B. M., White Jr., K. L. (1982). In vivo assessment of immunotoxicity. Environmental Health Perspectives 43:41-52.	55
1747837	Nakahama, T., Sarutani, S., Inouye, Y. (2000). Effects of chlorinated ethylenes on expression of rat CYP forms: Comparative study on correlation between biological activities and chemical structures. Journal of Health Science 46(4):251-258.	59
64411	Plaa, G. L., Larson, R. E. (1965). Relative nephrotoxic properties of chlorinated methane, ethane, and ethylene derivatives in mice. Toxicology and Applied Pharmacology 7(1):37-44.	65
2303853	Saldana-Ruiz, S., Boadas-Vaello, P., Sedo-Cabezon, L., Llorens, J. (2013). Reduced Systemic Toxicity and Preserved Vestibular Toxicity Following Co-treatment with Nitriles and CYP2E1 Inhibitors: a Mouse Model for Hair Cell Loss. JARO - Journal of the Association for Research in Otolaryngology 14(5):661-671.	69
Short-term (>1-30 days)		
200220	Barnes, D. W., Sanders, V. M., White, K. L., Jr, Shopp, G. M., Jr, Munson, A. E. (1985). Toxicology of trans-1,2-dichloroethylene in the mouse. Drug and Chemical Toxicology 8(5):373-392.	72

trans-1,2-Dichloroethylene

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1740886	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.	77
1414030	Hanioka, N., Jinno, H., Nishimura, T., Ando, M. (1998). Changes in hepatic cytochrome P450 enzymes by cis- and trans-1,2-dichloroethylenes in rat. Xenobiotica 28(1):41-51.	88
64411	Plaa, G. L., Larson, R. E. (1965). Relative nephrotoxic properties of chlorinated methane, ethane, and ethylene derivatives in mice. Toxicology and Applied Pharmacology 7(1):37-44.	92
5435222	Shopp, G. M., Sanders, V. M., White, K. L., Munson, A. E. (1985). Humoral and cell-mediated immune status of mice exposed to trans-1,2-dichloroethylene. Drug and Chemical Toxicology 8(5):393-407.	94
Subchronic (>30-91 days)		
200220	Barnes, D. W., Sanders, V. M., White, K. L., Jr, Shopp, G. M., Jr, Munson, A. E. (1985). Toxicology of trans-1,2-dichloroethylene in the mouse. Drug and Chemical Toxicology 8(5):373-392.	97
4154576	DuPont, (1998). trans-1,2-Dichloroethylene: 90-day inhalation toxicity study in rats.	106
1740886	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.	130
1740814	Hayes, J. R., Condie Jr., L. W., Egle Jr., J. L., Borzelleca, J. F. (1987). The acute and subchronic toxicity in rats of trans-1,2-dichloroethylene in drinking water. Journal of the American College of Toxicology 6(4):471-478.	142
5435222	Shopp, G. M., Sanders, V. M., White, K. L., Munson, A. E. (1985). Humoral and cell-mediated immune status of mice exposed to trans-1,2-dichloroethylene. Drug and Chemical Toxicology 8(5):393-407.	158
Chronic (>91 days)		
1740886	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.	164
1739657	Ress, N. B. (2002). NTP technical report on the toxicity studies of trans-1,2-dichloroethylene (CAS No. 156-60-5) administered in microcapsules in feed to F344/N rats and B6C3F1 mice. Toxicity Report Series, vol. 55 55:112 pp.	175
Reproductive/Developmental		
1741343	Hurt, M. E., Valentine, R., Alvarez, L. (1993). Developmental toxicity of inhaled trans-1,2-dichloroethylene in the rat. Fundamental and Applied Toxicology 20(2):225-230.	194

Isomer: 1,2-Dichloroethylene

Acute (less than or equal to 24 hr)

194679	Crebelli, R., Carere, A., Leopardi, P., Conti, L., Fassio, F., Raiteri, F., Barone, D., Ciliutti, P., Cinelli, S., Vericat, J. A. (1999). Evaluation of 10 aliphatic halogenated hydrocarbons in the mouse bone marrow micronucleus test. Mutagenesis 14(2):207-215.	204
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Isomer: cis-1,2-Dichloroethylene

trans-1,2-Dichloroethylene

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Acute (less than or equal to 24 hr)		
8875453	[Redacted] (1999). [Redacted] Trans-1,2-dichloroethylene and cis-1,2-dichloroethylene: Inhalation median lethal concentration (LC50) study in rats.	210
2310561	Eger, E. I., Halsey, M. J., Koblin, D. D., Laster, M. J., Ionescu, P., Königsberger, K., Fan, R., Nguyen, B. V., Hudlicky, T. (2001). The convulsant and anesthetic properties of cis-trans isomers of 1,2-dichlorohexafluorocyclobutane and 1,2-dichloroethylene. <i>Anesthesia and Analgesia</i> 93(4):922-927.	219
1748282	Jenkins, L. J., Trabulus, M. J., Murphy, S. D. (1972). Biochemical effects of 1,1-dichloroethylene in rats - Comparison with carbon-tetrachloride and 1,2-dichloroethylene. <i>Toxicology and Applied Pharmacology</i> 23(3):501-510.	221
1747837	Nakahama, T., Sarutani, S., Inouye, Y. (2000). Effects of chlorinated ethylenes on expression of rat CYP forms: Comparative study on correlation between biological activities and chemical structures. <i>Journal of Health Science</i> 46(4):251-258.	223
64411	Plaa, G. L., Larson, R. E. (1965). Relative nephrotoxic properties of chlorinated methane, ethane, and ethylene derivatives in mice. <i>Toxicology and Applied Pharmacology</i> 7(1):37-44.	229
Short-term (>1-30 days)		
5237	McCauley, P. T., Robinson, M., Daniel, F. B., Olson, G. R. (1995). The effects of subacute and subchronic oral exposure to cis-1,2-dichloroethylene in Sprague-Dawley rats. <i>Drug and Chemical Toxicology</i> 18(2-3):171-184.	233
64411	Plaa, G. L., Larson, R. E. (1965). Relative nephrotoxic properties of chlorinated methane, ethane, and ethylene derivatives in mice. <i>Toxicology and Applied Pharmacology</i> 7(1):37-44.	248
Subchronic (>30-91 days)		
5237	McCauley, P. T., Robinson, M., Daniel, F. B., Olson, G. R. (1995). The effects of subacute and subchronic oral exposure to cis-1,2-dichloroethylene in Sprague-Dawley rats. <i>Drug and Chemical Toxicology</i> 18(2-3):171-184.	250

Study Citation:	[Redacted] (1999). [Redacted] Trans-1,2-dichloroethylene and cis-1,2-dichloroethylene: Inhalation median lethal concentration (LC50) study in rats.			
Health Outcome(s):	Clinical signs (Clinical signs, gross necropsy)			
Reported Health Effect(s):	Clinical signs (Clinical signs, gross necropsy): Clinical signs of toxicity, gross necropsy			
Duration:	Acute (less than or equal to 24 hr) 4 hours			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	8875453			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1:	Test Substance Identity	High	The test substance was identified definitively (name, synonyms, CAS No.)
	Metric 2:	Test Substance Source	Low	The test substance was supplied by the sponsor, but no other information was provided. This appears to be a confidential study in which some of the identifying information has been redacted.
	Metric 3:	Test Substance Purity	High	The purity (>99%) and known impurities were provided.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	The appropriate negative control was included (a set of male and female rats exposed to air only).
	Metric 5:	Positive Controls	N/A	A positive control is not needed for this type of study.
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups, only that rats exhibiting a normal pattern of weight gain and no overt signs of disease were selected.
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and Storage of Test Substance	High	The vapor generation system was adequately described, and storage was not necessary as it was a single exposure.
	Metric 8:	Consistency of Exposure Administration	Medium	Details of exposure administration were not completely reported, but the missing information is unlikely to have a substantial impact on results.
	Metric 9:	Reporting of Doses/Concentrations	High	The test concentration mean, S.D., range, and number of samples taken were reported.
	Metric 10:	Exposure Frequency and Duration	High	The exposure duration and frequency were appropriate for the purpose of the study (acute lethality).
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The number of exposure groups and dose space were appropriate for the purpose of the study (acute lethality).
	Metric 12:	Exposure Route and Method	High	The route and method of exposure were reported and appropriate for the test substance.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	High	The test animal species, strain, sex, age, and starting body weights were reported. The source of the animals was redacted. The test species was appropriate for the outcome of interest (acute toxicity).
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were reported (temperature, humidity, light/dark cycle, diet, and water availability). The water source was redacted. There is no indication that any of these conditions differed between groups.
	Metric 15:	Number of Animals per Group	Medium	The number of animals per group was reported and acceptable for this type of study.

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Study Citation:	[Redacted] (1999). [Redacted] Trans-1,2-dichloroethylene and cis-1,2-dichloroethylene: Inhalation median lethal concentration (LC50) study in rats.		
Health Outcome(s):	Clinical signs (Clinical signs, gross necropsy)		
Reported Health Effect(s):	Clinical signs (Clinical signs, gross necropsy): Clinical signs of toxicity, gross necropsy		
Duration:	Acute (less than or equal to 24 hr) 4 hours		
Chemical:	trans-1,2-Dichloroethylene- Parent compound		
HERO ID:	8875453		
Domain	Metric	Rating	Comments
Domain 5: Outcome Assessment			
Metric 16:	Outcome Assessment Methodology	High	The outcome methodology was adequate and addressed the intended outcome (clinical signs/gross necropsy).
Metric 17:	Consistency of Outcome Assessment	Medium	No information was provided on the timing of the outcome assessment, but it is unlikely to impact results.
Metric 18:	Sampling Adequacy	High	The sampling was adequate for the intended outcome.
Metric 19:	Blinding of Assessors	Medium	Blinding was not reported, although the concern for bias was mitigated due to the simple nature of the outcome (basic clinical signs/gross necropsy).
Metric 20:	Negative Control Response	High	No effects were noted in the negative control group.
Domain 6: Confounding / Variable Control			
Metric 21:	Confounding Variables in Test Design and Procedures	Medium	There is no information to suggest or dismiss that confounders were present. All animals were accounted for, but some measures were not reported (breathing rates, food and water intake).
Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
Metric 23:	Data Presentation and Analysis	N/A	Statistical analysis was not conducted but is not required for the measured outcome (clinical signs/gross necropsy).
Metric 24:	Reporting of Data	High	Clinical signs and gross necropsy data were presented for individual animals.
Additional Comments: This form is associated with the trans-1,2-Dichloroethylene study.			
Overall Quality Determination		High	

Study Citation:	[Redacted] (1999). [Redacted] Trans-1,2-dichloroethylene and cis-1,2-dichloroethylene: Inhalation median lethal concentration (LC50) study in rats.			
Health Outcome(s):	Nutritional/Metabolic			
Reported Health Effect(s):	Nutritional/Metabolic: Body weight			
Duration:	Acute (less than or equal to 24 hr) 4 hours			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	8875453			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	The test substance was identified definitively (name, synonyms, CAS No.)	
	Metric 2: Test Substance Source	Low	The test substance was supplied by the sponsor, but no other information was provided. This appears to be a confidential study in which some of the identifying information has been redacted.	
	Metric 3: Test Substance Purity	High	The purity (>99%) and known impurities were provided.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	The appropriate negative control was included (a set of male and female rats exposed to air only).	
	Metric 5: Positive Controls	N/A	A positive control is not needed for this type of study.	
	Metric 6: Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups, only that rats exhibiting a normal pattern of weight gain and no overt signs of disease were selected.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	High	The vapor generation system was adequately described, and storage was not necessary as it was a single exposure.	
	Metric 8: Consistency of Exposure Administration	Medium	Details of exposure administration were not completely reported, but the missing information is unlikely to have a substantial impact on results.	
	Metric 9: Reporting of Doses/Concentrations	High	The test concentration mean, S.D., range, and number of samples taken were reported.	
	Metric 10: Exposure Frequency and Duration	High	The exposure duration and frequency were appropriate for the purpose of the study (acute lethality).	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	The number of exposure groups and dose space were appropriate for the purpose of the study (acute lethality).	
	Metric 12: Exposure Route and Method	High	The route and method of exposure were reported and appropriate for the test substance.	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	High	The test animal species, strain, sex, age, and starting body weights were reported. The source of the animals was redacted. The test species was appropriate for the outcome of interest (acute toxicity).	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were reported (temperature, humidity, light/dark cycle, diet, and water availability). The water source was redacted. There is no indication that any of these conditions differed between groups.	
	Metric 15: Number of Animals per Group	Medium	The number of animals per group was reported and acceptable for this type of study.	
Domain 5: Outcome Assessment				
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Study Citation:	[Redacted] (1999). [Redacted] Trans-1,2-dichloroethylene and cis-1,2-dichloroethylene: Inhalation median lethal concentration (LC50) study in rats.			
Health Outcome(s):	Nutritional/Metabolic			
Reported Health Effect(s):	Nutritional/Metabolic: Body weight			
Duration:	Acute (less than or equal to 24 hr) 4 hours			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	8875453			
Domain	Metric	Rating	Comments	
	Metric 16: Outcome Assessment Methodology	High	The outcome methodology was adequate and addressed the intended outcome (body weight effects).	
	Metric 17: Consistency of Outcome Assessment	Medium	No information was provided on the timing of the outcome assessment, but it is unlikely to impact results.	
	Metric 18: Sampling Adequacy	High	The sampling was adequate for the intended outcome.	
	Metric 19: Blinding of Assessors	N/A	Blinding was not reported, although it was a simple and objective measure (body weight).	
	Metric 20: Negative Control Response	High	No effects were noted in the negative control group.	
Domain 6: Confounding / Variable Control				
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	There is no information to suggest or dismiss that confounders were present. All animals were accounted for, but some measures were not reported (breathing rates, food and water intake).	
	Metric 22: Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.	
	Metric 23: Data Presentation and Analysis	High	Statistical analysis was not conducted, but individual body weight data were reported and sufficient to conduct an independent analysis.	
	Metric 24: Reporting of Data	High	Body weight data were presented for individual animals.	
Additional Comments:	None			

Overall Quality Determination**High**

Study Citation:	[Redacted] (1999). [Redacted] Trans-1,2-dichloroethylene and cis-1,2-dichloroethylene: Inhalation median lethal concentration (LC50) study in rats.			
Health Outcome(s):	Mortality			
Reported Health Effect(s):	Mortality: LC50			
Duration:	Acute (less than or equal to 24 hr) 4 hours			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	8875453			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	The test substance was identified definitively (name, synonyms, CAS No.)	
	Metric 2: Test Substance Source	Low	The test substance was supplied by the sponsor, but no other information was provided. This appears to be a confidential study in which some of the identifying information has been redacted.	
	Metric 3: Test Substance Purity	High	The purity (>99%) and known impurities were provided.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	The appropriate negative control was included (a set of male and female rats exposed to air only).	
	Metric 5: Positive Controls	N/A	A positive control is not needed for this type of study.	
	Metric 6: Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups, only that rats exhibiting a normal pattern of weight gain and no overt signs of disease were selected.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	High	The vapor generation system was adequately described, and storage was not necessary as it was a single exposure.	
	Metric 8: Consistency of Exposure Administration	Medium	Details of exposure administration were not completely reported, but the missing information is unlikely to have a substantial impact on results.	
	Metric 9: Reporting of Doses/Concentrations	High	The test concentration mean, S.D., range, and number of samples taken were reported.	
	Metric 10: Exposure Frequency and Duration	High	The exposure duration and frequency were appropriate for the purpose of the study (acute lethality).	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	The number of exposure groups and dose space were appropriate for the purpose of the study (acute lethality).	
	Metric 12: Exposure Route and Method	High	The route and method of exposure were reported and appropriate for the test substance.	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	High	The test animal species, strain, sex, age, and starting body weights were reported. The source of the animals was redacted. The test species was appropriate for the outcome of interest (acute toxicity).	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were reported (temperature, humidity, light/dark cycle, diet, and water availability). The water source was redacted. There is no indication that any of these conditions differed between groups.	
	Metric 15: Number of Animals per Group	Medium	The number of animals per group was reported and acceptable for this type of study.	
Domain 5: Outcome Assessment				
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Study Citation:	[Redacted] (1999). [Redacted] Trans-1,2-dichloroethylene and cis-1,2-dichloroethylene: Inhalation median lethal concentration (LC50) study in rats.			
Health Outcome(s):	Mortality			
Reported Health Effect(s):	Mortality: LC50			
Duration:	Acute (less than or equal to 24 hr) 4 hours			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	8875453			
Domain	Metric	Rating	Comments	
	Metric 16: Outcome Assessment Methodology	High	The outcome methodology was adequate and addressed the intended outcome (lethality).	
	Metric 17: Consistency of Outcome Assessment	Medium	No information was provided on the timing of the outcome assessment, but it is unlikely to impact results.	
	Metric 18: Sampling Adequacy	High	The sampling was adequate for the intended outcome.	
	Metric 19: Blinding of Assessors	N/A	Blinding was not reported and not required.	
	Metric 20: Negative Control Response	High	No effects were noted in the negative control group.	
Domain 6: Confounding / Variable Control				
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	There is no information to suggest or dismiss that confounders were present. All animals were accounted for, but some measures were not reported (breathing rates, food and water intake).	
	Metric 22: Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.	
	Metric 23: Data Presentation and Analysis	N/A	Statistical analysis was not conducted but is not required for mortality data.	
	Metric 24: Reporting of Data	High	Mortality data were presented across exposure groups and for individual animals.	
Additional Comments:	This form is associated with the trans-1,2-Dichloroethylene study.			
Overall Quality Determination		High		

Study Citation:	[Redacted] (1999). [Redacted] Trans-1,2-dichloroethylene and cis-1,2-dichloroethylene: Inhalation median lethal concentration (LC50) study in rats.			
Health Outcome(s):	Lung/Respiratory; Hepatic/Liver; Renal/Kidney; Cardiovascular;			
Reported Health Effect(s):	Lung/Respiratory: Lung histopathology; Hepatic/Liver: Liver histopathology; Renal/Kidney: Kidney histopathology; Cardiovascular: Heart histopathology;			
Duration:	Acute (less than or equal to 24 hr) 4 hours			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	8875453			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
Metric 1:	Test Substance Identity	High	All Outcomes: The test substance was identified definitively (name, synonyms, CAS No.)	
Metric 2:	Test Substance Source	Low	All Outcomes: The test substance was supplied by the sponsor, but no other information was provided. This appears to be a confidential study in which some of the identifying information has been redacted.	
Metric 3:	Test Substance Purity	High	All Outcomes: The purity (>99%) and known impurities were provided.	
Domain 2: Test Design				
Metric 4:	Negative and Vehicle Controls	High	All Outcomes: The appropriate negative control was included (a set of male and female rats exposed to air only).	
Metric 5:	Positive Controls	N/A	All Outcomes: A positive control is not needed for this type of study.	
Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: The study did not report how animals were allocated to study groups, only that rats exhibiting a normal pattern of weight gain and no overt signs of disease were selected.	
Domain 3: Exposure Characterization				
Metric 7:	Preparation and Storage of Test Substance	High	All Outcomes: The vapor generation system was adequately described, and storage was not necessary as it was a single exposure.	
Metric 8:	Consistency of Exposure Administration	Medium	All Outcomes: Details of exposure administration were not completely reported, but the missing information is unlikely to have a substantial impact on results.	
Metric 9:	Reporting of Doses/Concentrations	High	All Outcomes: The test concentration mean, S.D., range, and number of samples taken were reported.	
Metric 10:	Exposure Frequency and Duration	High	All Outcomes: The exposure duration and frequency were appropriate for the purpose of the study (acute lethality).	
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: The number of exposure groups and dose space were appropriate for the purpose of the study (acute lethality).	
Metric 12:	Exposure Route and Method	High	All Outcomes: The route and method of exposure were reported and appropriate for the test substance.	
Domain 4: Test Animals				
Metric 13:	Test Animal Characteristics	High	All Outcomes: The test animal species, strain, sex, age, and starting body weights were reported. The source of the animals was redacted. The test species was appropriate for the outcome of interest (acute toxicity).	
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: All husbandry conditions were reported (temperature, humidity, light/dark cycle, diet, and water availability). The water source was redacted. There is no indication that any of these conditions differed between groups.	
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Study Citation:	[Redacted] (1999). [Redacted] Trans-1,2-dichloroethylene and cis-1,2-dichloroethylene: Inhalation median lethal concentration (LC50) study in rats.			
Health Outcome(s):	Lung/Respiratory; Hepatic/Liver; Renal/Kidney; Cardiovascular;			
Reported Health Effect(s):	Lung/Respiratory: Lung histopathology; Hepatic/Liver: Liver histopathology; Renal/Kidney: Kidney histopathology; Cardiovascular: Heart histopathology;			
Duration:	Acute (less than or equal to 24 hr) 4 hours			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	8875453			
Domain	Metric	Rating	Comments	
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: The number of animals per group was reported and acceptable for this type of study.
Domain 5: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	Medium	Lung/Respiratory: The outcome methodology partially addressed the intended outcome (lung effects) as histology was conducted without examining lung weight or function.; Hepatic/Liver: The outcome methodology partially addressed the intended outcome (liver effects) as histology was conducted without examining liver weight or function.; Renal/Kidney: The outcome methodology partially addressed the intended outcome (kidney effects) as histology was conducted without examining kidney weight or function.; Cardiovascular: The outcome methodology partially addressed the intended outcome (heart effects) as histology was conducted without examining heart weight or function.
	Metric 17:	Consistency of Outcome Assessment	Medium	All Outcomes: No information was provided on the timing of the outcome assessment, but it is unlikely to impact results.
	Metric 18:	Sampling Adequacy	High	All Outcomes: The sampling was adequate for the intended outcome.
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding was not reported, although it is not recommended for screening level histopathology.
	Metric 20:	Negative Control Response	High	All Outcomes: No effects were noted in the negative control group.
Domain 6: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: There is no information to suggest or dismiss that confounders were present. All animals were accounted for, but some measures were not reported (breathing rates, food and water intake).
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	N/A	Lung/Respiratory: Statistical analysis was not conducted but is not required for the measured outcome (lung histopathology).; Hepatic/Liver: Statistical analysis was not conducted but is not required for the measured outcome (liver histopathology).; Renal/Kidney: Statistical analysis was not conducted but is not required for the measured outcome (kidney histopathology).; Cardiovascular: Statistical analysis was not conducted but is not required for the measured outcome (heart histopathology).
	Metric 24:	Reporting of Data	High	Lung/Respiratory: Lung histopathology data were presented for individual animals.; Hepatic/Liver: Liver histopathology data were presented for individual animals.; Renal/Kidney: Kidney histopathology data were presented for individual animals.; Cardiovascular: Heart histopathology data were presented for individual animals.
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Study Citation:	[Redacted] (1999). [Redacted] Trans-1,2-dichloroethylene and cis-1,2-dichloroethylene: Inhalation median lethal concentration (LC50) study in rats.
Health Outcome(s):	Lung/Respiratory; Hepatic/Liver; Renal/Kidney; Cardiovascular;
Reported Health Effect(s):	Lung/Respiratory: Lung histopathology; Hepatic/Liver: Liver histopathology; Renal/Kidney: Kidney histopathology; Cardiovascular: Heart histopathology;
Duration:	Acute (less than or equal to 24 hr) 4 hours
Chemical:	trans-1,2-Dichloroethylene- Parent compound
HERO ID:	8875453

Domain	Metric	Rating	Comments
Additional Comments:	This form is associated with the trans-1,2-Dichloroethylene study.		

Overall Quality Determination**High**

Study Citation:	Barnes, D. W., Sanders, V. M., White, K. L., Jr, Shopp, G. M., Jr, Munson, A. E. (1985). Toxicology of trans-1,2-dichloroethylene in the mouse. Drug and Chemical Toxicology 8(5):373-392.			
Health Outcome(s):	Mortality			
Reported Health Effect(s):	Mortality: LD10, LD50, and LD90 (survival over 14 days following a single oral administration).			
Duration:	Acute (less than or equal to 24 hr) Acute- single gavage			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	200220; Linked HERO ID(s): 200220, 62637, 5435222			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	Test substance was identified as trans-1,2-dichloroethylene.	
	Metric 2: Test Substance Source	High	The source of the test substance was Aldrich Chemical Co., Milwaukee, WI. Lot number was included.	
	Metric 3: Test Substance Purity	High	Test substance was 98% pure.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	N/A	Lethality study, negative control was not necessary.	
	Metric 5: Positive Controls	N/A	Positive control was not necessary for this study.	
	Metric 6: Randomized Allocation of Animals	Medium	The current study did not specify whether animals were randomly distributed across groups; however, the study followed methodological details reported in HERO ID 64563. This reference indicated that the study animals were randomized (method not specified).	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Medium	DCE was prepared on the day of administration and maintained in dark glassware at 4 °C until use. The test substance is volatile; it was not specified whether the bottles were sealed to prevent volatilization.	
	Metric 8: Consistency of Exposure Administration	High	Exposures were administered consistently across groups; the gavage volume (0.01 mL/g) was reported.	
	Metric 9: Reporting of Doses/Concentrations	Medium	A range of doses was reported. Nine doses ranging from 800-3500 mg/kg. From the results, 8 of the doses can be determined; however, it is not possible to know what the 9th dose was.	
	Metric 10: Exposure Frequency and Duration	High	Exposure duration was appropriate for study.	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	The study included nine exposure groups, and they were sufficient for the determination of LD50 values.	
	Metric 12: Exposure Route and Method	High	Exposure route was appropriate.	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	Medium	Test animal characteristics were not provided in the current study; however, some animal details were reported in White et al. 1985 (HERO 64563). The test animals were obtained from Charles River Breeding Laboratories, and the animal age was specified. Starting body weights were not provided.	
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Study Citation:	Barnes, D. W., Sanders, V. M., White, K. L., Jr, Shopp, G. M., Jr, Munson, A. E. (1985). Toxicology of trans-1,2-dichloroethylene in the mouse. Drug and Chemical Toxicology 8(5):373-392.			
Health Outcome(s):	Mortality			
Reported Health Effect(s):	Mortality: LD10, LD50, and LD90 (survival over 14 days following a single oral administration).			
Duration:	Acute (less than or equal to 24 hr) Acute- single gavage			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	200220; Linked HERO ID(s): 200220, 62637, 5435222			
Domain	Metric	Rating	Comments	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Medium	Husbandry conditions were not reported in this reference, but some methodological details are provided in White et al. 1985 (HERO 64563). The reference stated that food and water were available ad libitum and acceptable room temperature, and humidity targets were used. The photoperiod was 12 hrs. The number of animals per cage was not specified.	
	Metric 15: Number of Animals per Group	Low	The number of animals per group was not reported in the current study. The related methods paper White et al. (HERO 64563) reported that 8 mice/group were routinely used for the acute toxicity studies.	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	High	The study cited White et al. (HERO 64563) for methods. The methods described in white were appropriate and sensitive to the outcomes of interest.	
	Metric 17: Consistency of Outcome Assessment	Medium	Outcome assessment methods were described in White et al. (HERO 64563) and appeared to be consistent across study groups.	
	Metric 18: Sampling Adequacy	Low	Number of animals sampled/group was not reported.	
	Metric 19: Blinding of Assessors	N/A	Blinding was not necessary for this study.	
	Metric 20: Negative Control Response	N/A	Not applicable for this study.	
Domain 6: Confounding / Variable Control				
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	Study did not report all information to determine confounding, reported information did not identify differences between groups.	
	Metric 22: Health Outcomes Unrelated to Exposure	Medium	No information was provided to either to support or dismiss differences in groups in health outcomes or attrition.	
	Metric 23: Data Presentation and Analysis	High	The study used log probit analysis to determine LD50	
	Metric 24: Reporting of Data	High	Data were adequately reported.	
Additional Comments:	Re-Review QC: Shelley Stevens; sstevens@srcinc.comAdditional details were added to comments based on information provided in the study cited for methods (White et al.64563). Scores for the following metrics were changed: 6, 7, 8, 9, 11, 13, 14; and 16 and 23 for the gastrointestinal endpoint only.Form 2d for the acute toxicity study was revised.			

Overall Quality Determination**High**

Study Citation:	Barnes, D. W., Sanders, V. M., White, K. L., Jr, Shopp, G. M., Jr, Munson, A. E. (1985). Toxicology of trans-1,2-dichloroethylene in the mouse. Drug and Chemical Toxicology 8(5):373-392.			
Health Outcome(s):	Gastrointestinal			
Reported Health Effect(s):	Gastrointestinal: Lethality: Gross necropsy of stomach, small intestine			
Duration:	Acute (less than or equal to 24 hr) Acute- single gavage			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	200220; Linked HERO ID(s): 200220, 62637, 5435222			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	Test substance was identified as trans-1,2-dichloroethylene.	
	Metric 2: Test Substance Source	High	The source of the test substance was Aldrich Chemical Co., Milwaukee, WI. Lot number was included.	
	Metric 3: Test Substance Purity	High	Test substance was 98% pure.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	N/A	Lethality study, negative control was not necessary.	
	Metric 5: Positive Controls	N/A	Positive control was not necessary for this study.	
	Metric 6: Randomized Allocation of Animals	Medium	The current study did not specify whether animals were randomly distributed across groups; however, the study followed methodological details reported in HERO ID 64563. This reference indicated that the study animals were randomized (method not specified).	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Medium	DCE was prepared on the day of administration and maintained in dark glassware at 4 °C until use. The test substance is volatile; it was not specified whether the bottles were sealed to prevent volatilization.	
	Metric 8: Consistency of Exposure Administration	High	Exposures were administered consistently across groups; the gavage volume (0.01 mL/g) was reported.	
	Metric 9: Reporting of Doses/Concentrations	Medium	A range of doses was reported. Nine doses ranging from 800-3500 mg/kg. From the results, 8 of the doses can be determined; however, it is not possible to know what the 9th dose was.	
	Metric 10: Exposure Frequency and Duration	High	Exposure duration was appropriate for study.	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	The study included nine exposure groups, and they were sufficient for the determination of LD50 values.	
	Metric 12: Exposure Route and Method	High	Exposure route was appropriate.	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	Medium	Test animal characteristics were not provided in the current study; however, some animal details were reported in White et al. 1985 (HERO 64563). The test animals were obtained from Charles River Breeding Laboratories, and the animal age was specified. Starting body weights were not provided.	
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Study Citation:	Barnes, D. W., Sanders, V. M., White, K. L., Jr, Shopp, G. M., Jr, Munson, A. E. (1985). Toxicology of trans-1,2-dichloroethylene in the mouse. Drug and Chemical Toxicology 8(5):373-392.			
Health Outcome(s):	Gastrointestinal			
Reported Health Effect(s):	Gastrointestinal: Lethality: Gross necropsy of stomach, small intestine			
Duration:	Acute (less than or equal to 24 hr) Acute- single gavage			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	200220; Linked HERO ID(s): 200220, 62637, 5435222			
Domain	Metric	Rating	Comments	
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Husbandry conditions were not reported in this reference, but some methodological details are provided in White et al. 1985 (HERO 64563). The reference stated that food and water were available ad libitum and acceptable room temperature, and humidity targets were used. The photoperiod was 12 hrs. The number of animals per cage was not specified.
	Metric 15:	Number of Animals per Group	Low	The number of animals per group was not reported in the current study. The related methods paper White et al. (HERO 64563) reported that 8 mice/group were routinely used for the acute toxicity studies.
Domain 5: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	High	The study cited White et al. (HERO 64563) for methods. The methods described in white were appropriate and generally consistent with OECD TG 423, with a few omissions. Gross necropsy is not the most sensitive method for identifying organ-specific toxicity, but that was not the purpose of this study.
	Metric 17:	Consistency of Outcome Assessment	Medium	Outcome assessment methods were described in White et al. (HERO 64563) and appeared to be consistent across study groups.
	Metric 18:	Sampling Adequacy	Low	Number of animals sampled/group was not reported.
	Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary for this study.
	Metric 20:	Negative Control Response	N/A	Not applicable for this study.
Domain 6: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Study did not report all information to determine confounding, reported information did not identify differences between groups.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	No information was provided to either to support or dismiss differences in groups in health outcomes or attrition.
	Metric 23:	Data Presentation and Analysis	N/A	Acute lethality study with no control group.
	Metric 24:	Reporting of Data	Low	GI effects observed during necropsy were described qualitatively in the text, but no quantitative data or information about the significance or severity of the effect was included.
Additional Comments:	Re-Review QC: Shelley Stevens; sstevens@srcinc.comAdditional details were added to comments based on information provided in the study cited for methods (White et al.64563). Scores for the following metrics were changed: 6, 7, 8, 9, 11, 13, 14; and 16 and 23 for the gastrointestinal endpoint only.Form 2d for the acute toxicity study was revised.			

Overall Quality Determination**Medium**

Study Citation:	DuPont, (1988). Eye irritation test in rabbits of trans-1,2-dichloroethylene with cover letter dated 05/10/94 (sanitized).			
Health Outcome(s):	Irritation			
Reported Health Effect(s):	Irritation: Eye irritation			
Duration:	Acute (less than or equal to 24 hr) single instillation (unwashed) or 20 seconds (washed)			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	2310778			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1:	Test Substance Identity	High	The test substance was identified as trans-1,2-dichloroethylene; CAS No. 156-60-5). The physical form was a colorless liquid.
	Metric 2:	Test Substance Source	Low	The test substance was a product of PPG Industries, Inc. The batch/lot number was not provided and it was not reported if the test substance identity was certified by the source in the publication or analytically verified by the laboratory.
	Metric 3:	Test Substance Purity	High	The test substance purity was reported as 99.64%. Impurities were not identified.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	N/A	Negative controls are not required for eye irritation tests. Untreated eyes (left) served as the controls for each rabbit.
	Metric 5:	Positive Controls	N/A	Positive controls are not required for eye irritation tests.
	Metric 6:	Randomized Allocation of Animals	N/A	Randomization is not practical. Eye irritation was investigated in two rabbits.
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and Storage of Test Substance	Low	"The test material was assumed to be stable under the conditions of administration". Details regarding the preparation and storage of the test substance were not provided for the volatile substance.
	Metric 8:	Consistency of Exposure Administration	Medium	A 0.01 mL aliquot of the test substance was instilled into the conjunctival sac of the right eye of two rabbits. This is less than the recommended volume of 0.1 mL, but was sufficient to produce eye irritation in both animals. Details of exposure administration are mostly reported, but the missing information is unlikely to have a substantial impact on results.
	Metric 9:	Reporting of Doses/Concentrations	Medium	A 0.01 mL volume was used, but the concentration of the test substance was not specified. It appears the test substance was undiluted, but this was not specifically stated anywhere.
	Metric 10:	Exposure Frequency and Duration	High	The test substance was instilled into the conjunctival sac of the right eye and was either left unwashed or was washed out with lukewarm tap water 20 seconds following instillation of the test substance. This was appropriate to assess eye irritation.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	Justification for selection of the volume used (0.01 ml) was not provided. Current OECD guidelines recommend instilling 0.1 ml of the liquid test substance. However, the test volume was adequate to show results relevant to the outcome of interest (irritation).
	Metric 12:	Exposure Route and Method	High	The exposure method was appropriate for this test. The exposure method was adequately described.

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Study Citation:	DuPont, (1988). Eye irritation test in rabbits of trans-1,2-dichloroethylene with cover letter dated 05/10/94 (sanitized).		
Health Outcome(s):	Irritation		
Reported Health Effect(s):	Irritation: Eye irritation		
Duration:	Acute (less than or equal to 24 hr) single instillation (unwashed) or 20 seconds (washed)		
Chemical:	trans-1,2-Dichloroethylene- Parent compound		
HERO ID:	2310778		
Domain	Metric	Rating	Comments
Domain 4: Test Animals			
Metric 13:	Test Animal Characteristics	Medium	Young adult New Zealand White rabbits (2 females) were obtained from Hare Marland in Hewitt, NJ. Rabbits were quarantined, weighed and observed for 2 weeks but starting bodyweights were not reported. Actual ages of the animals were also not specified. Rabbits are appropriate for eye irritation assessments.
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	The target room temperature was 20 deg. C and humidity was 50%. Any variations were either small in magnitude or were brief. Animals were maintained on timer-controlled 12-hour light/dark cycles. Food and water were available ad libitum.
Metric 15:	Number of Animals per Group	Medium	2 animals were used in this test; it is recommended that just 1 animal be tested in an initial test to assess for severe effects, and if none are observed, additional confirmatory animals should also be tested. This test used 2 animals initially, and severely irritating effects were observed in both.
Domain 5: Outcome Assessment			
Metric 16:	Outcome Assessment Methodology	High	Eye reactions were observed at 1 and 4 hours and on days 1, 2, and 3. Eye lesions were scored using the Draize scale and the scale for biomicroscope classifications of corneal injury. No signs of irritation were observed on day 3, indicating this observation period was of sufficient duration, but the initial reactions were severe.
Metric 17:	Consistency of Outcome Assessment	High	Details of the outcome assessment protocol were reported and outcomes were assessed consistently across study groups using the same protocol in both rabbits.
Metric 18:	Sampling Adequacy	High	Both treated rabbits were evaluated for the outcomes of interest.
Metric 19:	Blinding of Assessors	N/A	Blinding of assessors is not required for eye irritation assessments.
Metric 20:	Negative Control Response	N/A	Negative controls are not required for eye irritation tests.
Domain 6: Confounding / Variable Control			
Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Although the study did not report all information to determine confounding, reported information did not identify differences among the tested animals.
Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure that could influence the outcome assessment.
Metric 23:	Data Presentation and Analysis	N/A	Statistical analysis is not required in an eye irritation test.
Metric 24:	Reporting of Data	High	Data for exposure-related findings were presented for all outcomes for each animal, with tabulated scores from the evaluations at 1 and 4 hours and on days 1, 2, and 3.
Additional Comments:	The study indicated eyes appeared normal by day 3 and were scored as 0; however, recovery seemed somewhat quick considering the severity of the lesions and reactions immediately following instillation of the test substance (severe corneal opacity and "copious bloody discharge").		

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Study Citation:	DuPont, (1988). Eye irritation test in rabbits of trans-1,2-dichloroethylene with cover letter dated 05/10/94 (sanitized).		
Health	Irritation		
Outcome(s):			
Reported Health	Irritation: Eye irritation		
Effect(s):			
Duration:	Acute (less than or equal to 24 hr) single instillation (unwashed) or 20 seconds (washed)		
Chemical:	trans-1,2-Dichloroethylene- Parent compound		
HERO ID:	2310778		
Domain	Metric	Rating	Comments
Overall Quality Determination		High	

Study Citation:	DuPont, (1988). Skin irritation test in rabbits of trans-1,2-dichloroethylene with cover letter dated 05/10/94 (sanitized).			
Health Outcome(s):	Irritation			
Reported Health Effect(s):	Irritation: Skin irritation			
Duration:	Acute (less than or equal to 24 hr) 24 hours			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	2310779			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
Metric 1:	Test Substance Identity	High	The test substance was identified as trans-1,2-dichloroethylene (CAS No. 156-60-5). The physical form was a colorless liquid.	
Metric 2:	Test Substance Source	Low	The test substance was a product of PPG Industries, Inc. The batch/lot number was not provided and it was not reported if the test substance identity was certified by the source in the publication or analytically verified by the laboratory.	
Metric 3:	Test Substance Purity	High	The test substance purity was reported as 99.64%. Impurities were not identified.	
Domain 2: Test Design				
Metric 4:	Negative and Vehicle Controls	N/A	Negative controls are not required for skin irritation studies. "The adjacent areas of the untreated skin were used for comparison".	
Metric 5:	Positive Controls	N/A	Positive controls are not required for skin irritation studies.	
Metric 6:	Randomized Allocation of Animals	N/A	Randomization is not necessary. All animals were administered the same occluded dose of 0.5 ml test substance.	
Domain 3: Exposure Characterization				
Metric 7:	Preparation and Storage of Test Substance	Low	"The test material was assumed to be stable under the conditions of administration". Details regarding the preparation and storage of the test substance were not provided for the volatile substance.	
Metric 8:	Consistency of Exposure Administration	High	Details of exposure administration were reported and exposures were administered consistently across study groups. A 0.5 mL aliquot of the test substance was applied to clipped skin on the backs of rabbits. This is an appropriate volume for skin irritation tests.	
Metric 9:	Reporting of Doses/Concentrations	Medium	A 0.5 mL volume was used, but the concentration of the test substance was not specified. It appears the test substance was undiluted, but this was not specifically stated.	
Metric 10:	Exposure Frequency and Duration	Medium	The test substance was applied to clipped skin under occlusion for 24 hours; 4 hours is usually recommended for acute dermal irritation studies under OECD TG 404.	
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	5 males and 1 female were dosed with 0.5 mL of test substance. This volume was sufficient to elicit an effect (mild irritation).	
Metric 12:	Exposure Route and Method	High	The chlorinated substances are volatile, and an occlusive dressing was appropriate to use. Dermal applications to clipped skin were appropriate to assess the skin irritation potential of the test substance. The exposure method was adequately described.	
Domain 4: Test Animals				
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Study Citation:	DuPont, (1988). Skin irritation test in rabbits of trans-1,2-dichloroethylene with cover letter dated 05/10/94 (sanitized).			
Health Outcome(s):	Irritation			
Reported Health Effect(s):	Irritation: Skin irritation			
Duration:	Acute (less than or equal to 24 hr) 24 hours			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	2310779			
Domain	Metric	Rating	Comments	
	Metric 13: Test Animal Characteristics	Medium	Young adult New Zealand White rabbits (1 female, 5 males) were obtained from Hare Marland in Hewitt, NJ. Rabbits were quarantined, weighed and observed for 2 weeks but starting bodyweights were not reported. Actual ages of the animals were also not specified. Rabbits are appropriate for skin irritation assessments.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	High	The target room temperature was 20 deg. C and humidity was 50%. Any variations were either small in magnitude or were brief. Animals were maintained on timer-controlled 12-hour light/dark cycles. Food and water were available ad libitum except during the 24-hour exposure period.	
	Metric 15: Number of Animals per Group	Medium	6 animals total were used; at least 3 animals are usually recommended.	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	Medium	Skin reactions were evaluated 24, 48, and 72 hours after the test substance was applied to skin and were scored using the Draize scale. OECD TG 404 recommends that skin reactions also be scored 60 minutes after the dermal exposure. Untreated skin adjacent to the application sited were used for comparison. However, erythema was still observed at 72 hours, and animals should have been observed for up to 14 days to examine re- versibility of the skin reactions.	
	Metric 17: Consistency of Outcome Assessment	High	Details of the outcome assessment protocol were reported and outcomes were assessed consistently across study group. Erythema and edema was scored 24, 48, and 72 hours after exposure using the Draize scale.	
	Metric 18: Sampling Adequacy	High	All animals (6 total) included in the study were evaluated for skin reactions following applications of the test substance.	
	Metric 19: Blinding of Assessors	N/A	Blinding of assessors is not required for skin irritation tests.	
	Metric 20: Negative Control Response	N/A	Negative controls are not required for skin irritation tests.	
Domain 6: Confounding / Variable Control				
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	3 other unidentified test substances were tested on the same animals, at different sites. It is unclear if this may have caused confounding.	
	Metric 22: Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure that could influence the outcome assessment.	
	Metric 23: Data Presentation and Analysis	N/A	Statistical analysis is not required in a skin irritation test.	
	Metric 24: Reporting of Data	High	Irritation scores were provided for each animal at 24, 48, and 72 hours, although the sex of each animal was not provided (only animal identification numbers).	
Additional Comments:	None			
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Study Citation:	DuPont, (1988). Skin irritation test in rabbits of trans-1,2-dichloroethylene with cover letter dated 05/10/94 (sanitized).		
Health	Irritation		
Outcome(s):			
Reported Health	Irritation: Skin irritation		
Effect(s):			
Duration:	Acute (less than or equal to 24 hr) 24 hours		
Chemical:	trans-1,2-Dichloroethylene- Parent compound		
HERO ID:	2310779		
Domain	Metric	Rating	Comments
Overall Quality Determination		High	

Study Citation:	Eger, E. I., Halsey, M. J., Koblin, D. D., Laster, M. J., Ionescu, P., Königsberger, K., Fan, R., Nguyen, B. V., Hudlicky, T. (2001). The convulsant and anesthetic properties of cis-trans isomers of 1,2-dichlorohexafluorocyclobutane and 1,2-dichloroethylene. <i>Anesthesia and Analgesia</i> 93(4):922-927.			
Health Outcome(s):	Neurological/Behavioral			
Reported Health Effect(s):	Neurological/Behavioral: Convulsant and anesthetic properties			
Duration:	Acute (less than or equal to 24 hr) Acute; trans-1,2-DCE			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	2310561			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
Metric 1:	Test Substance Identity	High	Test substance was clearly identified by standard nomenclature; structure also provided.	
Metric 2:	Test Substance Source	Low	A commercial source was identified; batch and lot numbers were not provided	
Metric 3:	Test Substance Purity	Medium	The purity of the purchased isomer was 98%. Enrichment of the 2N mixture for the trans isomer yielded an enriched mixture containing 7.8% cis and 92.2% trans-1,2-DCE. The overall purity was >99.8%.	
Domain 2: Test Design				
Metric 4:	Negative and Vehicle Controls	N/A	Not relevant to the study type	
Metric 5:	Positive Controls	N/A	Not relevant for the study type	
Metric 6:	Randomized Allocation of Animals	Low	Allocation method not described.	
Domain 3: Exposure Characterization				
Metric 7:	Preparation and Storage of Test Substance	Low	Generation of test substance atmospheres was partially described	
Metric 8:	Consistency of Exposure Administration	Low	Details of exposure administration were insufficiently reported to determine whether there was consistency of exposure between the two groups of 4 animals	
Metric 9:	Reporting of Doses/Concentrations	Uninformative	No administered exposure concentrations were explicitly reported. The test system was injected with amounts estimated to achieve approximately 60% of the predicted MAC	
Metric 10:	Exposure Frequency and Duration	Low	This information is not clearly reported. At least 20 min to reach equilibrium was indicated; another description in the text indicated it took 100 min to determine MAC	
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Uninformative	Concentrations were not provided, increasing concentrations (not specified) were added until an MAC was reached. There was a single group.	
Metric 12:	Exposure Route and Method	Low	Details of exposure administration were not clearly described.	
Domain 4: Test Animals				
Metric 13:	Test Animal Characteristics	Medium	Species, strain, sex, source, and body weight ranges were reported. Animal age was not provided.	
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Some animal husbandry conditions were reported: light/dark cycle, #/cage, and access to food and water.	
Metric 15:	Number of Animals per Group	Medium	There were 8 animal/group for some experiments, and 4/group for others. The numbers seemed to be appropriate for evaluating the outcome of interest.	
Domain 5: Outcome Assessment				

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Study Citation:	Eger, E. I., Halsey, M. J., Koblin, D. D., Laster, M. J., Ionescu, P., Königsberger, K., Fan, R., Nguyen, B. V., Hudlicky, T. (2001). The convulsant and anesthetic properties of cis-trans isomers of 1,2-dichlorohexafluorocyclobutane and 1,2-dichloroethylene. Anesthesia and Analgesia 93(4):922-927.			
Health Outcome(s):	Neurological/Behavioral			
Reported Health Effect(s):	Neurological/Behavioral: Convulsant and anesthetic properties			
Duration:	Acute (less than or equal to 24 hr) Acute; trans-1,2-DCE			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	2310561			
Domain		Metric	Rating	Comments
	Metric 16:	Outcome Assessment Methodology	Medium	Some outcome methods (e.g., determination olive oil/gas; octanol/gas; and saline/gas partition coefficients) were cited to another reference (FT not available)
	Metric 17:	Consistency of Outcome Assessment	Low	Consistency of outcome assessment was limited or not reported.
	Metric 18:	Sampling Adequacy	Low	Details regarding sampling of outcomes were not reported
	Metric 19:	Blinding of Assessors	N/A	Not necessary for this study type
	Metric 20:	Negative Control Response	N/A	No control groups were included
Domain 6: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design	Medium	The study did not report confounding variables
	Metric 22:	and Procedures Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	N/A	No comparisons were made
	Metric 24:	Reporting of Data	Medium	Means and measures of variance were reported for the outcomes of interest.
Additional Comments:	The purpose of the study was to investigate the correlation of convulsant and anesthetic properties with lipophilicity. The primary endpoint of interest was to determine the MAC (minimum alveolar concentration of anesthetic required to produce an absence of motor response to electrical stimulation of the tail in 50% of test rats) or immobility. Several metrics on this form were not applicable to the design of this study. This study does not provide usable data for evaluating the toxicity of the compound(s) of interest and is more informative for ADME.Additional experiments were performed to determine blood/gas partition coefficients as well as olive-oil/gas, octanol/gas, and saline/gas partition coefficients for each isomer, these were not considered in the evaluation.			

Overall Quality Determination**Uninformative**

Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.			
Health Outcome(s):	Hepatic/Liver; Renal/Kidney;			
Reported Health Effect(s):	Hepatic/Liver: Gross pathology of the liver (acute oral and i.p studies); histopathology of the liver (inhalation – all durations); serum chemistry (cholesterol, bilirubin, total protein, alkaline phosphatase, GOT, GPT, albumin, glucose; in inhalation acute studies and possibly 16-week duration); bile accumulation (acute inhalation); Renal/Kidney: Gross pathology of the kidney and bladder and hematuria (acute oral and i.p studies); histopathology (inhalation – all durations; no effects); serum chemistry (electrolytes, BUN, uric acid – inhalation acute durations);			
Duration:	Acute (less than or equal to 24 hr) Acute inhalation - 8hr			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740886			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
Metric 1:	Test Substance Identity	High	All Outcomes: The test substance was identified by a definitive name, trans-1,2-dichloroethylene.	
Metric 2:	Test Substance Source	Low	All Outcomes: The test substance was obtained from a commercial source (Merck). A batch or lot number was not reported, so this metric is rated Low.	
Metric 3:	Test Substance Purity	Low	All Outcomes: Purity or grade of the test substance was not reported.	
Domain 2: Test Design				
Metric 4:	Negative and Vehicle Controls	High	All Outcomes: It was specified that control animals were treated identically to the treated animals except that no test substance was added to the air (sham-exposed). This was also apparent from Table III, which showed controls for every exposure paradigm.	
Metric 5:	Positive Controls	N/A	All Outcomes: No positive controls are required for this study type.	
Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: The method of allocation of test animals was not reported.	
Domain 3: Exposure Characterization				
Metric 7:	Preparation and Storage of Test Substance	Medium	All Outcomes: Test substance preparation and generation of the vapor for inhalation exposures were reported with adequate detail. Test substance storage was not reported; therefore, this metric is rated as Medium.	
Metric 8:	Consistency of Exposure	High	All Outcomes: The acute exposures occurred daily between 12am-8am	
Metric 9:	Administration Reporting of Doses/Concentrations	Medium	All Outcomes: Target concentrations were reported without ambiguity. Analytical concentrations (gas chromatography) were not specified but were reported to be within 3% of target concentrations. Therefore, the lack of reporting analytical concentrations is not expected to have substantially impacted results.	
Metric 10:	Exposure Frequency and Duration	Medium	All Outcomes: Inhalation exposures were administered for 8 hours per day, which differs from the typical 6 hours per day. However, this difference is not expected to have substantially impacted results.	
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: The acute 8 hr exposures included multiple concentrations (200, 1000, or 3000 ppm) with uneven but adequate dose spacing.	
Metric 12:	Exposure Route and Method	Medium	All Outcomes: The route and exposure method were suited to the test substance. Air changes/hour was specified to be > 10. Whole-body exposure chambers were utilized. The test substance may condense at the higher concentrations tested for the acute exposures.	

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Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.		
Health Outcome(s):	Hepatic/Liver; Renal/Kidney;		
Reported Health Effect(s):	Hepatic/Liver: Gross pathology of the liver (acute oral and i.p studies); histopathology of the liver (inhalation – all durations); serum chemistry (cholesterol, bilirubin, total protein, alkaline phosphatase, GOT, GPT, albumin, glucose; in inhalation acute studies and possibly 16-week duration); bile accumulation (acute inhalation); Renal/Kidney: Gross pathology of the kidney and bladder and hematuria (acute oral and i.p studies); histopathology (inhalation – all durations; no effects); serum chemistry (electrolytes, BUN, uric acid – inhalation acute durations);		
Duration:	Acute (less than or equal to 24 hr) Acute inhalation - 8hr		
Chemical:	trans-1,2-Dichloroethylene- Parent compound		
HERO ID:	1740886		
Domain	Metric	Rating	Comments
Domain 4: Test Animals			
	Metric 13: Test Animal Characteristics	High	All Outcomes: Test animal species, strain, sex, and starting body weight were reported. The age of the test animals was specified to be "mature." The test animals were obtained from a commercial source and were appropriate for the study type.
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Medium	All Outcomes: Most husbandry conditions were reported. Light-dark cycle was not reported.
	Metric 15: Number of Animals per Group	Medium	Hepatic/Liver: 6 animals/group (female only) were utilized for all treatment and control groups. This is sufficient for an acute study and to conduct statistical analysis.; Renal/Kidney: 6-10 animals/group (female only) were utilized for all treatment and control groups. This is sufficient for an acute study and to conduct statistical analysis.
Domain 5: Outcome Assessment			
	Metric 16: Outcome Assessment Methodology	High	Hepatic/Liver: Histopathology (liver), standard clinical chemistry for liver parameters, and a measure of bile clearance were considered to be adequate to assess the outcome of interest.; Renal/Kidney: Histopathology and standard clinical chemistry were considered to be adequate to assess the outcome of interest. Organ weights were not measured.
	Metric 17: Consistency of Outcome Assessment	High	All Outcomes: Outcomes appeared to be assessed consistently across study groups. Protocols were provided.
	Metric 18: Sampling Adequacy	High	Hepatic/Liver: All 6 animals/group appear to have been sampled for histopathology based on Table III. Separate groups of animals were used for bile clearance experiments and the sampling was adequate.; Renal/Kidney: All 6 animals/group appear to have been sampled for histopathology based on Table III. The sampling for clinical chemistry indicates data were derived from 15 animals (controls), and from 10/group (treated).
	Metric 19: Blinding of Assessors	N/A	All Outcomes: Blinding is not required for initial histopathology.
	Metric 20: Negative Control Response	High	All Outcomes: Negative control responses were appropriate
Domain 6: Confounding / Variable Control			
	Metric 21: Confounding Variables in Test Design and Procedures	High	All Outcomes: No confounding variables were reported or identified.
	Metric 22: Health Outcomes Unrelated to Exposure	High	All Outcomes: There is no evidence of health outcomes unrelated to exposure.
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Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.			
Health Outcome(s):	Hepatic/Liver; Renal/Kidney;			
Reported Health Effect(s):	Hepatic/Liver: Gross pathology of the liver (acute oral and i.p studies); histopathology of the liver (inhalation – all durations); serum chemistry (cholesterol, bilirubin, total protein, alkaline phosphatase, GOT, GPT, albumin, glucose; in inhalation acute studies and possibly 16-week duration); bile accumulation (acute inhalation); Renal/Kidney: Gross pathology of the kidney and bladder and hematuria (acute oral and i.p studies); histopathology (inhalation – all durations; no effects); serum chemistry (electrolytes, BUN, uric acid – inhalation acute durations);			
Duration:	Acute (less than or equal to 24 hr) Acute inhalation - 8hr			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740886			
Domain	Metric	Rating	Comments	
	Metric 23: Data Presentation and Analysis	Low	Hepatic/Liver: For clinical chemistry, inappropriate statistical methods were utilized; first, multiple t-tests were conducted on the same data; second, normality was assumed without conducting a test for normality; and third, the t-tests conducted were one-tailed, which is not justified for all of the parameters tested (clinical chemistry parameters can either increase or decrease from controls). All of these statistical oversights contribute to substantially increasing the Type I error rate beyond the generally accepted rate of 5%; one-tailed t-tests alone doubles the Type I error rate. However, although information regarding distribution was not provided and an independent normality test is not possible, if normality is assumed then independent statistical analysis to compare means can be conducted given that means and SEM are provided. Means and SEMs could be extracted from Figure 3 and SEMs converted to SDs. Therefore, since independent statistical analysis is possible but would lack a normality test, this metric is rated as Low. For bile clearance data, one-tailed t-tests are justified but again lack a normality test. Histopathology data were not statistically analyzed, but sufficient information is provided for an independent analysis.; Renal/Kidney: For clinical chemistry, inappropriate statistical methods were utilized; first, multiple t-tests were conducted on the same data; second, normality was assumed without conducting a test for normality; and third, the t-tests conducted were one-tailed, which is not justified for all of the parameters tested (clinical chemistry parameters can either increase or decrease from controls). All of these statistical oversights contribute to substantially increasing the Type I error rate beyond the generally accepted rate of 5%; one-tailed t-tests alone doubles the Type I error rate. However, although information regarding distribution was not provided and an independent normality test is not possible, if normality is assumed then independent statistical analysis to compare means can be conducted given that means and SEM are provided. Means and SEMs could be extracted from Figure 3 and SEMs converted to SDs. Therefore, since independent statistical analysis is possible but would lack a normality test, this metric is rated as Low. Statistical analysis of histopathology data was not required (negative findings were reported qualitatively).	
	Metric 24: Reporting of Data	High	Hepatic/Liver: Data were adequately reported as means ± SEM or as incidences including levels of severity.; Renal/Kidney: Data were adequately reported as means ± SEM (clinical chemistry) or negative findings were reported qualitatively (histopathology)	
Additional Comments: None				

Overall Quality Determination**High**

Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.			
Health Outcome(s):	Lung/Respiratory			
Reported Health Effect(s):	Lung/Respiratory: Lungs: gross pathology (acute oral and i.p studies); histopathology (inhalation – all durations)			
Duration:	Acute (less than or equal to 24 hr) Acute inhalation - 8hr			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740886			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	The test substance was identified by a definitive name, trans-1,2-dichloroethylene.	
	Metric 2: Test Substance Source	Low	The test substance was obtained from a commercial source (Merck). A batch or lot number was not reported, so this metric is rated Low.	
	Metric 3: Test Substance Purity	Low	Purity or grade of the test substance was not reported.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	It was specified that control animals were treated identically to the treated animals except that no test substance was added to the air (sham-exposed). This was also apparent from Table III, which showed controls for every exposure paradigm.	
	Metric 5: Positive Controls	N/A	No positive controls are required for this study type.	
	Metric 6: Randomized Allocation of Animals	Low	The method of allocation of test animals was not reported.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Medium	Test substance preparation and generation of the vapor for inhalation exposures were reported with adequate detail. Test substance storage was not reported; therefore, this metric is rated as Medium.	
	Metric 8: Consistency of Exposure Administration	High	The acute exposures occurred daily between 12am-8am	
	Metric 9: Reporting of Doses/Concentrations	Medium	Target concentrations were reported without ambiguity. Analytical concentrations (gas chromatography) were not specified but were reported to be within 3% of target concentrations. Therefore, the lack of reporting analytical concentrations is not expected to have substantially impacted results.	
	Metric 10: Exposure Frequency and Duration	Medium	Inhalation exposures were administered for 8 hours per day, which differs from the typical 6 hours per day. However, this difference is not expected to have substantially impacted results.	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	The acute 8 hr exposures included multiple concentrations (200, 1000, or 3000 ppm) with uneven but adequate dose spacing.	
	Metric 12: Exposure Route and Method	Medium	The route and exposure method were suited to the test substance. Air changes/hour was specified to be > 10. Whole-body exposure chambers were utilized. The test substance may condense at the higher concentrations tested for the acute exposures.	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	High	Test animal species, strain, sex, and starting body weight were reported. The age of the test animals was specified to be "mature." The test animals were obtained from a commercial source and were appropriate for the study type.	
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Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.			
Health Outcome(s):	Lung/Respiratory			
Reported Health Effect(s):	Lung/Respiratory: Lungs: gross pathology (acute oral and i.p studies); histopathology (inhalation – all durations)			
Duration:	Acute (less than or equal to 24 hr) Acute inhalation - 8hr			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740886			
Domain	Metric	Rating	Comments	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Medium	Most husbandry conditions were reported. Light-dark cycle was not reported.	
	Metric 15: Number of Animals per Group	Medium	6 animals/group (female only) were utilized for all treatment and control groups. This is sufficient for an acute study and to conduct statistical analysis.	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	High	Histopathology was considered to be adequate to assess the outcome of interest. Organs were not weighed.	
	Metric 17: Consistency of Outcome Assessment	Medium	Outcomes appeared to be assessed consistently across study groups. A protocol for histopathology was provided.	
	Metric 18: Sampling Adequacy	High	All 6 animals/group appear to have been sampled for histopathology based on Table III.	
	Metric 19: Blinding of Assessors	N/A	Blinding is not required for initial histopathology.	
	Metric 20: Negative Control Response	High	Negative control responses were appropriate	
Domain 6: Confounding / Variable Control				
	Metric 21: Confounding Variables in Test Design and Procedures	High	No confounding variables were reported or identified.	
	Metric 22: Health Outcomes Unrelated to Exposure	High	There is no evidence of health outcomes unrelated to exposure.	
	Metric 23: Data Presentation and Analysis	High	Statistical analysis was not performed, but sufficient data were provided to allow for independent analysis.	
	Metric 24: Reporting of Data	High	Data were adequately reported as incidences including level of severity.	
Additional Comments:	None			
Overall Quality Determination		High		

Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.			
Health Outcome(s):	Musculoskeletal			
Reported Health Effect(s):	Musculoskeletal: Histopathology (quadriceps muscle; inhalation, all durations)			
Duration:	Acute (less than or equal to 24 hr) Acute inhalation - 8hr			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740886			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	The test substance was identified by a definitive name, trans-1,2-dichloroethylene.	
	Metric 2: Test Substance Source	Low	The test substance was obtained from a commercial source (Merck). A batch or lot number was not reported, so this metric is rated Low.	
	Metric 3: Test Substance Purity	Low	Purity or grade of the test substance was not reported.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	It was specified that control animals were treated identically to the treated animals except that no test substance was added to the air (sham-exposed). This was also apparent from Table III, which showed controls for every exposure paradigm.	
	Metric 5: Positive Controls	N/A	No positive controls are required for this study type.	
	Metric 6: Randomized Allocation of Animals	Low	The method of allocation of test animals was not reported.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Medium	Test substance preparation and generation of the vapor for inhalation exposures were reported with adequate detail. Test substance storage was not reported; therefore, this metric is rated as Medium.	
	Metric 8: Consistency of Exposure Administration	High	The acute exposures occurred daily between 12am-8am	
	Metric 9: Reporting of Doses/Concentrations	Medium	Target concentrations were reported without ambiguity. Analytical concentrations (gas chromatography) were not specified but were reported to be within 3% of target concentrations. Therefore, the lack of reporting analytical concentrations is not expected to have substantially impacted results.	
	Metric 10: Exposure Frequency and Duration	Medium	Inhalation exposures were administered for 8 hours per day, which differs from the typical 6 hours per day. However, this difference is not expected to have substantially impacted results.	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	The acute 8 hr exposures included multiple concentrations (200, 1000, or 3000 ppm) with uneven but adequate dose spacing.	
	Metric 12: Exposure Route and Method	Medium	The route and exposure method were suited to the test substance. Air changes/hour was specified to be > 10. Whole-body exposure chambers were utilized. The test substance may condense at the higher concentrations tested for the acute exposures.	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	High	Test animal species, strain, sex, and starting body weight were reported. The age of the test animals was specified to be "mature." The test animals were obtained from a commercial source and were appropriate for the study type.	
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Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.			
Health Outcome(s):	Musculoskeletal			
Reported Health Effect(s):	Musculoskeletal: Histopathology (quadriceps muscle; inhalation, all durations)			
Duration:	Acute (less than or equal to 24 hr) Acute inhalation - 8hr			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740886			
Domain	Metric	Rating	Comments	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Medium	Most husbandry conditions were reported. Light-dark cycle was not reported.	
	Metric 15: Number of Animals per Group	Medium	6 animals/group (female only) were utilized for all treatment and control groups. This is sufficient for an acute study and to conduct statistical analysis.	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	High	Histopathology was considered to be adequate to assess the outcome of interest.	
	Metric 17: Consistency of Outcome Assessment	Medium	Outcomes appeared to be assessed consistently across study groups. A protocol for histopathology was provided.	
	Metric 18: Sampling Adequacy	High	All 6 animals/group appear to have been sampled for histopathology based on Table III. Table III reports histopathology results for the lung and liver, but it is assumed that histopathology for all organs specified was carried out on these animals.	
	Metric 19: Blinding of Assessors	N/A	Blinding is not required for initial histopathology.	
	Metric 20: Negative Control Response	Low	Negative control responses were not explicitly reported	
Domain 6: Confounding / Variable Control				
	Metric 21: Confounding Variables in Test Design and Procedures	High	No confounding variables were reported or identified.	
	Metric 22: Health Outcomes Unrelated to Exposure	High	There is no evidence of health outcomes unrelated to exposure.	
	Metric 23: Data Presentation and Analysis	N/A	Statistical analysis was not necessary given the negative findings (qualitatively described).	
	Metric 24: Reporting of Data	High	Negative data were qualitatively described.	
Additional Comments:	None			
Overall Quality Determination		High		

Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.			
Health Outcome(s):	Cardiovascular			
Reported Health Effect(s):	Cardiovascular: Heart (gross pathology in acute oral and i.p studies); histopathology (inhalation – acute)			
Duration:	Acute (less than or equal to 24 hr) Acute inhalation - 8hr			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740886			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	The test substance was identified by a definitive name, trans-1,2-dichloroethylene.	
	Metric 2: Test Substance Source	Low	The test substance was obtained from a commercial source (Merck). A batch or lot number was not reported, so this metric is rated Low.	
	Metric 3: Test Substance Purity	Low	Purity or grade of the test substance was not reported.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	It was specified that control animals were treated identically to the treated animals except that no test substance was added to the air (sham-exposed). This was also apparent from Table III, which showed controls for every exposure paradigm.	
	Metric 5: Positive Controls	N/A	No positive controls are required for this study type.	
	Metric 6: Randomized Allocation of Animals	Low	The method of allocation of test animals was not reported.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Medium	Test substance preparation and generation of the vapor for inhalation exposures were reported with adequate detail. Test substance storage was not reported; therefore, this metric is rated as Medium.	
	Metric 8: Consistency of Exposure Administration	High	The acute exposures occurred daily between 12am-8am	
	Metric 9: Reporting of Doses/Concentrations	Medium	Target concentrations were reported without ambiguity. Analytical concentrations (gas chromatography) were not specified but were reported to be within 3% of target concentrations. Therefore, the lack of reporting analytical concentrations is not expected to have substantially impacted results.	
	Metric 10: Exposure Frequency and Duration	Medium	Inhalation exposures were administered for 8 hours per day, which differs from the typical 6 hours per day. However, this difference is not expected to have substantially impacted results.	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	The acute 8 hr exposures included multiple concentrations (200, 1000, or 3000 ppm) with uneven but adequate dose spacing.	
	Metric 12: Exposure Route and Method	Medium	The route and exposure method were suited to the test substance. Air changes/hour was specified to be > 10. Whole-body exposure chambers were utilized. The test substance may condense at the higher concentrations tested for the acute exposures.	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	High	Test animal species, strain, sex, and starting body weight were reported. The age of the test animals was specified to be "mature." The test animals were obtained from a commercial source and were appropriate for the study type.	
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Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.			
Health Outcome(s):	Cardiovascular			
Reported Health Effect(s):	Cardiovascular: Heart (gross pathology in acute oral and i.p studies); histopathology (inhalation – acute)			
Duration:	Acute (less than or equal to 24 hr) Acute inhalation - 8hr			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740886			
Domain	Metric	Rating	Comments	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Medium	Most husbandry conditions were reported. Light-dark cycle was not reported.	
	Metric 15: Number of Animals per Group	Medium	6 animals/group (female only) were utilized for all treatment and control groups. This is sufficient for an acute study and to conduct statistical analysis.	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	High	Histopathology (heart) was considered to be adequate to assess the outcome of interest.	
	Metric 17: Consistency of Outcome Assessment	Medium	Heart histopathology data were only reported for the 3000 ppm acute inhalation exposure and the corresponding control. A protocol for histopathology was provided.	
	Metric 18: Sampling Adequacy	High	All 6 animals/group appear to have been sampled for histopathology based on Table III. Table III reports histopathology results for the lung and liver, but it is assumed that histopathology for all organs specified was carried out on these animals.	
	Metric 19: Blinding of Assessors	N/A	Blinding is not required for initial histopathology.	
	Metric 20: Negative Control Response	Medium	Heart histopathology data were only reported for the 3000 ppm acute inhalation exposure and the corresponding control. It is assumed that no changes were observed in other groups, but no qualitative statement was provided.	
Domain 6: Confounding / Variable Control				
	Metric 21: Confounding Variables in Test Design and Procedures	High	No confounding variables were reported or identified.	
	Metric 22: Health Outcomes Unrelated to Exposure	High	No effects unrelated to exposure were reported or identified.	
	Metric 23: Data Presentation and Analysis	N/A	Statistical analysis was not necessary given the negative findings (qualitatively described).	
	Metric 24: Reporting of Data	Low	Heart histopathology data were only reported for the 3000 ppm acute inhalation exposure and the corresponding control. It is assumed that no changes were observed in other groups, but no qualitative statement was provided.	
Additional Comments: None				
Overall Quality Determination		High		

Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.			
Health Outcome(s):	Immune/Hematological			
Reported Health Effect(s):	Immune/Hematological: Histopathology (spleen; inhalation – all durations; no effects); hematology (WBC count, RBC count, Hgb, packed cell volume, MCV, MCH, MCHC; inhalation studies – acute duration)			
Duration:	Acute (less than or equal to 24 hr) Acute inhalation - 8hr			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740886			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	The test substance was identified by a definitive name, trans-1,2-dichloroethylene.	
	Metric 2: Test Substance Source	Low	The test substance was obtained from a commercial source (Merck). A batch or lot number was not reported, so this metric is rated Low.	
	Metric 3: Test Substance Purity	Low	Purity or grade of the test substance was not reported.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	It was specified that control animals were treated identically to the treated animals except that no test substance was added to the air (sham-exposed). This was also apparent from Table III, which showed controls for every exposure paradigm.	
	Metric 5: Positive Controls	N/A	No positive controls are required for this study type.	
	Metric 6: Randomized Allocation of Animals	Low	The method of allocation of test animals was not reported.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Medium	Test substance preparation and generation of the vapor for inhalation exposures were reported with adequate detail. Test substance storage was not reported; therefore, this metric is rated as Medium.	
	Metric 8: Consistency of Exposure Administration	High	The acute exposures occurred daily between 12am-8am	
	Metric 9: Reporting of Doses/Concentrations	Medium	Target concentrations were reported without ambiguity. Analytical concentrations (gas chromatography) were not specified but were reported to be within 3% of target concentrations. Therefore, the lack of reporting analytical concentrations is not expected to have substantially impacted results.	
	Metric 10: Exposure Frequency and Duration	Medium	Inhalation exposures were administered for 8 hours per day, which differs from the typical 6 hours per day. However, this difference is not expected to have substantially impacted results.	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	The acute 8 hr exposures included multiple concentrations (200, 1000, or 3000 ppm) with uneven but adequate dose spacing.	
	Metric 12: Exposure Route and Method	Medium	The route and exposure method were suited to the test substance. Air changes/hour was specified to be > 10. Whole-body exposure chambers were utilized. The test substance may condense at the higher concentrations tested for the acute exposures.	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	High	Test animal species, strain, sex, and starting body weight were reported. The age of the test animals was specified to be "mature." The test animals were obtained from a commercial source and were appropriate for the study type.	
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Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.			
Health Outcome(s):	Immune/Hematological			
Reported Health Effect(s):	Immune/Hematological: Histopathology (spleen; inhalation – all durations; no effects); hematology (WBC count, RBC count, Hgb, packed cell volume, MCV, MCH, MCHC; inhalation studies – acute duration)			
Duration:	Acute (less than or equal to 24 hr) Acute inhalation - 8hr			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740886			
Domain	Metric	Rating	Comments	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Medium	Most husbandry conditions were reported. Light-dark cycle was not reported.	
	Metric 15: Number of Animals per Group	Medium	6-10 animals/group (female only) were utilized for all treatment and control groups. This is sufficient for an acute study and to conduct statistical analysis.	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	High	Histopathology and standard hematology were considered to be adequate to assess the outcome of interest. Organ weights were not measured.	
	Metric 17: Consistency of Outcome Assessment	Medium	It appears that only the acute exposures at 200 and 1000 ppm (not 3000 ppm) were assessed for hematology. Otherwise, assessments appeared to be consistent across groups.	
	Metric 18: Sampling Adequacy	Low	The sample size for hematology measurements was not reported. All 6 animals/group appear to have been sampled for histopathology based on Table III. Table III reports histopathology results for the lung and liver, but it is assumed that histopathology for all organs specified was carried out on these animals.	
	Metric 19: Blinding of Assessors	N/A	Blinding is not required for initial histopathology or non-subjective outcomes (hematology).	
	Metric 20: Negative Control Response	High	Negative control responses for hematology were appropriate. Negative control responses for histopathology were not explicitly reported, but it was indicated that no hematological findings were observed, so this is presumed to include the controls.	
Domain 6: Confounding / Variable Control				
	Metric 21: Confounding Variables in Test Design and Procedures	High	No confounding variables were reported or identified.	
	Metric 22: Health Outcomes Unrelated to Exposure	High	There is no evidence of health outcomes unrelated to exposure.	
	Metric 23: Data Presentation and Analysis	Low	Statistical analysis was not necessary for negative pathology findings. For hematology, inappropriate statistical methods were utilized; first, multiple t-tests were conducted on the same data; second, normality was assumed without conducting a test for normality; and third, the t-tests conducted were one-tailed, which is not justified for all of the parameters tested (hematology parameters can either increase or decrease from controls). All of these statistical oversights contribute to substantially increasing the Type I error rate beyond the generally accepted rate of 5%; one-tailed t-tests alone doubles the Type I error rate. However, although information regarding distribution was not provided and an independent normality test is not possible, if normality is assumed then independent statistical analysis to compare means can be conducted given that means and SEM are provided. Means and SEMs could be extracted from Figure 3 and SEMs converted to SDs. Therefore, since independent statistical analysis is possible but would lack a normality test, this metric is rated as Low.	
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Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.
Health Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Immune/Hematological: Histopathology (spleen; inhalation – all durations; no effects); hematology (WBC count, RBC count, Hgb, packed cell volume, MCV, MCH, MCHC; inhalation studies – acute duration)
Duration:	Acute (less than or equal to 24 hr) Acute inhalation - 8hr
Chemical:	trans-1,2-Dichloroethylene- Parent compound
HERO ID:	1740886

Domain	Metric	Rating	Comments
	Metric 24: Reporting of Data	High	Data were adequately reported as means $\pm$ SEM (hematology) or negative findings were reported qualitatively (histopathology)

Additional Comments: None

Overall Quality Determination**High**

Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.		
Health Outcome(s):	Neurological/Behavioral		
Reported Health Effect(s):	Neurological/Behavioral: Neurological/behavioral clinical signs (acute oral and ip and inhalation – all durations); histopathology brain and peripheral nerves (inhalation – all durations, no effects)		
Duration:	Acute (less than or equal to 24 hr) Acute inhalation - 8hr		
Chemical:	trans-1,2-Dichloroethylene- Parent compound		
HERO ID:	1740886		
Domain	Metric	Rating	Comments
Domain 1: Test Substance			
	Metric 1: Test Substance Identity	High	The test substance was identified by a definitive name, trans-1,2-dichloroethylene.
	Metric 2: Test Substance Source	Low	The test substance was obtained from a commercial source (Merck). A batch or lot number was not reported, so this metric is rated Low.
	Metric 3: Test Substance Purity	Low	Purity or grade of the test substance was not reported.
Domain 2: Test Design			
	Metric 4: Negative and Vehicle Controls	High	It was specified that control animals were treated identically to the treated animals except that no test substance was added to the air (sham-exposed). This was also apparent from Table III, which showed controls for every exposure paradigm.
	Metric 5: Positive Controls	N/A	No positive controls are required for this study type.
	Metric 6: Randomized Allocation of Animals	Low	The method of allocation of test animals was not reported.
Domain 3: Exposure Characterization			
	Metric 7: Preparation and Storage of Test Substance	Medium	Test substance preparation and generation of the vapor for inhalation exposures were reported with adequate detail. Test substance storage was not reported; therefore, this metric is rated as Medium.
	Metric 8: Consistency of Exposure Administration	High	The acute exposures occurred daily between 12am-8am
	Metric 9: Reporting of Doses/Concentrations	Medium	Target concentrations were reported without ambiguity. Analytical concentrations (gas chromatography) were not specified but were reported to be within 3% of target concentrations. Therefore, the lack of reporting analytical concentrations is not expected to have substantially impacted results.
	Metric 10: Exposure Frequency and Duration	Medium	Inhalation exposures were administered for 8 hours per day, which differs from the typical 6 hours per day. However, this difference is not expected to have substantially impacted results.
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	The acute 8 hr exposures included multiple concentrations (200, 1000, or 3000 ppm) with uneven but adequate dose spacing.
	Metric 12: Exposure Route and Method	Medium	The route and exposure method were suited to the test substance. Air changes/hour was specified to be > 10. Whole-body exposure chambers were utilized. The test substance may condense at the higher concentrations tested for the acute exposures.
Domain 4: Test Animals			
	Metric 13: Test Animal Characteristics	High	Test animal species, strain, sex, and starting body weight were reported. The age of the test animals was specified to be "mature." The test animals were obtained from a commercial source and were appropriate for the study type.
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Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.			
Health Outcome(s):	Neurological/Behavioral			
Reported Health Effect(s):	Neurological/Behavioral: Neurological/behavioral clinical signs (acute oral and ip and inhalation – all durations); histopathology brain and peripheral nerves (inhalation – all durations, no effects)			
Duration:	Acute (less than or equal to 24 hr) Acute inhalation - 8hr			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740886			
Domain	Metric	Rating	Comments	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Medium	Most husbandry conditions were reported. Light-dark cycle was not reported.	
	Metric 15: Number of Animals per Group	Medium	6 animals/group (female only) were utilized for all treatment and control groups. This is sufficient for an acute study and to conduct statistical analysis	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	Medium	Histopathology (brain, sciatic nerve) and clinical signs were considered to be adequate to assess the outcome of interest. The study authors were specifically interested in acute neurotoxicity (CNS depression), which was the basis of the TLV-MAC (200 ppm) that was the focus of the study. This would be appropriately addressed by noting clinical signs of toxicity during exposure administration. A protocol for animal observations (frequency/duration) was not provided.	
	Metric 17: Consistency of Outcome Assessment	Medium	Outcomes appeared to be assessed consistently across study groups. A protocol for histopathology was provided, but not for clinical observations.	
	Metric 18: Sampling Adequacy	High	It is unclear whether all 6 animals/group were sampled for clinical signs. All 6 animals/group appear to have been sampled for histopathology based on Table III. Table III reports histopathology results for the lung and liver, but it is assumed that histopathology for all organs specified was carried out on these animals.	
	Metric 19: Blinding of Assessors	N/A	Blinding is not required for initial histopathology. Blinding was not specified for clinical observations, but generally is not included in acute exposure studies.	
	Metric 20: Negative Control Response	High	Negative controls responded appropriately.	
Domain 6: Confounding / Variable Control				
	Metric 21: Confounding Variables in Test Design and Procedures	High	No confounding variables were reported or identified.	
	Metric 22: Health Outcomes Unrelated to Exposure	High	No effects unrelated to exposure were reported or identified.	
	Metric 23: Data Presentation and Analysis	N/A	Statistical analysis was not necessary given the negative findings (qualitatively described).	
	Metric 24: Reporting of Data	High	Negative data were qualitatively described.	
Additional Comments:	None			
Overall Quality Determination		High		

Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.			
Health Outcome(s):	Mortality			
Reported Health Effect(s):	Mortality: Mortality (acute oral and i,p studies)			
Duration:	Acute (less than or equal to 24 hr) Single dose i.p. (rats and mice)			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740886			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	The test substance was identified by a definitive name, trans-1,2-dichloroethylene.	
	Metric 2: Test Substance Source	Low	The test substance was obtained from a commercial source (Merck). A batch or lot number was not reported, so this metric is rated Low.	
	Metric 3: Test Substance Purity	Low	Purity or grade of the test substance was not reported.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	N/A	No negative controls are necessary for acute lethality determination.	
	Metric 5: Positive Controls	N/A	No positive controls are required for this study type.	
	Metric 6: Randomized Allocation of Animals	Low	The method of allocation of test animals was not reported.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Medium	Test substance preparation in vehicle was reported. Test substance storage was not reported for the volatile substance; therefore, this metric is rated Medium.	
	Metric 8: Consistency of Exposure Administration	High	Test substances were administered consistently across treatment groups (dose levels); gavage volume was consistent and not excessive.	
	Metric 9: Reporting of Doses/Concentrations	High	Doses were reported without ambiguity.	
	Metric 10: Exposure Frequency and Duration	High	Single doses are appropriate for an acute lethality test.	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	The number of dose groups and dose spacing were adequate for the purpose of the study. A range of responses were observed.	
	Metric 12: Exposure Route and Method	High	The route and exposure method were appropriate for the purpose of the study.	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	High	Test animal species, strain, sex, and starting body weight were reported. The age of the test animals was specified to be "mature." The test animals were obtained from a commercial source and were appropriate for the study type.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Medium	Most husbandry conditions were reported. Light-dark cycle was not reported.	
	Metric 15: Number of Animals per Group	Medium	10 animals/group (female only) were utilized for all treatment groups.	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	High	Number of deaths and time of death are appropriate to determine the LD50.	
	Metric 17: Consistency of Outcome Assessment	High	Outcomes appeared to be assessed consistently across study groups. A protocol is provided.	
	Metric 18: Sampling Adequacy	High	All 10 animals/group were observed for mortality after dosing.	
	Metric 19: Blinding of Assessors	N/A	No subjective outcomes were assessed.	
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Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.			
Health Outcome(s):	Mortality			
Reported Health Effect(s):	Mortality: Mortality (acute oral and i,p studies)			
Duration:	Acute (less than or equal to 24 hr) Single dose i.p. (rats and mice)			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740886			
Domain	Metric	Rating	Comments	
	Metric 20: Negative Control Response	N/A	No negative controls were necessary for the acute lethality test.	
Domain 6: Confounding / Variable Control				
	Metric 21: Confounding Variables in Test Design and Procedures	High	No confounding variables were reported or identified.	
	Metric 22: Health Outcomes Unrelated to Exposure	High	No effects unrelated to exposure were reported or identified.	
	Metric 23: Data Presentation and Analysis	High	Statistical analysis was described and appropriate for the data.	
	Metric 24: Reporting of Data	High	Data were reported adequately.	
Additional Comments:	None			
Overall Quality Determination		High		

Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.			
Health Outcome(s):	Neurological/Behavioral			
Reported Health Effect(s):	Neurological/Behavioral: Neurological/behavioral clinical signs (acute oral and ip and inhalation – all durations); histopathology brain and peripheral nerves (inhalation – all durations, no effects)			
Duration:	Acute (less than or equal to 24 hr) Single dose i.p. (rats and mice)			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740886			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1:	Test Substance Identity	High	The test substance was identified by a definitive name, trans-1,2-dichloroethylene.
	Metric 2:	Test Substance Source	Low	The test substance was obtained from a commercial source (Merck). A batch or lot number was not reported, so this metric is rated Low.
	Metric 3:	Test Substance Purity	Low	Purity or grade of the test substance was not reported.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	N/A	No negative controls are necessary for acute lethality determination.
	Metric 5:	Positive Controls	N/A	No positive controls are required for this study type.
	Metric 6:	Randomized Allocation of Animals	Low	The method of allocation of test animals was not reported.
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and Storage of Test Substance	Medium	Test substance preparation in vehicle was reported. Test substance storage was not reported for the volatile substance; therefore, this metric is rated Medium.
	Metric 8:	Consistency of Exposure Administration	High	Test substances were administered consistently across treatment groups (dose levels); gavage volume was consistent within each species and not excessive.
	Metric 9:	Reporting of Doses/Concentrations	High	Doses were reported without ambiguity.
	Metric 10:	Exposure Frequency and Duration	High	Single doses are appropriate for an acute lethality test.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The number of dose groups and dose spacing were adequate for the purpose of the study. A range of responses were observed.
	Metric 12:	Exposure Route and Method	High	The route and exposure method were appropriate for the purpose of the study.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	High	Test animal species, strain, sex, and starting body weight were reported. The age of the test animals was specified to be "mature." The test animals were obtained from a commercial source and were appropriate for the study type.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Most husbandry conditions were reported. Light-dark cycle was not reported.
	Metric 15:	Number of Animals per Group	Medium	10 animals/group (female only) were utilized for all treatment groups.
Domain 5: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	Low	The details of the outcome assessment were not described in the study methods, but based on the reported results, animals were observed for behavioral changes. The duration and frequency of the observation were not specified. Clinical signs alone are not typically a sensitive measure for assessing neurological effects but are consistent with the endpoints evaluated in an acute lethality study.

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Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.			
Health Outcome(s):	Neurological/Behavioral			
Reported Health Effect(s):	Neurological/Behavioral: Neurological/behavioral clinical signs (acute oral and ip and inhalation – all durations); histopathology brain and peripheral nerves (inhalation – all durations, no effects)			
Duration:	Acute (less than or equal to 24 hr) Single dose i.p. (rats and mice)			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740886			
Domain	Metric		Rating	Comments
	Metric 17:	Consistency of Outcome Assessment	Low	Since no methods for this outcome assessment were provided, it is unclear whether the outcome was assessed consistently across groups.
	Metric 18:	Sampling Adequacy	Medium	Although it was not explicitly stated, it appears that all 10 animals/group were observed.
	Metric 19:	Blinding of Assessors	N/A	Blinding is not required in acute lethality studies, although clinical observations may be subjective in nature.
	Metric 20:	Negative Control Response	N/A	No negative controls were necessary for the acute lethality test.
Domain 6: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	High	No confounding variables were reported or identified.
	Metric 22:	Health Outcomes Unrelated to Exposure	High	No effects unrelated to exposure were reported or identified.
	Metric 23:	Data Presentation and Analysis	N/A	Statistical analysis was not necessary because no control or comparator group was used.
	Metric 24:	Reporting of Data	Low	Symptoms were qualitatively described in a table. The incidences and timing (other than following injection) were not specified.
Additional Comments: None				

Overall Quality Determination**Medium**

Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.			
Health Outcome(s):	Gastrointestinal; Lung/Respiratory; Lung/Respiratory; Hepatic/Liver; Hepatic/Liver; Renal/Kidney;			
Reported Health Effect(s):	Gastrointestinal: Gastrointestinal (gross pathology in acute oral and i.p studies); Lung/Respiratory: Lungs: gross pathology (acute oral and i.p studies); histopathology (inhalation – all durations); Lung/Respiratory: Lungs: gross pathology (acute oral and i.p studies); histopathology (inhalation – all durations); Hepatic/Liver: Gross pathology of the liver (acute oral and i.p studies); histopathology of the liver (inhalation – all durations); serum chemistry (cholesterol, bilirubin, total protein, alkaline phosphatase, GOT, GPT, albumin, glucose; in inhalation acute studies and possibly 16-week duration); bile accumulation (acute inhalation); Hepatic/Liver: Gross pathology of the liver (acute oral and i.p studies); histopathology of the liver (inhalation – all durations); serum chemistry (cholesterol, bilirubin, total protein, alkaline phosphatase, GOT, GPT, albumin, glucose; in inhalation acute studies and possibly 16-week duration); bile accumulation (acute inhalation); Renal/Kidney: Gross pathology of the kidney and bladder and hematuria (acute oral and i.p studies); histopathology (inhalation – all durations; no effects); serum chemistry (electrolytes, BUN, uric acid – inhalation acute durations);			
Duration:	Acute (less than or equal to 24 hr) Single dose i.p. (rats and mice)			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740886			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	All Outcomes: The test substance was identified by a definitive name, trans-1,2-dichloroethylene.	
	Metric 2: Test Substance Source	Low	All Outcomes: The test substance was obtained from a commercial source (Merck). A batch or lot number was not reported, so this metric is rated Low.	
	Metric 3: Test Substance Purity	Low	All Outcomes: Purity or grade of the test substance was not reported.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	N/A	All Outcomes: No negative controls are necessary for acute lethality determination.	
	Metric 5: Positive Controls	N/A	All Outcomes: No positive controls are required for this study type.	
	Metric 6: Randomized Allocation of Animals	Low	All Outcomes: The method of allocation of test animals was not reported.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Medium	All Outcomes: Test substance preparation in vehicle was reported. Test substance storage was not reported for the volatile substance; therefore, this metric is rated Medium.	
	Metric 8: Consistency of Exposure Administration	High	All Outcomes: Test substances were administered consistently across treatment groups (dose levels); gavage volume was consistent within each species and not excessive.	
	Metric 9: Reporting of Doses/Concentrations	High	All Outcomes: Doses were reported without ambiguity.	
	Metric 10: Exposure Frequency and Duration	High	All Outcomes: Single doses are appropriate for an acute lethality test.	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: The number of dose groups and dose spacing were adequate for the purpose of the study. A range of responses were observed.	
	Metric 12: Exposure Route and Method	High	All Outcomes: The route and exposure method were appropriate for the purpose of the study.	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	High	All Outcomes: Test animal species, strain, sex, and starting body weight were reported. The age of the test animals was specified to be "mature." The test animals were obtained from a commercial source and were appropriate for the study type.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Medium	All Outcomes: Most husbandry conditions were reported. Light-dark cycle was not reported.	
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Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.			
Health Outcome(s):	Gastrointestinal; Lung/Respiratory; Lung/Respiratory; Hepatic/Liver; Hepatic/Liver; Renal/Kidney;			
Reported Health Effect(s):	Gastrointestinal: Gastrointestinal (gross pathology in acute oral and i.p studies); Lung/Respiratory: Lungs: gross pathology (acute oral and i.p studies); histopathology (inhalation – all durations); Lung/Respiratory: Lungs: gross pathology (acute oral and i.p studies); histopathology (inhalation – all durations); Hepatic/Liver: Gross pathology of the liver (acute oral and i.p studies); histopathology of the liver (inhalation – all durations); serum chemistry (cholesterol, bilirubin, total protein, alkaline phosphatase, GOT, GPT, albumin, glucose; in inhalation acute studies and possibly 16-week duration); bile accumulation (acute inhalation); Hepatic/Liver: Gross pathology of the liver (acute oral and i.p studies); histopathology of the liver (inhalation – all durations); serum chemistry (cholesterol, bilirubin, total protein, alkaline phosphatase, GOT, GPT, albumin, glucose; in inhalation acute studies and possibly 16-week duration); bile accumulation (acute inhalation); Renal/Kidney: Gross pathology of the kidney and bladder and hematuria (acute oral and i.p studies); histopathology (inhalation – all durations; no effects); serum chemistry (electrolytes, BUN, uric acid – inhalation acute durations);			
Duration:	Acute (less than or equal to 24 hr) Single dose i.p. (rats and mice)			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740886			
Domain	Metric	Rating	Comments	
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: 10 animals/group (female only) were utilized for all treatment groups.
Domain 5: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	Medium	All Outcomes: The details of the outcome assessment were not described in the study methods, but based on the reported results, animals were examined for gross pathological changes. Gross pathology is generally not considered to be the most sensitive outcome to asses organ toxicity but is consistent with endpoints typically included in an acute lethality study and, therefore, was appropriate for this study type.
	Metric 17:	Consistency of Outcome Assessment	High	All Outcomes: Animals from all groups were examined post-mortem for gross pathological changes.
	Metric 18:	Sampling Adequacy	Medium	All Outcomes: Sampling was not explicitly stated, but it is assumed that all animals were grossly examined.
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding is not required in acute lethality studies, and is generally not applied when conducting gross examinations.
	Metric 20:	Negative Control Response	N/A	All Outcomes: No negative controls were necessary for the acute lethality test.
Domain 6: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	High	All Outcomes: No confounding variables were reported or identified.
	Metric 22:	Health Outcomes Unrelated to Exposure	High	All Outcomes: No effects unrelated to exposure were reported or identified.
	Metric 23:	Data Presentation and Analysis	N/A	All Outcomes: Statistical analysis was not necessary because no control or comparator group was used.
	Metric 24:	Reporting of Data	Low	All Outcomes: Gross changes were qualitatively described in a table legend. The incidences and severity were not consistently described.
Additional Comments:	None			

Overall Quality Determination**High**

Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.			
Health Outcome(s):	Mortality			
Reported Health Effect(s):	Mortality: Mortality (acute oral and i,p studies)			
Duration:	Acute (less than or equal to 24 hr) Single dose p.o. (rats)			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740886			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
Metric 1:	Test Substance Identity	High	The test substance was identified by a definitive name, trans-1,2-dichloroethylene.	
Metric 2:	Test Substance Source	Low	The test substance was obtained from a commercial source (Merck). A batch or lot number was not reported, so this metric is rated Low.	
Metric 3:	Test Substance Purity	Low	Purity or grade of the test substance was not reported.	
Domain 2: Test Design				
Metric 4:	Negative and Vehicle Controls	N/A	No negative controls are necessary for acute lethality determination.	
Metric 5:	Positive Controls	N/A	No positive controls are required for this study type.	
Metric 6:	Randomized Allocation of Animals	Low	The method of allocation of test animals was not reported.	
Domain 3: Exposure Characterization				
Metric 7:	Preparation and Storage of Test Substance	Medium	Test substance preparation in vehicle was reported. Test substance storage was not reported for the volatile substance; therefore, this metric is rated Medium.	
Metric 8:	Consistency of Exposure Administration	Low	Test substances were administered consistently across treatment groups (dose levels); gavage volume was consistent. However, the gavage volume was excessive at 10 mL/kg test substance in olive oil followed by 15 mL/kg water.	
Metric 9:	Reporting of Doses/Concentrations	High	Doses were reported without ambiguity.	
Metric 10:	Exposure Frequency and Duration	High	Single doses are appropriate for an acute lethality test.	
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The number of dose groups and dose spacing were adequate for the purpose of the study. A range of responses were observed.	
Metric 12:	Exposure Route and Method	High	The route and exposure method were appropriate for the purpose of the study.	
Domain 4: Test Animals				
Metric 13:	Test Animal Characteristics	High	Test animal species, strain, sex, and starting body weight were reported. The age of the test animals was specified to be "mature." The test animals were obtained from a commercial source and were appropriate for the study type.	
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Most husbandry conditions were reported. Light-dark cycle was not reported.	
Metric 15:	Number of Animals per Group	Medium	10 animals/group (female only) were utilized for all treatment groups.	
Domain 5: Outcome Assessment				
Metric 16:	Outcome Assessment Methodology	High	Number of deaths and time of death are appropriate to determine the LD50.	
Metric 17:	Consistency of Outcome Assessment	High	Outcomes appeared to be assessed consistently across study groups. A protocol is provided.	
Metric 18:	Sampling Adequacy	High	All 10 animals/group were observed for mortality after dosing.	
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Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.			
Health Outcome(s):	Mortality			
Reported Health Effect(s):	Mortality: Mortality (acute oral and i,p studies)			
Duration:	Acute (less than or equal to 24 hr) Single dose p.o. (rats)			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740886			
Domain	Metric	Rating	Comments	
	Metric 19:	Blinding of Assessors	N/A	No subjective outcomes were assessed.
	Metric 20:	Negative Control Response	N/A	No negative controls were necessary for the acute lethality test.
Domain 6: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	High	No confounding variables were reported or identified.
	Metric 22:	Health Outcomes Unrelated to Exposure	High	No effects unrelated to exposure were reported or identified.
	Metric 23:	Data Presentation and Analysis	High	Statistical analysis was described and appropriate for the data.
	Metric 24:	Reporting of Data	High	Data were reported adequately.
Additional Comments:	None			
Overall Quality Determination		High		

Study Citation:	Hayes, J. R., Condie Jr., L. W., Egle Jr., J. L., Borzelleca, J. F. (1987). The acute and subchronic toxicity in rats of trans-1,2-dichloroethylene in drinking water. Journal of the American College of Toxicology 6(4):471-478.			
Health Outcome(s):	Mortality			
Reported Health Effect(s):	Mortality: Mortality and LD50 in the acute oral toxicity study. No test substance-related mortalities in the 90-day study.			
Duration:	Acute (less than or equal to 24 hr) Acute (single dose/1 day)			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740814			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	The test substance was identified as trans-1,2-dichloroethylene (CASN 156-60-5).	
	Metric 2: Test Substance Source	High	The test substance was obtained from Aldrich Chemical Company (Milwaukee, WI). Lot number 5201 J.J.	
	Metric 3: Test Substance Purity	High	Purity was reported to be 98%.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	N/A	Negative controls are not necessary for this study type.	
	Metric 5: Positive Controls	N/A	Not applicable for this study type.	
	Metric 6: Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study treatment groups.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Medium	”Trans-1,2-DCE was administered as a solution in corn oil for the acute studies (450-850 mg/ml).” No additional details on preparation of test substance were provided. No storage details were provided, however, this is unlikely to impact the results of a single dose acute duration study.	
	Metric 8: Consistency of Exposure Administration	High	A single gavage dose was administered. Gavage volume was 10 ml/kg.	
	Metric 9: Reporting of Doses/Concentrations	Uninformative	Study authors report that five dose groups were included in the study, however, the administered doses were not reported.	
	Metric 10: Exposure Frequency and Duration	High	Test substance was administered as a single dose via gavage. This is appropriate for an acute study.	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	Uninformative	Study authors report that five dose groups were included in the study, however, the administered doses were not reported.	
	Metric 12: Exposure Route and Method	High	The route (oral) and method (gavage) of exposure were reported and were suited to the test substance.	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	High	The test animal species, strain, sex, age, and starting body weight were reported, and the test animal was obtained from a commercial source.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were reported and were adequate.	
	Metric 15: Number of Animals per Group	Medium	10 rats/sex were included in each exposure group.	

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Study Citation:	Hayes, J. R., Condie Jr., L. W., Egle Jr., J. L., Borzelleca, J. F. (1987). The acute and subchronic toxicity in rats of trans-1,2-dichloroethylene in drinking water. Journal of the American College of Toxicology 6(4):471-478.
Health Outcome(s):	Mortality
Reported Health Effect(s):	Mortality: Mortality and LD50 in the acute oral toxicity study. No test substance-related mortalities in the 90-day study.
Duration:	Acute (less than or equal to 24 hr) Acute (single dose/1 day)
Chemical:	trans-1,2-Dichloroethylene- Parent compound
HERO ID:	1740814

Domain	Metric	Rating	Comments
Domain 5: Outcome Assessment			
	Metric 16: Outcome Assessment Methodology	High	Animals were observed hourly for mortality for the first 9 hours after test substance administration and then twice daily (at least 5 hours apart) for the next 14 days.
	Metric 17: Consistency of Outcome Assessment	High	Details of the outcome assessment protocol were reported and outcomes were assessed consistently across study groups.
	Metric 18: Sampling Adequacy	High	Reported information indicates the study used adequate sampling for the outcome(s) of interest
	Metric 19: Blinding of Assessors	N/A	Not necessary for this study type.
	Metric 20: Negative Control Response	N/A	Negative controls are not required for this study type.
Domain 6: Confounding / Variable Control			
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	Although the study did not report all information to determine confounding, reported information did not identify differences among study groups.
	Metric 22: Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure that could influence the outcome assessment.
	Metric 23: Data Presentation and Analysis	High	LD50 values and confidence limits were determined by the method of Litchfield and Wilcoxon.
	Metric 24: Reporting of Data	Uninformative	LD50 values were reported for male and female rats, however, the underlying mortality data at each dose group was not reported.

Additional Comments: None

Overall Quality Determination**Low**

Study Citation:	Hayes, J. R., Condie Jr., L. W., Egle Jr., J. L., Borzelleca, J. F. (1987). The acute and subchronic toxicity in rats of trans-1,2-dichloroethylene in drinking water. Journal of the American College of Toxicology 6(4):471-478.			
Health Outcome(s):	Neurological/Behavioral			
Reported Health Effect(s):	Neurological/Behavioral: Neurological effects (depression, ataxia, and depressed respiration) were reported in the acute oral toxicity study. No effects on mean or relative (to body weight) brain weight and no effects on general appearance or signs of intoxication (i.e., potential evidence of neurotoxicity) were reported in the 90-day study.			
Duration:	Acute (less than or equal to 24 hr) Acute (single dose/1 day)			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740814			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	The test substance was identified as trans-1,2-dichloroethylene (CASN 156-60-5).	
	Metric 2: Test Substance Source	High	The test substance was obtained from Aldrich Chemical Company (Milwaukee, WI). Lot number 5201 J.J.	
	Metric 3: Test Substance Purity	High	Purity was reported to be 98%.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	N/A	Negative controls are not necessary for this study type.	
	Metric 5: Positive Controls	N/A	Not applicable for this study type.	
	Metric 6: Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study treatment groups.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Medium	Trans-1,2-DCE was administered as a solution in corn oil for the acute studies (450-850 mg/ml). No additional details on preparation of test substance were provided. No storage details were provided, however, this is unlikely to impact the results of a single dose acute duration study.	
	Metric 8: Consistency of Exposure	High	A single gavage dose was administered. Gavage volume was 10 ml/kg.	
	Metric 9: Administration Reporting of Doses/Concentrations	Uninformative	Study authors report that five dose groups were included in the study, however, the administered doses were not reported.	
	Metric 10: Exposure Frequency and Duration	High	Test substance was administered as a single dose via gavage. This is appropriate for an acute study.	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	Uninformative	Study authors report that five dose groups were included in the study, however, the administered doses were not reported.	
	Metric 12: Exposure Route and Method	High	The route (oral) and method (gavage) of exposure were reported and were suited to the test substance.	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	High	The test animal species, strain, sex, age, and starting body weight were reported, and the test animal was obtained from a commercial source.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were reported and were adequate.	
	Metric 15: Number of Animals per Group	Medium	10 rats/sex were included in each exposure group.	
Domain 5: Outcome Assessment				

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Study Citation:	Hayes, J. R., Condie Jr., L. W., Egle Jr., J. L., Borzelleca, J. F. (1987). The acute and subchronic toxicity in rats of trans-1,2-dichloroethylene in drinking water. Journal of the American College of Toxicology 6(4):471-478.			
Health Outcome(s):	Neurological/Behavioral			
Reported Health Effect(s):	Neurological/Behavioral: Neurological effects (depression, ataxia, and depressed respiration) were reported in the acute oral toxicity study. No effects on mean or relative (to body weight) brain weight and no effects on general appearance or signs of intoxication (i.e., potential evidence of neurotoxicity) were reported in the 90-day study.			
Duration:	Acute (less than or equal to 24 hr) Acute (single dose/1 day)			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740814			
Domain	Metric	Rating	Comments	
	Metric 16: Outcome Assessment Methodology	High	Hourly observations were made for the first 9 hours after test substance administration and then twice daily (at least 5 hours apart) for the next 14 days.	
	Metric 17: Consistency of Outcome Assessment	High	Details of the outcome assessment protocol were reported and outcomes were assessed consistently across study groups.	
	Metric 18: Sampling Adequacy	High	Reported information indicates the study used adequate sampling for the outcome(s) of interest	
	Metric 19: Blinding of Assessors	N/A	Not necessary for this study type.	
	Metric 20: Negative Control Response	N/A	Negative controls are not required for this study type.	
Domain 6: Confounding / Variable Control				
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	Although the study did not report all information to determine confounding, reported information did not identify differences among study groups.	
	Metric 22: Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure that could influence the outcome assessment.	
	Metric 23: Data Presentation and Analysis	Uninformative	No statistical analysis was performed on the incidence of clinical observations. Sufficient data was not provided to allow for an independent analysis.	
	Metric 24: Reporting of Data	Uninformative	Study authors state "Central nervous system depression, ataxia, and depressed respiration were observed at all doses; the severity was dose-dependent." No additional information/data is reported, and the overall incidence of clinical observations is not reported, nor is the data broken out by dose group or sex.	
Additional Comments: None				
Overall Quality Determination		Uninformative		

Study Citation:	Jenkins, L. J., Trabulus, M. J., Murphy, S. D. (1972). Biochemical effects of 1,1-dichloroethylene in rats - Comparison with carbon-tetrachloride and 1,2-dichloroethylene. Toxicology and Applied Pharmacology 23(3):501-510.			
Health Outcome(s):	Hepatic/Liver			
Reported Health Effect(s):	Hepatic/Liver: Plasma ALT, ALP and liver enzymes (glucose-6-phosphatase, tyrosine transaminase, alkaline phosphatase)			
Duration:	Acute (less than or equal to 24 hr) Single dose			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1748282			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1:	Test Substance Identity	High	Test substance was identified as trans 1,2-dichloroethylene.
	Metric 2:	Test Substance Source	High	The source of the test substance was K & K Laboratories, Inc., Plainview, NY.
	Metric 3:	Test Substance Purity	Low	The test substance purity not reported.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	Negative controls received the vehicle corn oil.
	Metric 5:	Positive Controls	N/A	Positive control was not required in this study.
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated.
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and Storage of Test Substance	Medium	Storage is not reported however the assay is a single dose study so this is unlikely to have a substantial impact.
	Metric 8:	Consistency of Exposure Administration	High	Exposure was administered consistently across study groups. Gavage volume was appropriate (2ml/kg).
	Metric 9:	Reporting of Doses/Concentrations	Medium	Only the nominal level was reported but this is unlikely to have a substantial impact on results.
	Metric 10:	Exposure Frequency and Duration	High	Exposure to test substance was appropriate (single exposure).
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	There were minor limitations on concentrations (full range of responses not seen); justification for choosing doses was not provided.
	Metric 12:	Exposure Route and Method	High	The route of exposure was appropriate.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Medium	Age of rats were not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Temperature, humidity, and light-dark cycle were not reported.
	Metric 15:	Number of Animals per Group	Low	The number of animals evaluated/group was reported to be 3-4, which is lower than is typically used for this type of study.
Domain 5: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	Medium	Liver and serum enzymes were measured, however, liver histology or weights were not evaluated.
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Study Citation:	Jenkins, L. J., Trabulus, M. J., Murphy, S. D. (1972). Biochemical effects of 1,1-dichloroethylene in rats - Comparison with carbon-tetrachloride and 1,2-dichloroethylene. Toxicology and Applied Pharmacology 23(3):501-510.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	Hepatic/Liver: Plasma ALT, ALP and liver enzymes (glucose-6-phosphatase, tyrosine transaminase, alkaline phosphatase)
Duration:	Acute (less than or equal to 24 hr) Single dose
Chemical:	trans-1,2-Dichloroethylene- Parent compound
HERO ID:	1748282

Domain	Metric	Rating	Comments
	Metric 17: Consistency of Outcome Assessment	Medium	Details of protocols were minimal and cited in other papers. Authors state all animals were sacrificed between 10am and noon.
	Metric 18: Sampling Adequacy	Low	The number of animals evaluated/group was adequate n= 3-4. The small number of animals per group could have impacted the number of results that could have been found to be statistically significant.
	Metric 19: Blinding of Assessors	N/A	Blinding was not necessary for this study because outcomes were not subjective.
	Metric 20: Negative Control Response	High	The negative control responses were appropriate.
Domain 6: Confounding / Variable Control			
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	Although the study did not report all information to determine confounding, reported information did not identify differences among study groups.
	Metric 22: Health Outcomes Unrelated to Exposure	Medium	No information was provided to either to support or dismiss differences in groups in health outcomes or attrition.
	Metric 23: Data Presentation and Analysis	Low	Statistical analysis was performed but not described adequately.
	Metric 24: Reporting of Data	High	Outcome data were reported sufficiently.

Additional Comments: None

Overall Quality Determination**Medium**

Study Citation:	Munson, A. E., Sanders, V. M., Douglas, K. A., Sain, L. E., Kauffmann, B. M., White Jr., K. L. (1982). In vivo assessment of immunotoxicity. Environmental Health Perspectives 43:41-52.			
Health Outcome(s):	Mortality			
Reported Health Effect(s):	Mortality: LD50			
Duration:	Acute (less than or equal to 24 hr) acute			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	62637; Linked HERO ID(s): 200220, 62637, 5435222			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	The test substance was identified definitively as trans 1,2-dichloroethylene test substance was obtained from commercial source and lot # provided The purity was not reported in the current study, but was reported as 98% pure in a linked study (HERO 200220) for the same lot number.	
	Metric 2: Test Substance Source	High		
	Metric 3: Test Substance Purity	Medium		
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	N/A	Negative control not required for study type	
	Metric 5: Positive Controls	N/A	Not necessary for the study type	
	Metric 6: Randomized Allocation of Animals	Low	The study did not specify how animals were allocated into groups.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Medium	Preparation and storage conditions were incompletely reported but unlikely to affect results.	
	Metric 8: Consistency of Exposure Administration	High	Exposures were administered consistently across groups; the gavage volume (0.01 mL/g) was reported.	
	Metric 9: Reporting of Doses/Concentrations	Low	The doses were not reported in the current study, which is not uncommon for some LD50 studies. A companion paper, Barnes et al., reported using nine doses ranging from 800 to 3500 mg/kg. The female LD50 (95% CI) value for Barnes et al. was 2391 (2055-2788) compared with 2391 (2056-2788) in the current study. These two linked papers appear to share other datasets (e.g., a 14-day study that is reviewed under Barnes et al.), so it is possible the datasets for acute toxicity were the same; however, this is unclear, and the male LD50 values were not an exact match. The dosing information reported in Barnes et al. is sufficient to score this metric as a Low.	
	Metric 10: Exposure Frequency and Duration	High	Single administration was appropriate for the study.	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	Medium	The number of groups and spacing were not reported in the current study, but were sufficient to determine LD50 values. A companion paper, Barnes et al., reported using nine doses ranging from 800 to 3500 mg/kg. Another companion study, White et al. (HERO 64563), which reports methods used in these linked studies, states that at least 6 dose levels were used for acute toxicity studies.	
	Metric 12: Exposure Route and Method	High	The route and method of exposure was suited to the test substance.	
Domain 4: Test Animals				
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Study Citation:	Munson, A. E., Sanders, V. M., Douglas, K. A., Sain, L. E., Kauffmann, B. M., White Jr., K. L. (1982). In vivo assessment of immunotoxicity. Environmental Health Perspectives 43:41-52.			
Health Outcome(s):	Mortality			
Reported Health Effect(s):	Mortality: LD50			
Duration:	Acute (less than or equal to 24 hr) acute			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	62637; Linked HERO ID(s): 200220, 62637, 5435222			
Domain	Metric	Rating	Comments	
	Metric 13: Test Animal Characteristics	Medium	Animal characteristics were reported, except for starting body weight. Animals were obtained from a commercial source and are appropriate.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	High	Animal husbandry conditions were reported and consistent across groups.	
	Metric 15: Number of Animals per Group	Low	The number of animals per group was not reported in the current study. The related methods paper White et al. (HERO 64563) reported that 8 mice/group were routinely used for the acute toxicity studies.	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	High	The assessment methodology was appropriate for the outcome of interest.	
	Metric 17: Consistency of Outcome Assessment	Medium	outcome assessment appeared to be consistent across study groups	
	Metric 18: Sampling Adequacy	Low	Not reported	
	Metric 19: Blinding of Assessors	N/A	not necessary	
	Metric 20: Negative Control Response	N/A	not necessary	
Domain 6: Confounding / Variable Control				
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	there were not reported differences among groups	
	Metric 22: Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups	
	Metric 23: Data Presentation and Analysis	High	Used log probit analysis to determine LD50	
	Metric 24: Reporting of Data	High	data were reported for all groups by sex	
Additional Comments:	QC review by Shelley Stevens (SRC), sstevens@srcinc.com. Forms for the 14-day study on trans 1,2-dichloroethylene were removed (to be reviewed under Barnes et al. HERO 200220).Added form 2b for "other" clinical signs; added form 2b for "other" gross necropsy.Added additional form 3 for the acute toxicity study on trans-1,2-dichloroethylne for clinical signs. No form was added for gross necropsy because the results were not reported. In the existing form 3: Comments were edited to correct grammar or with additional information from linked studies. Scores for metrics 3 and 9 were changed. Updated form 2d.No changes to 1,2-dichloroethane forms were made.The overall score changed from a Low to a Med.			

Overall Quality Determination**Medium**

Study Citation:	Munson, A. E., Sanders, V. M., Douglas, K. A., Sain, L. E., Kauffmann, B. M., White Jr., K. L. (1982). In vivo assessment of immunotoxicity. Environmental Health Perspectives 43:41-52.			
Health Outcome(s):	Clinical signs (Clinical signs)			
Reported Health Effect(s):	Clinical signs (Clinical signs): Acute toxicity: Observations for overt toxicological effects			
Duration:	Acute (less than or equal to 24 hr) acute			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	62637; Linked HERO ID(s): 200220, 62637, 5435222			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	The test substance was identified definitively as trans 1,2-dichloroethylene test substance was obtained from commercial source and lot # provided	
	Metric 2: Test Substance Source	High		
	Metric 3: Test Substance Purity	Medium		
			The purity was not reported in the current study, but was reported as 98% pure in a linked study (HERO 200220) for the same lot number.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	N/A	Negative control not required for study type	
	Metric 5: Positive Controls	N/A	Not necessary for the study type	
	Metric 6: Randomized Allocation of Animals	Low	The study did not specify how animals were allocated into groups.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Medium	preparation and storage conditions were incompletely reported but unlikely to affect results	
	Metric 8: Consistency of Exposure Administration	High	Exposures were administered consistently across groups; the gavage volume (0.01 mL/g) was reported.	
	Metric 9: Reporting of Doses/Concentrations	Low	The doses were not reported in the current study, which is not uncommon for some LD50 studies. A companion paper, Barnes et al., reported using nine doses ranging from 800 to 3500 mg/kg. The female LD50 (95% CI) value for Barnes et al. was 2391 (2055-2788) compared with 2391 (2056-2788) in the current study. These two linked papers appear to share other datasets (e.g., a 14-day study that is reviewed under Barnes et al.), so it is possible the datasets for acute toxicity were the same; however, this is unclear, and the male LD50 values were not an exact match. The dosing information reported in Barnes et al. is sufficient to score this metric as a Low.	
	Metric 10: Exposure Frequency and Duration	High	Single administration was appropriate for the study.	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	Medium	The number of groups and spacing were not reported in the current study, but were sufficient to determine LD50 values. A companion paper, Barnes et al., reported using nine doses ranging from 800 to 3500 mg/kg. Another companion study, White et al. (HERO 64563), which reports methods used in these linked studies, states that at least 6 dose levels were used for acute toxicity studies.	
	Metric 12: Exposure Route and Method	High	The route and method of exposure was suited to the test substance.	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	Medium	Animal characteristics were reported, except for starting body weight. Animals were obtained from a commercial source and are appropriate.	
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Study Citation:	Munson, A. E., Sanders, V. M., Douglas, K. A., Sain, L. E., Kauffmann, B. M., White Jr., K. L. (1982). In vivo assessment of immunotoxicity. Environmental Health Perspectives 43:41-52.
Health Outcome(s):	Clinical signs (Clinical signs)
Reported Health Effect(s):	Clinical signs (Clinical signs): Acute toxicity: Observations for overt toxicological effects
Duration:	Acute (less than or equal to 24 hr) acute
Chemical:	trans-1,2-Dichloroethylene- Parent compound
HERO ID:	62637; Linked HERO ID(s): 200220, 62637, 5435222

Domain	Metric	Rating	Comments
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	High	Animal husbandry conditions were reported and consistent across groups.
	Metric 15: Number of Animals per Group	Low	The number of animals per group was not reported in the current study. The related methods paper White et al. (HERO 64563) reported that 8 mice/group were routinely used for the acute toxicity studies.
Domain 5: Outcome Assessment			
	Metric 16: Outcome Assessment Methodology	High	The outcome methods were clearly reported and consistent with those described in OECD TG 423. Observations for clinical signs are not the most sensitive methods for identifying specific organ toxicity, but that is not the purpose of this study type.
	Metric 17: Consistency of Outcome Assessment	Medium	outcome assessment appeared to be consistent across study groups
	Metric 18: Sampling Adequacy	Low	Not reported
	Metric 19: Blinding of Assessors	N/A	not necessary
	Metric 20: Negative Control Response	N/A	not necessary
Domain 6: Confounding / Variable Control			
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	there were not reported differences among groups
	Metric 22: Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups
	Metric 23: Data Presentation and Analysis	High	Used log probit analysis to determine LD50
	Metric 24: Reporting of Data	Low	Results were qualitatively described and were not distinguished by group or sex.

Additional Comments: None

Overall Quality Determination**Medium**

Study Citation:	Nakahama, T., Sarutani, S., Inouye, Y. (2000). Effects of chlorinated ethylenes on expression of rat CYP forms: Comparative study on correlation between biological activities and chemical structures. Journal of Health Science 46(4):251-258.			
Health Outcome(s):	Nutritional/Metabolic			
Reported Health Effect(s):	Nutritional/Metabolic: Change in body weight			
Duration:	Acute (less than or equal to 24 hr) Single injection- trans-1,2-dichloroethylene			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1747837			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance	Metric 1: Test Substance Identity	High	Test substance was identified as cis-1,2-dichloroethylene.	
	Metric 2: Test Substance Source	High	The source of the test substance was Aldrich Chemical Co. (USA).	
	Metric 3: Test Substance Purity	Low	The purity of test substance was not reported.	
Domain 2: Test Design	Metric 4: Negative and Vehicle Controls	High	Appropriate negative controls were included (corn-oil dosing).	
	Metric 5: Positive Controls	N/A	A positive control was not needed.	
	Metric 6: Randomized Allocation of Animals	Low	The study does not report how animals were allocated.	
Domain 3: Exposure Characterization	Metric 7: Preparation and Storage of Test Substance	Low	The preparation and storage of test substance were not reported. Given the volatility of the test substance this information is needed.	
	Metric 8: Consistency of Exposure Administration	Low	The volume of test substance or corn oil per body weight administered was not reported.	
	Metric 9: Reporting of Doses/Concentrations	High	Dose was reported without ambiguity.	
	Metric 10: Exposure Frequency and Duration	High	Exposure frequency was appropriate (single injection).	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	Low	Only one dose was studied, and justification was not provided.	
	Metric 12: Exposure Route and Method	High	Route of exposure was appropriate.	
Domain 4: Test Animals	Metric 13: Test Animal Characteristics	Medium	Starting body weights were reported as approximately 200 g (exact body weight was not provided). The sex of the animals was only reported in the abstract.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were not reported.	
	Metric 15: Number of Animals per Group	Medium	The numbers of animals/group were appropriate (n=4-6).	
Domain 5: Outcome Assessment	Metric 16: Outcome Assessment Methodology	High	The outcome assessment methodology addresses the outcome of interest.	
	Metric 17: Consistency of Outcome Assessment	Medium	The timing of body weight measurements was reported and it is assumed the methodology was applied consistently. However, the method of how the animals were sacrificed was not reported.	

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Study Citation:	Nakahama, T., Sarutani, S., Inouye, Y. (2000). Effects of chlorinated ethylenes on expression of rat CYP forms: Comparative study on correlation between biological activities and chemical structures. Journal of Health Science 46(4):251-258.
Health Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Nutritional/Metabolic: Change in body weight
Duration:	Acute (less than or equal to 24 hr) Single injection- trans-1,2-dichloroethylene
Chemical:	trans-1,2-Dichloroethylene- Parent compound
HERO ID:	1747837

Domain	Metric	Rating	Comments
	Metric 18: Sampling Adequacy	High	The number of animals evaluated was adequate for outcomes of interest.
	Metric 19: Blinding of Assessors	N/A	Blinding was not needed to assess outcomes.
	Metric 20: Negative Control Response	High	The negative control response was appropriate.
Domain 6: Confounding / Variable Control			
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	Body weight changes were identified, but not food/water intake differences.
	Metric 22: Health Outcomes Unrelated to Exposure	Medium	There was no information to support or dismiss the suggestion of health outcomes differences unrelated to exposure.
	Metric 23: Data Presentation and Analysis	High	Statistical analysis was performed and appropriate.
	Metric 24: Reporting of Data	Medium	Data were reported for changes to body weight as the mean of the percent change in body weight +/- S.E (n=4-6). The actual body weights of the mice during the course of the study were not reported.

Additional Comments: The main goal of the study is to characterize changes to cytochrome P450 activity and protein content. Therefore, the only endpoints used to evaluate organ toxicity was changes to liver and lung weights. As this was an acute, single dose study, there may not have been a significant dosing window to show a change in organ weights, and the route of administration may not be the best choice to study acute pulmonary toxicity.

Overall Quality Determination

Medium

Study Citation:	Nakahama, T., Sarutani, S., Inouye, Y. (2000). Effects of chlorinated ethylenes on expression of rat CYP forms: Comparative study on correlation between biological activities and chemical structures. Journal of Health Science 46(4):251-258.			
Health Outcome(s):	Hepatic/Liver			
Reported Health Effect(s):	Hepatic/Liver: Change in liver weight			
Duration:	Acute (less than or equal to 24 hr) Single injection- trans-1,2-dichloroethylene			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1747837			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	Test substance was identified as cis-1,2-dichloroethylene.	
	Metric 2: Test Substance Source	High	The source of the test substance was Aldrich Chemical Co. (USA).	
	Metric 3: Test Substance Purity	Low	The purity of test substance was not reported.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	Appropriate negative controls were included (corn-oil dosing).	
	Metric 5: Positive Controls	N/A	A positive control was not needed.	
	Metric 6: Randomized Allocation of Animals	Low	The study does not report how animals were allocated.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Low	The preparation and storage of test substance were not reported. Given the volatility of the test substance this information is needed.	
	Metric 8: Consistency of Exposure Administration	Low	The volume of test substance or corn oil per body weight administered was not reported.	
	Metric 9: Reporting of Doses/Concentrations	High	Dose was reported without ambiguity.	
	Metric 10: Exposure Frequency and Duration	High	Exposure frequency was appropriate (single injection).	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	Low	Only one dose was studied, and justification was not provided.	
	Metric 12: Exposure Route and Method	High	The route and method of exposure was appropriate for a volatile compound.	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	Medium	Starting body weights were reported as approximately 200 g (exact body weight was not provided). The sex of the animals was only reported in the abstract.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were not reported.	
	Metric 15: Number of Animals per Group	Medium	The numbers of animals/group were appropriate (n=4-6).	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	Medium	The only measure of hepatic toxicity was changes to liver weight. No serum chemistry or histopathology was performed.	
	Metric 17: Consistency of Outcome Assessment	Medium	There was incomplete reporting of minor detail of outcome assessment protocol execution, but these are unlikely to substantially impact results.	
	Metric 18: Sampling Adequacy	High	The number of animals evaluated was adequate for outcomes of interest.	
	Metric 19: Blinding of Assessors	N/A	Blinding was not needed to assess outcomes.	

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Study Citation:	Nakahama, T., Sarutani, S., Inouye, Y. (2000). Effects of chlorinated ethylenes on expression of rat CYP forms: Comparative study on correlation between biological activities and chemical structures. Journal of Health Science 46(4):251-258.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	Hepatic/Liver: Change in liver weight
Duration:	Acute (less than or equal to 24 hr) Single injection- trans-1,2-dichloroethylene
Chemical:	trans-1,2-Dichloroethylene- Parent compound
HERO ID:	1747837

Domain	Metric	Rating	Comments
Metric 20:	Negative Control Response	High	The negative control response was appropriate.
Domain 6: Confounding / Variable Control			
Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Body weight changes were identified, but not food/water intake differences.
Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information to support or dismiss the suggestion of health outcomes differences unrelated to exposure.
Metric 23:	Data Presentation and Analysis	High	Statistical analysis was performed and appropriate.
Metric 24:	Reporting of Data	Medium	Data were reported for changes to liver weights as the mean +/- S.E (n=4-6). Liver weights were reported g/100 g body weight. The absolute weights were not reported.

Additional Comments: The main goal of the study is to characterize changes to cytochrome P450 activity and protein content. Therefore, the only endpoints used to evaluate organ toxicity was changes to liver and lung weights. As this was an acute, single dose study, there may not have been a significant dosing window to show a change in organ weights, and the route of administration may not be the best choice to study acute pulmonary toxicity.

Overall Quality Determination

Medium

Study Citation:	Nakahama, T., Sarutani, S., Inouye, Y. (2000). Effects of chlorinated ethylenes on expression of rat CYP forms: Comparative study on correlation between biological activities and chemical structures. Journal of Health Science 46(4):251-258.			
Health Outcome(s):	Lung/Respiratory			
Reported Health Effect(s):	Lung/Respiratory: Change in lung weight			
Duration:	Acute (less than or equal to 24 hr) Single injection- trans-1,2-dichloroethylene			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1747837			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	Test substance was identified as cis-1,2-dichloroethylene.	
	Metric 2: Test Substance Source	High	The source of the test substance was Aldrich Chemical Co. (USA).	
	Metric 3: Test Substance Purity	Low	The purity of test substance was not reported.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	Appropriate negative controls were included (corn-oil dosing).	
	Metric 5: Positive Controls	N/A	A positive control was not needed.	
	Metric 6: Randomized Allocation of Animals	Low	The study does not report how animals were allocated.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Low	The preparation and storage of test substance were not reported. Given the volatility of the test substance this information is needed.	
	Metric 8: Consistency of Exposure Administration	Low	The volume of test substance or corn oil per body weight administered was not reported.	
	Metric 9: Reporting of Doses/Concentrations	High	Dose was reported without ambiguity.	
	Metric 10: Exposure Frequency and Duration	High	Exposure frequency was appropriate (single injection).	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	Low	Only one dose was studied, and justification was not provided.	
	Metric 12: Exposure Route and Method	Medium	Route of exposure was appropriate for a volatile compound. However, as this looked to assess toxicity to the lung the route of administration was not the most appropriate. Inhalation would have been the best choice for this type of assay.	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	Medium	Starting body weights were reported as approximately 200 g (exact body weight was not provided). The sex of the animals was only reported in the abstract.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were not reported.	
	Metric 15: Number of Animals per Group	Medium	The numbers of animals/group were appropriate (n=4-6).	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	Medium	The only measure of pulmonary toxicity was changes to lung weight. No histopathology or assessment of pulmonary function was performed.	
	Metric 17: Consistency of Outcome Assessment	Medium	There was incomplete reporting of minor detail of outcome assessment protocol execution, but these are unlikely to substantially impact results.	

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Study Citation:	Nakahama, T., Sarutani, S., Inouye, Y. (2000). Effects of chlorinated ethylenes on expression of rat CYP forms: Comparative study on correlation between biological activities and chemical structures. Journal of Health Science 46(4):251-258.
Health Outcome(s):	Lung/Respiratory
Reported Health Effect(s):	Lung/Respiratory: Change in lung weight
Duration:	Acute (less than or equal to 24 hr) Single injection- trans-1,2-dichloroethylene
Chemical:	trans-1,2-Dichloroethylene- Parent compound
HERO ID:	1747837

Domain	Metric	Rating	Comments
	Metric 18: Sampling Adequacy	High	The number of animals evaluated was adequate for outcomes of interest.
	Metric 19: Blinding of Assessors	N/A	Blinding was not needed to assess outcomes.
	Metric 20: Negative Control Response	High	The negative control response was appropriate.
Domain 6: Confounding / Variable Control			
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	Body weight changes were identified, but not food/water intake differences.
	Metric 22: Health Outcomes Unrelated to Exposure	Medium	There was no information to support or dismiss the suggestion of health outcomes differences unrelated to exposure.
	Metric 23: Data Presentation and Analysis	High	Statistical analysis was performed and appropriate.
	Metric 24: Reporting of Data	Medium	Data were reported for changes to lung weights as the mean +/- S.E (n=4-6). Lung weights were reported g/100 g body weight. The absolute weights were not reported.
Additional Comments:	The main goal of the study is to characterize changes to cytochrome P450 activity and protein content. Therefore, the only endpoints used to evaluate organ toxicity was changes to liver and lung weights. As this was an acute, single dose study, there may not have been a significant dosing window to show a change in organ weights, and the route of administration may not be the best choice to study acute pulmonary toxicity.		

Overall Quality Determination**Medium**

Study Citation:	Plaa, G. L., Larson, R. E. (1965). Relative nephrotoxic properties of chlorinated methane, ethane, and ethylene derivatives in mice. Toxicology and Applied Pharmacology 7(1):37-44.			
Health Outcome(s):	Renal/Kidney			
Reported Health Effect(s):	Renal/Kidney: Urinary glucose and protein; renal histopathology			
Duration:	Acute (less than or equal to 24 hr) Acute- single dose			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	64411			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1:	Test Substance Identity	High	Test substance was identified as trans-1,2-dichloroethylene.
	Metric 2:	Test Substance Source	Low	The source of the test substance was not reported.
	Metric 3:	Test Substance Purity	Low	The purity of the test substance was not reported.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	Uninformative	Details of negative control are not reported. It appears the data on the negative controls come from historic data. The strain, age, sex of the animals are not provided nor is information on if the animals were sham or untreated.
	Metric 5:	Positive Controls	N/A	Not applicable for this study.
	Metric 6:	Randomized Allocation of Animals	Low	Authors do not report if how study groups were formed.
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and Storage of Test Substance	Low	Preparation and storage conditions were not properly reported given the volatility of the test substance.
	Metric 8:	Consistency of Exposure Administration	Medium	Details of exposure administration are incomplete.
	Metric 9:	Reporting of Doses/Concentrations	High	Exposure doses were reported without ambiguity.
	Metric 10:	Exposure Frequency and Duration	High	Exposure and frequency were appropriate for outcome studied.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	There were minor limitation in dose spacing.
	Metric 12:	Exposure Route and Method	High	Route of exposure was i.p. injection.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Low	The source and age of the mice was not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were not reported.
	Metric 15:	Number of Animals per Group	Medium	The number of animals exposed/group was not reported as 10 in each group (Table 4 legend).
Domain 5: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	Medium	Some details regarding the outcome assessment methodology were lacking (e.g how long urine was collected for).

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Study Citation:	Plaa, G. L., Larson, R. E. (1965). Relative nephrotoxic properties of chlorinated methane, ethane, and ethylene derivatives in mice. Toxicology and Applied Pharmacology 7(1):37-44.			
Health Outcome(s):	Renal/Kidney			
Reported Health Effect(s):	Renal/Kidney: Urinary glucose and protein; renal histopathology			
Duration:	Acute (less than or equal to 24 hr) Acute- single dose			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	64411			
Domain	Metric	Rating	Comments	
	Metric 17: Consistency of Outcome Assessment	High	Outcomes were assessed consistently across study groups.	
	Metric 18: Sampling Adequacy	Medium	The sampling was adequate (all surviving mice)	
	Metric 19: Blinding of Assessors	N/A	Blinding was not necessary for outcomes studied.	
	Metric 20: Negative Control Response	High	Negative control responses for urinary parameters were reported in text and were appropriate for some outcomes.	
Domain 6: Confounding / Variable Control				
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	Study did not report all information to determine confounding, reported information did not identify differences among study groups.	
	Metric 22: Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure.	
	Metric 23: Data Presentation and Analysis	Low	Statistics analysis were not performed. Significance of increased urinary glucose or protein was determined by a cutoff number set by the authors.	
	Metric 24: Reporting of Data	Medium	Incidence data is provided for presence of urinary glucose or protein above cutoff level. The measured level of glucose and protein would be more useful.	

Additional Comments: Study is rated as unacceptable based on lack of information regarding the negative control.

Overall Quality Determination

Uninformative

Study Citation:	Plaa, G. L., Larson, R. E. (1965). Relative nephrotoxic properties of chlorinated methane, ethane, and ethylene derivatives in mice. Toxicology and Applied Pharmacology 7(1):37-44.			
Health Outcome(s):	Mortality			
Reported Health Effect(s):	Mortality: Mortality			
Duration:	Acute (less than or equal to 24 hr) Acute- single dose			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	64411			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
Metric 1:	Test Substance Identity	High	Test substance was identified as trans-1,2-dichloroethylene.	
Metric 2:	Test Substance Source	Low	The source of the test substance was not reported.	
Metric 3:	Test Substance Purity	Low	The purity of the test substance was not reported.	
Domain 2: Test Design				
Metric 4:	Negative and Vehicle Controls	Uninformative	Details of negative control are not reported. It appears the data on the negative controls come from historic data. The strain, age, sex of the animals are not provided nor is information on if the animals were sham or untreated.	
Metric 5:	Positive Controls	N/A	Not applicable for this study.	
Metric 6:	Randomized Allocation of Animals	Low	Authors do not report if how study groups were formed.	
Domain 3: Exposure Characterization				
Metric 7:	Preparation and Storage of Test Substance	Low	Preparation and storage conditions were not properly reported given the volatility of the test substance.	
Metric 8:	Consistency of Exposure Administration	Medium	Details of exposure administration are incomplete.	
Metric 9:	Reporting of Doses/Concentrations	High	Exposure doses were reported without ambiguity.	
Metric 10:	Exposure Frequency and Duration	High	Exposure and frequency were appropriate for outcome studied.	
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	There were minor limitation in dose spacing.	
Metric 12:	Exposure Route and Method	High	Route of exposure was i.p. injection.	
Domain 4: Test Animals				
Metric 13:	Test Animal Characteristics	Low	The source and age of the mice was not reported.	
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were not reported.	
Metric 15:	Number of Animals per Group	Medium	The number of animals exposed/group was not reported as 10 in each group (Table 4 legend).	
Domain 5: Outcome Assessment				
Metric 16:	Outcome Assessment Methodology	Medium	Details regarding the outcome assessment methodology were lacking.	
Metric 17:	Consistency of Outcome Assessment	High	Outcomes were assessed consistently across study groups.	
Metric 18:	Sampling Adequacy	Medium	The sampling was adequate.	
Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary for outcomes studied.	

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Study Citation:	Plaa, G. L., Larson, R. E. (1965). Relative nephrotoxic properties of chlorinated methane, ethane, and ethylene derivatives in mice. Toxicology and Applied Pharmacology 7(1):37-44.			
Health Outcome(s):	Mortality			
Reported Health Effect(s):	Mortality: Mortality			
Duration:	Acute (less than or equal to 24 hr) Acute- single dose			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	64411			
Domain	Metric		Rating	Comments
	Metric 20:	Negative Control Response	Low	Negative control responses was not reported.
Domain 6: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Study did not report all information to determine confounding, reported information did not identify differences among study groups.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure.
	Metric 23:	Data Presentation and Analysis	High	Statistics analysis were not performed but data is presented so that independent analysis can be done.
	Metric 24:	Reporting of Data	High	Mortality data is adequately presented.
Additional Comments: Study is rated as unacceptable based on lack of information regarding the negative control.				

Overall Quality Determination**Uninformative**

Study Citation:	Saldana-Ruiz, S., Boadas-Vaello, P., Sedo-Cabezón, L., Llorens, J. (2013). Reduced Systemic Toxicity and Preserved Vestibular Toxicity Following Co-treatment with Nitriles and CYP2E1 Inhibitors: a Mouse Model for Hair Cell Loss. JARO - Journal of the Association for Research in Otolaryngology 14(5):661-671.			
Health Outcome(s):	Ocular/Sensory; Ocular/Sensory;			
Reported Health Effect(s):	Ocular/Sensory: Vestibular function assessed via behavioral observations (i.e., observed for circling, retropulsion, abnormal head movements) and functional battery (tail hang reflex, righting reflex, air righting reflex tests) and histology of vestibular sensory epithelia; Ocular/Sensory: Vestibular function assessed via behavioral observations (i.e., observed for circling, retropulsion, abnormal head movements) and functional battery (tail hang reflex, righting reflex, air righting reflex tests) and histology of vestibular sensory epithelia;			
Duration:	Acute (less than or equal to 24 hr) 3 ip doses over 24.5 hours - Swiss mice			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	2303853			
Domain		Metric	Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test Substance Identity	High	All Outcomes: Test substance identified as trans-1,2-dichloroethylene. CASRN and chemical structure not provided.
	Metric 2:	Test Substance Source	High	All Outcomes: The test substance was obtained from a commercial source (Sigma-Aldrich Química S.A.). Lot/Batch number not reported.
	Metric 3:	Test Substance Purity	High	All Outcomes: Test substance purity was reported to be 98%.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Concurrent negative controls received vehicle (corn oil)
	Metric 5:	Positive Controls	N/A	All Outcomes: Not required for study type
	Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: Study states that "animals were assigned to group treatments in a pseudorandom order."
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and Storage of Test Substance	Low	All Outcomes: Information on preparation and storage was not reported
	Metric 8:	Consistency of Exposure Administration	High	All Outcomes: "TDCE ...was administered i.p. in 6 ml/kg of corn oil" and mice recieved "TDCE at 0 (corn oil, vehicle control) or 100 mg/kg,administered 30 min before and 6 and 24 h after administration of allylnitrile."
	Metric 9:	Reporting of Doses/Concentrations	Medium	All Outcomes: Nominal ip doses of 100 mg/kg were reported, however, doses were not analytically verified.
	Metric 10:	Exposure Frequency and Duration	Medium	All Outcomes: 3 ip doses of 100 mg/kg test substance over a 24.5 hour period may not be sufficient to induce vestibular toxicity of the test substance; however, this duration was sufficient for other substances tested in the study.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	All Outcomes: Although the goal of this study was not to have a dose-dependent effect, only one dose level was administered, and this dose did not induce any vestibular toxicity.
	Metric 12:	Exposure Route and Method	High	All Outcomes: The test substance was administered via ip injection. This was considered appropriate for the study type.
Domain 4: Test Animals				

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Study Citation:	Saldana-Ruiz, S., Boadas-Vaello, P., Sedo-Cabezón, L., Llorens, J. (2013). Reduced Systemic Toxicity and Preserved Vestibular Toxicity Following Co-treatment with Nitriles and CYP2E1 Inhibitors: a Mouse Model for Hair Cell Loss. JARO - Journal of the Association for Research in Otolaryngology 14(5):661-671.			
Health Outcome(s):	Ocular/Sensory; Ocular/Sensory;			
Reported Health Effect(s):	Ocular/Sensory: Vestibular function assessed via behavioral observations (i.e., observed for circling, retropulsion, abnormal head movements) and functional battery (tail hang reflex, righting reflex, air righting reflex tests) and histology of vestibular sensory epithelia; Ocular/Sensory: Vestibular function assessed via behavioral observations (i.e., observed for circling, retropulsion, abnormal head movements) and functional battery (tail hang reflex, righting reflex, air righting reflex tests) and histology of vestibular sensory epithelia;			
Duration:	Acute (less than or equal to 24 hr) 3 ip doses over 24.5 hours - Swiss mice			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	2303853			
Domain	Metric	Rating	Comments	
	Metric 13: Test Animal Characteristics	Medium	Ocular/Sensory: "male RjOrl:Swiss/CD-1 (Swiss) mice purchased from Janvier (Le-Genest-Saint-Isle, France)." Age and starting body weight were not reported.; Ocular/Sensory: "male or female 129S1/SvImJ (129S1) mice from a local colony established by breeding pairs obtained from the Jackson Laboratory (Bar Harbor, ME, USA)." Age and starting body weight were not reported.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Low	All Outcomes: Husbandry conditions were not sufficiently reported to evaluate if husbandry was adequate and whether differences occurred between control and exposed populations. Diet, housing, and bedding were reported; temperature, relative humidity, and light/dark cycle were not reported.	
	Metric 15: Number of Animals per Group	Low	Ocular/Sensory: Study authors state that 2-4 animals were included in each treatment group, however, additional details were not provided.; Ocular/Sensory: The number of animals per group was not reported.	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	High	All Outcomes: Vestibular toxicity was determined using a battery of behavioral tests and histologic examination. These tests and histologic examination procedures were adequately described and sensitive for the outcome of interest.	
	Metric 17: Consistency of Outcome Assessment	Medium	Ocular/Sensory: "Vestibular dysfunction was assessed 2–3, 7, and 21 days after nitrile exposure, and histological analysis was performed 4–5 weeks after dosing" indicating some minor difference in the timing of the outcome assessment across groups. However, these uncertainties are unlikely to have substantial impact on results.; Ocular/Sensory: Vestibular dysfunction was assessed 2–3, 7, and 21 days after nitrile exposure, and histological analysis was performed 4–5 weeks after dosing indicating some minor difference in the timing of the outcome assessment across groups. However, these uncertainties are unlikely to have substantial impact on results.	
	Metric 18: Sampling Adequacy	Low	Ocular/Sensory: Details regarding sampling of outcomes were not reported.; Ocular/Sensory: Details regarding sampling of outcomes were not reported	
	Metric 19: Blinding of Assessors	High	All Outcomes: "The same experimenter was responsible for dosing and behavioral analysis. However, animals were assigned to group treatments in a pseudorandom order and the rating sheets did not contain treatment information, so the experimenter performed the behavioral assessment under blind conditions"	
	Metric 20: Negative Control Response	High	All Outcomes: Negative control response reported and appeared appropriate	
Domain 6: Confounding / Variable Control				
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Study Citation:	Saldana-Ruiz, S., Boadas-Vaello, P., Sedo-Cabezón, L., Llorens, J. (2013). Reduced Systemic Toxicity and Preserved Vestibular Toxicity Following Co-treatment with Nitriles and CYP2E1 Inhibitors: a Mouse Model for Hair Cell Loss. JARO - Journal of the Association for Research in Otolaryngology 14(5):661-671.
Health Outcome(s):	Ocular/Sensory; Ocular/Sensory;
Reported Health Effect(s):	Ocular/Sensory: Vestibular function assessed via behavioral observations (i.e., observed for circling, retropulsion, abnormal head movements) and functional battery (tail hang reflex, righting reflex, air righting reflex tests) and histology of vestibular sensory epithelia; Ocular/Sensory: Vestibular function assessed via behavioral observations (i.e., observed for circling, retropulsion, abnormal head movements) and functional battery (tail hang reflex, righting reflex, air righting reflex tests) and histology of vestibular sensory epithelia;
Duration:	Acute (less than or equal to 24 hr) 3 ip doses over 24.5 hours - Swiss mice
Chemical:	trans-1,2-Dichloroethylene- Parent compound
HERO ID:	2303853

Domain	Metric	Rating	Comments
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	All Outcomes: Body weight, food and water intake were not reported.
	Metric 22: Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23: Data Presentation and Analysis	High	All Outcomes: Statistical methods were clearly described or had only minor omissions and were appropriate for the dataset(s).
	Metric 24: Reporting of Data	Low	All Outcomes: Behavioral data are presented as mean $\pm$ standard error of raw scores of all vestibular dysfunction tests/observations. Data from individual tests/observations are not reported. Histologic findings are not adequately reported.

Additional Comments: None

Overall Quality Determination**Medium**

Study Citation:	Barnes, D. W., Sanders, V. M., White, K. L., Jr, Shopp, G. M., Jr, Munson, A. E. (1985). Toxicology of trans-1,2-dichloroethylene in the mouse. Drug and Chemical Toxicology 8(5):373-392.			
Health Outcome(s):	Renal/Kidney; Hepatic/Liver; Reproductive/Developmental; Lung/Respiratory; Gastrointestinal; Immune/Hematological;			
Reported Health Effect(s):	Renal/Kidney: Drinking water: Kidney weight, serum BUN, creatinine, glucose, calcium, sodium, chloride, potassiumGavage: Kidney weight, BUN; Hepatic/Liver: Drinking water: Serum ALT, AST, ALP, LDH, liver weight, and hepatic microsomal activitiesGavage: Serum LDH, ALT and liver weight; Reproductive/Developmental: Gavage study: Testes weightDrinking water: Testes weight; Lung/Respiratory: Lung weight; Gastrointestinal: Lethality: Gross necropsy of stomach, small intestine; Immune/Hematological: Hematology parameters, spleen and thymus weight;			
Duration:	Short-term (>1-30 days) 14-day gavage			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	200220; Linked HERO ID(s): 200220, 62637, 5435222			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	All Outcomes: Test substance was identified as trans-1,2-dichloroethylene.	
	Metric 2: Test Substance Source	High	All Outcomes: The source of the test substance was Aldrich Chemical Co., Milwaukee, WI. Lot number was included.	
	Metric 3: Test Substance Purity	High	All Outcomes: Test substance was 98% pure.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	All Outcomes: Negative control was appropriate (vehicle; 10% emulphor in deionised water).	
	Metric 5: Positive Controls	N/A	All Outcomes: Positive control was not necessary for this study.	
	Metric 6: Randomized Allocation of Animals	Medium	All Outcomes: The current study did not specify whether animals were randomly distributed across groups; however, the study followed methodological details reported in HERO ID 64563. This reference indicated that the study animals were randomized (method not specified).	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Medium	All Outcomes: DCE was prepared on the day of administration and maintained in dark glassware at 4 °C until use. The test substance is volatile; it was not specified whether the bottles were sealed to prevent volatilization.	
	Metric 8: Consistency of Exposure Administration	High	All Outcomes: Exposures were administered consistently across groups; the gavage volume (0.01 mL/g) was reported.	
	Metric 9: Reporting of Doses/Concentrations	Medium	All Outcomes: Doses are reported as mg/kg without ambiguity and were based on LD50 values. The study did not specify whether the test solutions for the gavage study were analytically verified.	
	Metric 10: Exposure Frequency and Duration	High	All Outcomes: Exposure duration was appropriate for study a range-finding study.	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: The number of dose groups and spacing were appropriate (range of response obtained and doses were justified).	
	Metric 12: Exposure Route and Method	High	All Outcomes: Exposure route was appropriate.	
Domain 4: Test Animals				
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Study Citation:	Barnes, D. W., Sanders, V. M., White, K. L., Jr, Shopp, G. M., Jr, Munson, A. E. (1985). Toxicology of trans-1,2-dichloroethylene in the mouse. Drug and Chemical Toxicology 8(5):373-392.
Health Outcome(s):	Renal/Kidney; Hepatic/Liver; Reproductive/Developmental; Lung/Respiratory; Gastrointestinal; Immune/Hematological;
Reported Health Effect(s):	Renal/Kidney: Drinking water: Kidney weight, serum BUN, creatinine, glucose, calcium, sodium, chloride, potassiumGavage: Kidney weight, BUN; Hepatic/Liver: Drinking water: Serum ALT, AST, ALP, LDH, liver weight, and hepatic microsomal activitiesGavage: Serum LDH, ALT and liver weight; Reproductive/Developmental: Gavage study: Testes weightDrinking water: Testes weight; Lung/Respiratory: Lung weight; Gastrointestinal: Lethality: Gross necropsy of stomach, small intestine; Immune/Hematological: Hematology parameters, spleen and thymus weight;
Duration:	Short-term (>1-30 days) 14-day gavage
Chemical:	trans-1,2-Dichloroethylene- Parent compound
HERO ID:	200220; Linked HERO ID(s): 200220, 62637, 5435222

Domain	Metric	Rating	Comments
	Metric 13: Test Animal Characteristics	Medium	All Outcomes: Test animal characteristics were not provided in the current study; however, some animal details were reported in White et al. 1985 (HERO 64563). The test animals were obtained from Charles River Breeding Laboratories and the animal age was specified. Starting body weights were not provided.
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Medium	All Outcomes: Husbandry conditions were not reported in this reference, but some methodological details are provided in White et al. 1985 (HERO 64563). The reference stated that food and water were available ad libitum and acceptable room temperature, and humidity targets were used. The photoperiod was 12 hrs. The number of animals per cage was not specified.
	Metric 15: Number of Animals per Group	Low	All Outcomes: The total number of animals treated/group were not reported.
Domain 5: Outcome Assessment			
	Metric 16: Outcome Assessment Methodology	High	All Outcomes: Outcome assessment methods were described in detail in White et al. 1985 (HERO 64563), with some details also provided in HERO IDs 200220 and 62637. The outcome assessment methods were appropriate for the study type. Histological examinations are typically not included in range-finding studies.
	Metric 17: Consistency of Outcome Assessment	Medium	All Outcomes: Outcome assessment methods were described in White et al. (HERO 64563) and appeared to be consistent across study groups.
	Metric 18: Sampling Adequacy	High	All Outcomes: The number of animals sampled were reported and appropriate. Organ weights and serum enzymes are reported for 9-10 animals per treatment group.
	Metric 19: Blinding of Assessors	N/A	All Outcomes: Blinding was not necessary for this study.
	Metric 20: Negative Control Response	High	All Outcomes: Negative control response was appropriate.
Domain 6: Confounding / Variable Control			
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	All Outcomes: Study did not report all information to determine confounding, reported information did not identify differences between groups.
	Metric 22: Health Outcomes Unrelated to Exposure	Medium	All Outcomes: No information was provided to either to support or dismiss differences in groups in health outcomes or attrition.
	Metric 23: Data Presentation and Analysis	High	All Outcomes: Statistical analysis was appropriate.
	Metric 24: Reporting of Data	High	All Outcomes: Absolute the relative organ weights to body were reported as means and SE. Hematology and blood chemistry were reported as means and SE. Relative organ weights to brain weights were reported as negative in the text.
Additional Comments: None			

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Study Citation:	Barnes, D. W., Sanders, V. M., White, K. L., Jr, Shopp, G. M., Jr, Munson, A. E. (1985). Toxicology of trans-1,2-dichloroethylene in the mouse. Drug and Chemical Toxicology 8(5):373-392.		
Health Outcome(s):	Renal/Kidney; Hepatic/Liver; Reproductive/Developmental; Lung/Respiratory; Gastrointestinal; Immune/Hematological;		
Reported Health Effect(s):	Renal/Kidney: Drinking water: Kidney weight, serum BUN, creatinine, glucose, calcium, sodium, chloride, potassiumGavage: Kidney weight, BUN; Hepatic/Liver: Drinking water: Serum ALT, AST, ALP, LDH, liver weight, and hepatic microsomal activitiesGavage: Serum LDH, ALT and liver weight; Reproductive/Developmental: Gavage study: Testes weightDrinking water: Testes weight; Lung/Respiratory: Lung weight; Gastrointestinal: Lethality: Gross necropsy of stomach, small intestine; Immune/Hematological: Hematology parameters, spleen and thymus weight;		
Duration:	Short-term (>1-30 days) 14-day gavage		
Chemical:	trans-1,2-Dichloroethylene- Parent compound		
HERO ID:	200220; Linked HERO ID(s): 200220, 62637, 5435222		
Domain	Metric	Rating	Comments
Overall Quality Determination		High	

Study Citation:	Barnes, D. W., Sanders, V. M., White, K. L., Jr, Shopp, G. M., Jr, Munson, A. E. (1985). Toxicology of trans-1,2-dichloroethylene in the mouse. Drug and Chemical Toxicology 8(5):373-392.			
Health Outcome(s):	Nutritional/Metabolic			
Reported Health Effect(s):	Nutritional/Metabolic: Body weightWater consumption (drinking water study)			
Duration:	Short-term (>1-30 days) 14-day gavage			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	200220; Linked HERO ID(s): 200220, 62637, 5435222			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1:	Test Substance Identity	High	Test substance was identified as trans-1,2-dichloroethylene.
	Metric 2:	Test Substance Source	High	The source of the test substance was Aldrich Chemical Co., Milwaukee, WI. Lot number was included.
	Metric 3:	Test Substance Purity	High	Test substance was 98% pure.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	Negative control was appropriate (vehicle; 10% emulphor in deionised water).
	Metric 5:	Positive Controls	N/A	Positive control was not necessary for this study.
	Metric 6:	Randomized Allocation of Animals	Medium	The current study did not specify whether animals were randomly distributed across groups; however, the study followed methodological details reported in HERO ID 64563. This reference indicated that the study animals were randomized (method not specified).
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and Storage of Test Substance	Medium	DCE was prepared on the day of administration and maintained in dark glassware at 4 °C until use. The test substance is volatile; it was not specified whether the bottles were sealed to prevent volatilization.
	Metric 8:	Consistency of Exposure Administration	High	Exposures were administered consistently across groups; the gavage volume (0.01 mL/g) was reported.
	Metric 9:	Reporting of Doses/Concentrations	Medium	Doses are reported as mg/kg without ambiguity and were based on LD50 values. The study did not specify whether the test solutions for the gavage study were analytically verified.
	Metric 10:	Exposure Frequency and Duration	High	Exposure duration was appropriate for study a range-finding study.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The number of dose groups and spacing were appropriate (range of response obtained and doses were justified).
	Metric 12:	Exposure Route and Method	High	Exposure route was appropriate.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Medium	Test animal characteristics were not provided in the current study; however, some animal details were reported in White et al. 1985 (HERO 64563). The test animals were obtained from Charles River Breeding Laboratories and the animal age was specified. Starting body weights were not provided.
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Study Citation:	Barnes, D. W., Sanders, V. M., White, K. L., Jr, Shopp, G. M., Jr, Munson, A. E. (1985). Toxicology of trans-1,2-dichloroethylene in the mouse. Drug and Chemical Toxicology 8(5):373-392.			
Health Outcome(s):	Nutritional/Metabolic			
Reported Health Effect(s):	Nutritional/Metabolic: Body weightWater consumption (drinking water study)			
Duration:	Short-term (>1-30 days) 14-day gavage			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	200220; Linked HERO ID(s): 200220, 62637, 5435222			
Domain	Metric	Rating	Comments	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Medium	Husbandry conditions were not reported in this reference, but some methodological details are provided in White et al. 1985 (HERO 64563). The reference stated that food and water were available ad libitum and acceptable room temperature, and humidity targets were used. The photoperiod was 12 hrs. The number of animals per cage was not specified.	
	Metric 15: Number of Animals per Group	Low	The total number of animals treated/group were not reported.	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	High	Outcome assessment methods were described in detail in White et al. 1985 (HERO 64563), with some details also provided in HERO IDs 200220 and 62637. The outcome assessment methods were appropriate for the study type.	
	Metric 17: Consistency of Outcome Assessment	Medium	Outcome assessment methods were described in White et al. (HERO 64563) and appeared to be consistent across study groups.	
	Metric 18: Sampling Adequacy	High	The number of animals sampled were reported and appropriate. Organ weights and serum enzymes are reported for 9-10 animals per treatment group.	
	Metric 19: Blinding of Assessors	N/A	Blinding was not necessary for this study.	
	Metric 20: Negative Control Response	High	Negative control response was appropriate.	
Domain 6: Confounding / Variable Control				
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	Study did not report all information to determine confounding, reported information did not identify differences between groups.	
	Metric 22: Health Outcomes Unrelated to Exposure	Medium	No information was provided to either to support or dismiss differences in groups in health outcomes or attrition.	
	Metric 23: Data Presentation and Analysis	High	Statistical analysis was appropriate.	
	Metric 24: Reporting of Data	Medium	Body weight gain was reported as negative in the text.	
Additional Comments:	Re-Review QC Shelley Stevens (sstevens@srcinc.com)Scores were updated for metrics: 4, 6, 7, 8, 9, 10, 11, 13, 14, and 16; 24 was changed for nutritional/metabolic. Additional details were added to other metric comments. Form 2d was revised. Details from Barnes et al. (200220) and White et al. 64563 were included.			
Overall Quality Determination		High		

Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.			
Health Outcome(s):	Lung/Respiratory			
Reported Health Effect(s):	Lung/Respiratory: Lungs: gross pathology (acute oral and i.p studies); histopathology (inhalation – all durations)			
Duration:	Short-term (>1-30 days) 8hr/day, 5days/week for 1 or 2 weeks			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740886			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	The test substance was identified by a definitive name, trans-1,2-dichloroethylene.	
	Metric 2: Test Substance Source	Low	The test substance was obtained from a commercial source (Merck). A batch or lot number was not reported, so this metric is rated Low.	
	Metric 3: Test Substance Purity	Low	Purity or grade of the test substance was not reported.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	It was specified that control animals were treated identically to the treated animals except that no test substance was added to the air (sham-exposed). This was also apparent from Table III, which showed controls for every exposure paradigm.	
	Metric 5: Positive Controls	N/A	No positive controls are required for this study type.	
	Metric 6: Randomized Allocation of Animals	Low	The method of allocation of test animals was not reported.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Medium	Test substance preparation and generation of the vapor for inhalation exposures were reported with adequate detail. Test substance storage was not reported; therefore, this metric is rated as Medium.	
	Metric 8: Consistency of Exposure Administration	High	Exposures occurred daily between 12am-8am	
	Metric 9: Reporting of Doses/Concentrations	Medium	Target concentrations were reported without ambiguity. Analytical concentrations (gas chromatography) were not specified but were reported to be within 3% of target concentrations. Therefore, the lack of reporting analytical concentrations is not expected to have substantially impacted results.	
	Metric 10: Exposure Frequency and Duration	Medium	Inhalation exposures were administered for 8 hours per day, which differs from the typical 6 hours per day. However, this difference is not expected to have substantially impacted results.	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	Only a single concentration is tested. However, the aim of the study was to evaluate the effects of this concentration (200 ppm, the TLV/MAC in many countries at the time of the study) across multiple timepoints, rather than multiple concentrations at one time-point. Therefore, this is not considered to have significantly impacted results or to have significantly hampered conclusions.	
	Metric 12: Exposure Route and Method	Medium	The route and exposure method were suited to the test substance. Air changes/hour was specified to be > 10. Whole-body exposure chambers were utilized. The test substance may condense at the higher concentrations tested for the acute exposures.	
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Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.			
Health Outcome(s):	Lung/Respiratory			
Reported Health Effect(s):	Lung/Respiratory: Lungs: gross pathology (acute oral and i.p studies); histopathology (inhalation – all durations)			
Duration:	Short-term (>1-30 days) 8hr/day, 5days/week for 1 or 2 weeks			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740886			
Domain	Metric	Rating	Comments	
Domain 4: Test Animals				
Metric 13:	Test Animal Characteristics	High	Test animal species, strain, sex, and starting body weight were reported. The age of the test animals was specified to be "mature." The test animals were obtained from a commercial source and were appropriate for the study type.	
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Most husbandry conditions were reported. Light-dark cycle was not reported.	
Metric 15:	Number of Animals per Group	Medium	6 animals/group (female only) were utilized for all treatment and control groups. This is sufficient for a short-term study and to conduct statistical analysis.	
Domain 5: Outcome Assessment				
Metric 16:	Outcome Assessment Methodology	High	Histopathology was considered to be adequate to assess the outcome of interest. Organ weights were not measured.	
Metric 17:	Consistency of Outcome Assessment	High	Outcomes appeared to be assessed consistently across study groups. A protocol for histopathology was provided.	
Metric 18:	Sampling Adequacy	High	All 6 animals/group appear to have been sampled for histopathology based on Table III.	
Metric 19:	Blinding of Assessors	N/A	Blinding is not required for initial histopathology.	
Metric 20:	Negative Control Response	High	Negative control responses were adequate	
Domain 6: Confounding / Variable Control				
Metric 21:	Confounding Variables in Test Design and Procedures	High	No confounding variables were reported or identified.	
Metric 22:	Health Outcomes Unrelated to Exposure	High	No effects unrelated to exposure were reported or identified.	
Metric 23:	Data Presentation and Analysis	High	Statistical analysis was not performed, but sufficient data were provided to allow for independent analysis.	
Metric 24:	Reporting of Data	High	Data were adequately reported as incidences including level of severity.	
Additional Comments:	None			
Overall Quality Determination		High		

Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.			
Health Outcome(s):	Musculoskeletal			
Reported Health Effect(s):	Musculoskeletal: Histopathology (quadriceps muscle; inhalation, all durations)			
Duration:	Short-term (>1-30 days) 8hr/day, 5days/week for 1 or 2 weeks			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740886			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	The test substance was identified by a definitive name, trans-1,2-dichloroethylene.	
	Metric 2: Test Substance Source	Low	The test substance was obtained from a commercial source (Merck). A batch or lot number was not reported, so this metric is rated Low.	
	Metric 3: Test Substance Purity	Low	Purity or grade of the test substance was not reported.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	It was specified that control animals were treated identically to the treated animals except that no test substance was added to the air (sham-exposed). This was also apparent from Table III, which showed controls for every exposure paradigm.	
	Metric 5: Positive Controls	N/A	No positive controls are required for this study type.	
	Metric 6: Randomized Allocation of Animals	Low	The method of allocation of test animals was not reported.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Medium	Test substance preparation and generation of the vapor for inhalation exposures were reported with adequate detail. Test substance storage was not reported; therefore, this metric is rated as Medium.	
	Metric 8: Consistency of Exposure Administration	High	Exposures occurred daily between 12am-8am	
	Metric 9: Reporting of Doses/Concentrations	Medium	Target concentrations were reported without ambiguity. Analytical concentrations (gas chromatography) were not specified but were reported to be within 3% of target concentrations. Therefore, the lack of reporting analytical concentrations is not expected to have substantially impacted results.	
	Metric 10: Exposure Frequency and Duration	Medium	Inhalation exposures were administered for 8 hours per day, which differs from the typical 6 hours per day. However, this difference is not expected to have substantially impacted results.	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	Only a single concentration is tested. However, the aim of the study was to evaluate the effects of this concentration (200 ppm, the TLV/MAC in many countries at the time of the study) across multiple timepoints, rather than multiple concentrations at one time-point. Therefore, this is not considered to have significantly impacted results or to have significantly hampered conclusions.	
	Metric 12: Exposure Route and Method	Medium	The route and exposure method were suited to the test substance. Air changes/hour was specified to be > 10. Whole-body exposure chambers were utilized. The test substance may condense at the higher concentrations tested for the acute exposures.	
Domain 4: Test Animals				
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Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.			
Health Outcome(s):	Musculoskeletal			
Reported Health Effect(s):	Musculoskeletal: Histopathology (quadriceps muscle; inhalation, all durations)			
Duration:	Short-term (>1-30 days) 8hr/day, 5days/week for 1 or 2 weeks			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740886			
Domain	Metric	Rating	Comments	
	Metric 13: Test Animal Characteristics	High	Test animal species, strain, sex, and starting body weight were reported. The age of the test animals was specified to be "mature." The test animals were obtained from a commercial source and were appropriate for the study type.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Medium	Most husbandry conditions were reported. Light-dark cycle was not reported.	
	Metric 15: Number of Animals per Group	Medium	6 animals/group (female only) were utilized for all treatment and control groups. This is sufficient for a short-term study and to conduct statistical analysis.	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	High	Histopathology was considered to be adequate to assess the outcome of interest. Organ weights were not measured.	
	Metric 17: Consistency of Outcome Assessment	High	Outcomes appeared to be assessed consistently across study groups. A protocol for histopathology was provided.	
	Metric 18: Sampling Adequacy	High	All 6 animals/group appear to have been sampled for histopathology based on Table III. Table III reports histopathology results for the lung and liver, but it is assumed that histopathology for all organs specified was carried out on these animals.	
	Metric 19: Blinding of Assessors	N/A	Blinding is not required for initial histopathology.	
	Metric 20: Negative Control Response	Low	Only data for organs with evidence of lesions were reported.	
Domain 6: Confounding / Variable Control				
	Metric 21: Confounding Variables in Test Design and Procedures	High	No confounding variables were reported or identified.	
	Metric 22: Health Outcomes Unrelated to Exposure	High	No effects unrelated to exposure were reported or identified.	
	Metric 23: Data Presentation and Analysis	N/A	Statistical analysis was not necessary given the supposed negative findings.	
	Metric 24: Reporting of Data	High	Negative results were qualitatively reported.	
Additional Comments: None				
Overall Quality Determination		High		

Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.			
Health Outcome(s):	Cardiovascular			
Reported Health Effect(s):	Cardiovascular: Heart (gross pathology in acute oral and i.p studies); histopathology (inhalation – acute)			
Duration:	Short-term (>1-30 days) 8hr/day, 5days/week for 1 or 2 weeks			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740886			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	The test substance was identified by a definitive name, trans-1,2-dichloroethylene.	
	Metric 2: Test Substance Source	Low	The test substance was obtained from a commercial source (Merck). A batch or lot number was not reported, so this metric is rated Low.	
	Metric 3: Test Substance Purity	Low	Purity or grade of the test substance was not reported.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	It was specified that control animals were treated identically to the treated animals except that no test substance was added to the air (sham-exposed). This was also apparent from Table III, which showed controls for every exposure paradigm.	
	Metric 5: Positive Controls	N/A	No positive controls are required for this study type.	
	Metric 6: Randomized Allocation of Animals	Low	The method of allocation of test animals was not reported.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Medium	Test substance preparation and generation of the vapor for inhalation exposures were reported with adequate detail. Test substance storage was not reported; therefore, this metric is rated as Medium.	
	Metric 8: Consistency of Exposure Administration	High	Exposures occurred daily between 12am-8am	
	Metric 9: Reporting of Doses/Concentrations	Medium	Target concentrations were reported without ambiguity. Analytical concentrations (gas chromatography) were not specified but were reported to be within 3% of target concentrations. Therefore, the lack of reporting analytical concentrations is not expected to have substantially impacted results.	
	Metric 10: Exposure Frequency and Duration	Medium	Inhalation exposures were administered for 8 hours per day, which differs from the typical 6 hours per day. However, this difference is not expected to have substantially impacted results.	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	Only a single concentration is tested. However, the aim of the study was to evaluate the effects of this concentration (200 ppm, the TLV/MAC in many countries at the time of the study) across multiple timepoints, rather than multiple concentrations at one time-point. Therefore, this is not considered to have significantly impacted results or to have significantly hampered conclusions.	
	Metric 12: Exposure Route and Method	Medium	The route and exposure method were suited to the test substance. Air changes/hour was specified to be > 10. Whole-body exposure chambers were utilized. The test substance may condense at the higher concentrations tested for the acute exposures.	
Domain 4: Test Animals				
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Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.			
Health Outcome(s):	Cardiovascular			
Reported Health Effect(s):	Cardiovascular: Heart (gross pathology in acute oral and i.p studies); histopathology (inhalation – acute)			
Duration:	Short-term (>1-30 days) 8hr/day, 5days/week for 1 or 2 weeks			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740886			
Domain	Metric	Rating	Comments	
	Metric 13: Test Animal Characteristics	High	Test animal species, strain, sex, and starting body weight were reported. The age of the test animals was specified to be "mature." The test animals were obtained from a commercial source and were appropriate for the study type.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Medium	Most husbandry conditions were reported. Light-dark cycle was not reported.	
	Metric 15: Number of Animals per Group	Medium	6 animals/group (female only) were utilized for all treatment and control groups. This is sufficient for a short-term study and to conduct statistical analysis.	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	High	Histopathology was considered to be adequate to assess the outcome of interest. Organ weights were not measured.	
	Metric 17: Consistency of Outcome Assessment	High	Outcomes appeared to be assessed consistently across study groups. A protocol for histopathology was provided.	
	Metric 18: Sampling Adequacy	High	All 6 animals/group appear to have been sampled for histopathology based on Table III. Table III reports histopathology results for the lung and liver, but it is assumed that histopathology for all organs specified was carried out on these animals.	
	Metric 19: Blinding of Assessors	N/A	Blinding is not required for initial histopathology.	
	Metric 20: Negative Control Response	Low	Only data for organs with evidence of lesions were reported.	
Domain 6: Confounding / Variable Control				
	Metric 21: Confounding Variables in Test Design and Procedures	High	No confounding variables were reported or identified.	
	Metric 22: Health Outcomes Unrelated to Exposure	High	No effects unrelated to exposure were reported or identified.	
	Metric 23: Data Presentation and Analysis	N/A	Statistical analysis was not necessary given the supposed negative findings.	
	Metric 24: Reporting of Data	Uninformative	Heart histopathology data were only reported for the 3000 ppm acute inhalation exposure and corresponding control. Negative findings were not described qualitatively; therefore, the results for this outcome for this exposure duration were not reported.	

Additional Comments: None

Overall Quality Determination**Uninformative**

Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.			
Health Outcome(s):	Renal/Kidney; Immune/Hematological; Hepatic/Liver;			
Reported Health Effect(s):	Renal/Kidney: Gross pathology of the kidney and bladder and hematuria (acute oral and i.p studies); histopathology (inhalation – all durations; no effects); serum chemistry (electrolytes, BUN, uric acid – inhalation acute durations); Immune/Hematological: Histopathology (spleen; inhalation – all durations; no effects); hematology (WBC count, RBC count, Hgb, packed cell volume, MCV, MCH, MCHC; inhalation studies – acute duration); Hepatic/Liver: Gross pathology of the liver (acute oral and i.p studies); histopathology of the liver (inhalation – all durations); serum chemistry (cholesterol, bilirubin, total protein, alkaline phosphatase, GOT, GPT, albumin, glucose; in inhalation acute studies and possibly 16-week duration); bile accumulation (acute inhalation);			
Duration:	Short-term (>1-30 days) 8hr/day, 5days/week for 1 or 2 weeks			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740886			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	All Outcomes: The test substance was identified by a definitive name, trans-1,2-dichloroethylene.	
	Metric 2: Test Substance Source	Low	All Outcomes: The test substance was obtained from a commercial source (Merck). A batch or lot number was not reported, so this metric is rated Low.	
	Metric 3: Test Substance Purity	Low	All Outcomes: Purity or grade of the test substance was not reported.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	All Outcomes: It was specified that control animals were treated identically to the treated animals except that no test substance was added to the air (sham-exposed). This was also apparent from Table III, which showed controls for every exposure paradigm.	
	Metric 5: Positive Controls	N/A	All Outcomes: No positive controls are required for this study type.	
	Metric 6: Randomized Allocation of Animals	Low	All Outcomes: The method of allocation of test animals was not reported.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Medium	All Outcomes: Test substance preparation and generation of the vapor for inhalation exposures were reported with adequate detail. Test substance storage was not reported; therefore, this metric is rated as Medium.	
	Metric 8: Consistency of Exposure Administration	High	All Outcomes: Exposures occurred daily between 12am-8am	
	Metric 9: Reporting of Doses/Concentrations	Medium	All Outcomes: Target concentrations were reported without ambiguity. Analytical concentrations (gas chromatography) were not specified but were reported to be within 3% of target concentrations. Therefore, the lack of reporting analytical concentrations is not expected to have substantially impacted results.	
	Metric 10: Exposure Frequency and Duration	Medium	All Outcomes: Inhalation exposures were administered for 8 hours per day, which differs from the typical 6 hours per day. However, this difference is not expected to have substantially impacted results.	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: Only a single concentration is tested. However, the aim of the study was to evaluate the effects of this concentration (200 ppm, the TLV/MAC in many countries at the time of the study) across multiple timepoints, rather than multiple concentrations at one timepoint. Therefore, this is not considered to have significantly impacted results or to have significantly hampered conclusions.	

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Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.			
Health Outcome(s):	Renal/Kidney; Immune/Hematological; Hepatic/Liver;			
Reported Health Effect(s):	Renal/Kidney: Gross pathology of the kidney and bladder and hematuria (acute oral and i.p studies); histopathology (inhalation – all durations; no effects); serum chemistry (electrolytes, BUN, uric acid – inhalation acute durations); Immune/Hematological: Histopathology (spleen; inhalation – all durations; no effects); hematology (WBC count, RBC count, Hgb, packed cell volume, MCV, MCH, MCHC; inhalation studies – acute duration); Hepatic/Liver: Gross pathology of the liver (acute oral and i.p studies); histopathology of the liver (inhalation – all durations); serum chemistry (cholesterol, bilirubin, total protein, alkaline phosphatase, GOT, GPT, albumin, glucose; in inhalation acute studies and possibly 16-week duration); bile accumulation (acute inhalation);			
Duration:	Short-term (>1-30 days) 8hr/day, 5days/week for 1 or 2 weeks			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740886			
Domain		Metric	Rating	Comments
	Metric 12:	Exposure Route and Method	Medium	All Outcomes: The route and exposure method were suited to the test substance. Air changes/hour was specified to be > 10. Whole-body exposure chambers were utilized. The test substance may condense at the higher concentrations tested for the acute exposures.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	High	All Outcomes: Test animal species, strain, sex, and starting body weight were reported. The age of the test animals was specified to be "mature." The test animals were obtained from a commercial source and were appropriate for the study type.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	All Outcomes: Most husbandry conditions were reported. Light-dark cycle was not reported.
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: 6 animals/group (female only) were utilized for all treatment and control groups. This is sufficient for a short-term study and to conduct statistical analysis.
Domain 5: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	Medium	Renal/Kidney: Histopathology was considered to be adequate to assess the outcome of interest; however, clinical chemistry and organ weights were not measured and these endpoints are typically included in repeat dose experiments.; Immune/Hematological: Histopathology was considered to be adequate to assess the outcome of interest; however, hematology and organ weights were not measured and these endpoints are typically included in repeat dose experiments.; Hepatic/Liver: Histopathology was considered to be adequate to assess the outcome of interest; however, clinical chemistry and organ weights were not measured and these endpoints are typically included in repeat dose experiments.
	Metric 17:	Consistency of Outcome Assessment	High	All Outcomes: Outcomes appeared to be assessed consistently across study groups. A protocol for histopathology was provided.
	Metric 18:	Sampling Adequacy	High	All Outcomes: All 6 animals/group appear to have been sampled for histopathology based on Table III.
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding is not required for initial histopathology.
	Metric 20:	Negative Control Response	High	All Outcomes: Negative control responses were adequate
Domain 6: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	High	All Outcomes: No confounding variables were reported or identified.
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Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.
Health Outcome(s):	Renal/Kidney; Immune/Hematological; Hepatic/Liver;
Reported Health Effect(s):	Renal/Kidney: Gross pathology of the kidney and bladder and hematuria (acute oral and i.p studies); histopathology (inhalation – all durations; no effects); serum chemistry (electrolytes, BUN, uric acid – inhalation acute durations); Immune/Hematological: Histopathology (spleen; inhalation – all durations; no effects); hematology (WBC count, RBC count, Hgb, packed cell volume, MCV, MCH, MCHC; inhalation studies – acute duration); Hepatic/Liver: Gross pathology of the liver (acute oral and i.p studies); histopathology of the liver (inhalation – all durations); serum chemistry (cholesterol, bilirubin, total protein, alkaline phosphatase, GOT, GPT, albumin, glucose; in inhalation acute studies and possibly 16-week duration); bile accumulation (acute inhalation);
Duration:	Short-term (>1-30 days) 8hr/day, 5days/week for 1 or 2 weeks
Chemical:	trans-1,2-Dichloroethylene- Parent compound
HERO ID:	1740886

Domain	Metric	Rating	Comments
	Metric 22: Health Outcomes Unrelated to Exposure	High	All Outcomes: No effects unrelated to exposure were reported or identified.
	Metric 23: Data Presentation and Analysis	High	All Outcomes: Statistical analysis was not performed, but sufficient data were provided to allow for independent analysis.
	Metric 24: Reporting of Data	High	All Outcomes: Data were adequately reported as incidences including level of severity.

Additional Comments: None

Overall Quality Determination**High**

Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.		
Health Outcome(s):	Neurological/Behavioral		
Reported Health Effect(s):	Neurological/Behavioral: Neurological/behavioral clinical signs (acute oral and ip and inhalation – all durations); histopathology brain and peripheral nerves (inhalation – all durations, no effects)		
Duration:	Short-term (>1-30 days) 8hr/day, 5days/week for 1 or 2 weeks		
Chemical:	trans-1,2-Dichloroethylene- Parent compound		
HERO ID:	1740886		
Domain	Metric	Rating	Comments
Domain 1: Test Substance			
	Metric 1: Test Substance Identity	High	The test substance was identified by a definitive name, trans-1,2-dichloroethylene.
	Metric 2: Test Substance Source	Low	The test substance was obtained from a commercial source (Merck). A batch or lot number was not reported, so this metric is rated Low.
	Metric 3: Test Substance Purity	Low	Purity or grade of the test substance was not reported.
Domain 2: Test Design			
	Metric 4: Negative and Vehicle Controls	High	It was specified that control animals were treated identically to the treated animals except that no test substance was added to the air (sham-exposed). This was also apparent from Table III, which showed controls for every exposure paradigm.
	Metric 5: Positive Controls	N/A	No positive controls are required for this study type.
	Metric 6: Randomized Allocation of Animals	Low	The method of allocation of test animals was not reported.
Domain 3: Exposure Characterization			
	Metric 7: Preparation and Storage of Test Substance	Medium	Test substance preparation and generation of the vapor for inhalation exposures were reported with adequate detail. Test substance storage was not reported; therefore, this metric is rated as Medium.
	Metric 8: Consistency of Exposure Administration	High	The acute exposures occurred daily between 12am-8am
	Metric 9: Reporting of Doses/Concentrations	Medium	Target concentrations were reported without ambiguity. Analytical concentrations (gas chromatography) were not specified but were reported to be within 3% of target concentrations. Therefore, the lack of reporting analytical concentrations is not expected to have substantially impacted results.
	Metric 10: Exposure Frequency and Duration	Medium	Inhalation exposures were administered for 8 hours per day, which differs from the typical 6 hours per day. However, this difference is not expected to have substantially impacted results.
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	Only a single concentration is tested. However, the aim of the study was to evaluate the effects of this concentration (200 ppm, the TLV/MAC in many countries at the time of the study) across multiple timepoints, rather than multiple concentrations at one time-point. Therefore, this is not considered to have significantly impacted results or to have significantly hampered conclusions.
	Metric 12: Exposure Route and Method	Medium	The route and exposure method were suited to the test substance. Air changes/hour was specified to be > 10. Whole-body exposure chambers were utilized. The test substance may condense at the higher concentrations tested for the acute exposures.
Domain 4: Test Animals			
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Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.			
Health Outcome(s):	Neurological/Behavioral			
Reported Health Effect(s):	Neurological/Behavioral: Neurological/behavioral clinical signs (acute oral and ip and inhalation – all durations); histopathology brain and peripheral nerves (inhalation – all durations, no effects)			
Duration:	Short-term (>1-30 days) 8hr/day, 5days/week for 1 or 2 weeks			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740886			
Domain	Metric	Rating	Comments	
	Metric 13: Test Animal Characteristics	High	Test animal species, strain, sex, and starting body weight were reported. The age of the test animals was specified to be "mature." The test animals were obtained from a commercial source and were appropriate for the study type.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Medium	Most husbandry conditions were reported. Light-dark cycle was not reported.	
	Metric 15: Number of Animals per Group	Medium	6 animals/group (female only) were utilized for all treatment and control groups. This is sufficient for a short-term study and to conduct statistical analysis.	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	Medium	Histopathology (brain, sciatic nerve) and clinical signs were considered to be adequate to assess the outcome of interest. The study authors were specifically interested in acute neurotoxicity (CNS depression), which was the basis of the TLV-MAC (200 ppm) that was the focus of the study. This would be appropriately addressed by noting clinical signs of toxicity during exposure administration. A protocol for animal observations (frequency/duration) was not provided.	
	Metric 17: Consistency of Outcome Assessment	Medium	Outcomes appeared to be assessed consistently across study groups. A protocol for histopathology was provided, but not for clinical observations.	
	Metric 18: Sampling Adequacy	High	It is unclear whether all 6 animals/group were sampled for clinical signs. All 6 animals/group appear to have been sampled for histopathology based on Table III. Table III reports histopathology results for the lung and liver, but it is assumed that histopathology for all organs specified was carried out on these animals.	
	Metric 19: Blinding of Assessors	N/A	Blinding is not required for initial histopathology. Blinding was not specified for clinical observations.	
	Metric 20: Negative Control Response	High	Negative controls responded appropriately.	
Domain 6: Confounding / Variable Control				
	Metric 21: Confounding Variables in Test Design and Procedures	High	No confounding variables were reported or identified.	
	Metric 22: Health Outcomes Unrelated to Exposure	High	No effects unrelated to exposure were reported or identified.	
	Metric 23: Data Presentation and Analysis	N/A	Statistical analysis was not necessary given the negative findings (qualitatively described).	
	Metric 24: Reporting of Data	High	Negative data were qualitatively described.	
Additional Comments:	None			

Overall Quality Determination**High**

Study Citation:	Hanioka, N., Jinno, H., Nishimura, T., Ando, M. (1998). Changes in hepatic cytochrome P450 enzymes by cis- and trans-1,2-dichloroethylenes in rat. Xenobiotica 28(1):41-51.		
Health Outcome(s):	Hepatic/Liver; Immune/Hematological; Nutritional/Metabolic; Hepatic/Liver; Immune/Hematological; Nutritional/Metabolic;		
Reported Health Effect(s):	Hepatic/Liver: Liver weights, P450-dependent-monooxygenase activities and P450 protein levels in liver microsomes; Immune/Hematological: Spleen and thymus weights; Nutritional/Metabolic: Body weight changes; Hepatic/Liver: Liver weights, P450-dependent-monooxygenase activities and P450 protein levels in liver microsomes; Immune/Hematological: Spleen and thymus weights; Nutritional/Metabolic: Body weight changes;		
Duration:	Short-term (>1-30 days) 4 days -trans-DCE		
Chemical:	trans-1,2-Dichloroethylene- Parent compound		
HERO ID:	1414030		
Domain	Metric	Rating	Comments
Domain 1: Test Substance			
	Metric 1: Test Substance Identity	High	Hepatic/Liver: nomenclature was provided; Immune/Hematological: Chemical nomenclature provided; Nutritional/Metabolic: Nomenclature was provided; Hepatic/Liver: Nomenclature was provided; Immune/Hematological: Nomenclature was provided; Nutritional/Metabolic: Nomenclature provided
	Metric 2: Test Substance Source	Low	All Outcomes: Batch lot/number was not reported
	Metric 3: Test Substance Purity	Medium	Hepatic/Liver: Purity of isomers reported at >99%. Impurities, residual chemicals were identified and the chemical of interest was the main component.; Immune/Hematological: Impurities, residual chemicals, were identified and the chemical of interest was the main component.; Nutritional/Metabolic: Impurities, residual chemicals, were identified and the chemical of interest was the main component.; Hepatic/Liver: Impurities, residual chemicals, were identified and the chemical of interest was the main component.; Immune/Hematological: Impurities, residual chemicals, were identified and the chemical of interest was the main component.; Nutritional/Metabolic: Impurities, residual chemicals, were identified and the chemical of interest was the main component.
Domain 2: Test Design			
	Metric 4: Negative and Vehicle Controls	High	All Outcomes: Vehicle only used as control
	Metric 5: Positive Controls	N/A	All Outcomes: Positive control not required for this study type
	Metric 6: Randomized Allocation of Animals	Low	All Outcomes: Random allocation was not reported
Domain 3: Exposure Characterization			
	Metric 7: Preparation and Storage of Test Substance	Low	All Outcomes: Storage and preparation of the test substance was not reported
	Metric 8: Consistency of Exposure Administration	High	All Outcomes: single dose
	Metric 9: Reporting of Doses/Concentrations	High	All Outcomes: Single i.p. dose 7.5 mmol/kg/2.0 mL corn oil
	Metric 10: Exposure Frequency and Duration	High	All Outcomes: Single i.p. dose for 4 consecutive days (table 1)
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	Medium	All Outcomes: Dose selection based on previous unpublished study.
	Metric 12: Exposure Route and Method	High	All Outcomes: i.p. exposure sufficient to evaluate body and organ weight changes
Domain 4: Test Animals			

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Study Citation:	Hanioka, N., Jinno, H., Nishimura, T., Ando, M. (1998). Changes in hepatic cytochrome P450 enzymes by cis- and trans-1,2-dichloroethylenes in rat. Xenobiotica 28(1):41-51.			
Health Outcome(s):	Hepatic/Liver; Immune/Hematological; Nutritional/Metabolic; Hepatic/Liver; Immune/Hematological; Nutritional/Metabolic;			
Reported Health Effect(s):	Hepatic/Liver: Liver weights, P450-dependent-monooxygenase activities and P450 protein levels in liver microsomes; Immune/Hematological: Spleen and thymus weights; Nutritional/Metabolic: Body weight changes; Hepatic/Liver: Liver weights, P450-dependent-monooxygenase activities and P450 protein levels in liver microsomes; Immune/Hematological: Spleen and thymus weights; Nutritional/Metabolic: Body weight changes;			
Duration:	Short-term (>1-30 days) 4 days -trans-DCE			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1414030			
Domain	Metric	Rating	Comments	
	Metric 13: Test Animal Characteristics	High	All Outcomes: Age, bodyweights, and colony source were reported	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: Feed, water, light/dark cycle, plastic cages, temperature, humidity, and acclimation period reported.	
	Metric 15: Number of Animals per Group	Medium	All Outcomes: 4 animals/group	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	High	Hepatic/Liver: No significant differences in liver weights in males and females; Immune/Hematological: No significant changes in spleen or thymus weights for males or females; Nutritional/Metabolic: No significant changes in body weights in females. Significantly decreased body weight changes in males.; Hepatic/Liver: No significant differences in liver weights in males and females.; Immune/Hematological: No significant changes in spleen or thymus weights for males or females; Nutritional/Metabolic: No significant changes in body weights females. Significantly decreased body weight changes in males.	
	Metric 17: Consistency of Outcome Assessment	High	Hepatic/Liver: Outcomes were assessed consistently across groups; Immune/Hematological: Outcomes were assessed consistently across groups; Nutritional/Metabolic: Organ weights were assessed consistently across study groups; Hepatic/Liver: Outcomes were assessed consistently across groups; Immune/Hematological: spleen and thymus weights were assessed consistently for control and treated male and female rats; Nutritional/Metabolic: Body weight changes were assessed and reported consistently for control and treated male and female rats	
	Metric 18: Sampling Adequacy	High	Hepatic/Liver: Adequate sampling was used to assess outcomes; Immune/Hematological: Adequate sampling was used to assess outcomes; Nutritional/Metabolic: Sample size was adequate to assess and observe the differences across study groups; Hepatic/Liver: The study used adequate sampling; Immune/Hematological: Sampling was adequate to observe effects from DCE across treated groups and sexes; Nutritional/Metabolic: The study used adequate sampling	
	Metric 19: Blinding of Assessors	N/A	All Outcomes: Blinding of assessors not required for the exams conducted (organ and body weights)	
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Study Citation:	Hanioka, N., Jinno, H., Nishimura, T., Ando, M. (1998). Changes in hepatic cytochrome P450 enzymes by cis- and trans-1,2-dichloroethylenes in rat. Xenobiotica 28(1):41-51.			
Health Outcome(s):	Hepatic/Liver; Immune/Hematological; Nutritional/Metabolic; Hepatic/Liver; Immune/Hematological; Nutritional/Metabolic;			
Reported Health Effect(s):	Hepatic/Liver: Liver weights, P450-dependent-monooxygenase activities and P450 protein levels in liver microsomes; Immune/Hematological: Spleen and thymus weights; Nutritional/Metabolic: Body weight changes; Hepatic/Liver: Liver weights, P450-dependent-monooxygenase activities and P450 protein levels in liver microsomes; Immune/Hematological: Spleen and thymus weights; Nutritional/Metabolic: Body weight changes;			
Duration:	Short-term (>1-30 days) 4 days -trans-DCE			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1414030			
Domain	Metric	Rating	Comments	
Metric 20:	Negative Control Response	Medium	Hepatic/Liver: No significant differences in liver weights between treated and untreated animals. There was a sex difference in P450 and fp1levels in the control or trans -1,2-DCE rat. There were sex differences in all P450-dependent monooxygenaseactivities in the control, and cis- and trans -1,2-DCE rat. The CYP1A2 protein levels in the female control, and cis- and trans -1,2-DCE-treated rat were higher than that in the male control.; Immune/Hematological: No significant differences in organ weight changes (spleen and thymus) between male and female rats in the control groups versus treated; Nutritional/Metabolic: Significant (p<0.01) differences in body weight set changes between male and female rats in the control groups; Hepatic/Liver: No significant differences in liver weights between treated and untreated animals. There was a sex difference in P450 and fp1levels in the control or trans -1,2-DCE rat. There were sex differences in all P450-dependent monooxygenaseactivities in the control, and cis- and trans -1,2-DCE rat. The CYP1A2 protein levels in the female control, and cis- and trans -1,2-DCE-treated rat were higher than that in the male control.; Immune/Hematological: Significant (p<0.01) differences in body weight set changes between male and female rats in the control groups; Nutritional/Metabolic: Significant (p<0.01) differences in body weight set changes between male and female rats in the control groups	
Domain 6: Confounding / Variable Control				
Metric 21:	Confounding Variables in Test Design and Procedures	High	Hepatic/Liver: Relevant information was provided tor treated versus control animals.; Immune/Hematological: All relevant information was provided; Nutritional/Metabolic: All information was provided to determine that there was no confounding bias existing; Hepatic/Liver: All relevant study information was provided; Immune/Hematological: all information was provided to determine no confounding bias; Nutritional/Metabolic: The study reported all information to determine that there was no confounding bias	
Metric 22:	Health Outcomes Unrelated to Exposure	High	All Outcomes: End of pg 4 - "rats... remained healthy in appearance and normal in behavior during the study"	
Metric 23:	Data Presentation and Analysis	High	Hepatic/Liver: Appropriate statistical analysis was conducted (student's t=test).; Immune/Hematological: Appropriate statistical methods were used (student's t-test); Nutritional/Metabolic: Appropriate statistical methods were applied; Hepatic/Liver: Appropriate statistical methods were used; Immune/Hematological: Appropriate statistical methods were clearly described; Nutritional/Metabolic: Appropriate statistical methods were used	
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Study Citation:	Hanioka, N., Jinno, H., Nishimura, T., Ando, M. (1998). Changes in hepatic cytochrome P450 enzymes by cis- and trans-1,2-dichloroethylenes in rat. Xenobiotica 28(1):41-51.			
Health Outcome(s):	Hepatic/Liver; Immune/Hematological; Nutritional/Metabolic; Hepatic/Liver; Immune/Hematological; Nutritional/Metabolic;			
Reported Health Effect(s):	Hepatic/Liver: Liver weights, P450-dependent-monooxygenase activities and P450 protein levels in liver microsomes; Immune/Hematological: Spleen and thymus weights; Nutritional/Metabolic: Body weight changes; Hepatic/Liver: Liver weights, P450-dependent-monooxygenase activities and P450 protein levels in liver microsomes; Immune/Hematological: Spleen and thymus weights; Nutritional/Metabolic: Body weight changes;			
Duration:	Short-term (>1-30 days) 4 days -trans-DCE			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1414030			
Domain	Metric	Rating	Comments	
Metric 24:	Reporting of Data	High	Hepatic/Liver: Data were presented on the effects of DCE on liver weights, liver enzymes and proteins; Immune/Hematological: All information was provided to assess spleen and thymus outcomes; Nutritional/Metabolic: Data for exposure-related findings, including means and standard deviations, were presented for all outcomes by exposure group and sex; Hepatic/Liver: Data for exposure-related findings were presented for all liver outcomes by exposure group and sex; Immune/Hematological: Data was reported for liver weights, enzymes and proteins across exposure groups and sexes; Nutritional/Metabolic: Data on changes in body weights were presented across exposure groups and for both sexes	
Additional Comments: trans-1,2-DCE				
Overall Quality Determination		High		

Study Citation:	Plaa, G. L., Larson, R. E. (1965). Relative nephrotoxic properties of chlorinated methane, ethane, and ethylene derivatives in mice. Toxicology and Applied Pharmacology 7(1):37-44.			
Health Outcome(s):	Renal/Kidney			
Reported Health Effect(s):	Renal/Kidney: Urinary glucose and protein; renal histopathology			
Duration:	Short-term (>1-30 days) Short-term- 3 days			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	64411			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
Metric 1:	Test Substance Identity	High	Test substance was identified as trans-1,2-dichloroethylene.	
Metric 2:	Test Substance Source	Low	The source of the test substance was not reported.	
Metric 3:	Test Substance Purity	Low	The purity of the test substance was not reported.	
Domain 2: Test Design				
Metric 4:	Negative and Vehicle Controls	Uninformative	Details of negative control are not reported. It appears the data on the negative controls come from historic data. The strain, age, sex of the animals are not provided nor is information on if the animals were sham or untreated.	
Metric 5:	Positive Controls	N/A	Not applicable for this study.	
Metric 6:	Randomized Allocation of Animals	Low	Authors do not report if how study groups were formed.	
Domain 3: Exposure Characterization				
Metric 7:	Preparation and Storage of Test Substance	Low	Preparation and storage conditions were not properly reported given the volatility of the test substance.	
Metric 8:	Consistency of Exposure Administration	Medium	Details of exposure administration are incomplete.	
Metric 9:	Reporting of Doses/Concentrations	High	Exposure doses were reported without ambiguity.	
Metric 10:	Exposure Frequency and Duration	High	Exposure and frequency were appropriate for outcome studied.	
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	The one dose studied was the highest one that did not cause lethality.	
Metric 12:	Exposure Route and Method	High	Route of exposure was i.p. injection.	
Domain 4: Test Animals				
Metric 13:	Test Animal Characteristics	Low	The source and age of mice were not reported.	
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were not reported.	
Metric 15:	Number of Animals per Group	Low	The number of animals/group were not reported.	
Domain 5: Outcome Assessment				
Metric 16:	Outcome Assessment Methodology	Low	Some details regarding the outcome assessment methodology were lacking (e.g how long urine was collected for, histological evaluations)	
Metric 17:	Consistency of Outcome Assessment	High	Outcomes were assessed consistently across study groups.	

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Study Citation:	Plaa, G. L., Larson, R. E. (1965). Relative nephrotoxic properties of chlorinated methane, ethane, and ethylene derivatives in mice. Toxicology and Applied Pharmacology 7(1):37-44.			
Health Outcome(s):	Renal/Kidney			
Reported Health Effect(s):	Renal/Kidney: Urinary glucose and protein; renal histopathology			
Duration:	Short-term (> 1-30 days) Short-term- 3 days			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	64411			
Domain	Metric	Rating	Comments	
	Metric 18: Sampling Adequacy	Uninformative	Histology was not performed on controls.	
	Metric 19: Blinding of Assessors	N/A	Blinding was not necessary for outcomes studied.	
	Metric 20: Negative Control Response	Low	Negative control histology was not reported.	
Domain 6: Confounding / Variable Control				
	Metric 21: Confounding Variables in Test Design and Procedures	Low	Potential confounding variables were not reported.	
	Metric 22: Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure.	
	Metric 23: Data Presentation and Analysis	High	Statistical analysis was not performed; independent statistics could be done.	
	Metric 24: Reporting of Data	Low	Combistix analysis data were not presented.	
Additional Comments:	Lack of information on the negative control group makes the study unacceptable.			

Overall Quality Determination**Uninformative**

Study Citation:	Shopp, G. M., Sanders, V. M., White, K. L., Munson, A. E. (1985). Humoral and cell-mediated immune status of mice exposed to trans-1,2-dichloroethylene. Drug and Chemical Toxicology 8(5):393-407.		
Health Outcome(s):	Immune/Hematological		
Reported Health Effect(s):	Immune/Hematological: Cellular and humoral response		
Duration:	Short-term (>1-30 days) 14 day- gavage		
Chemical:	trans-1,2-Dichloroethylene- Parent compound		
HERO ID:	5435222; Linked HERO ID(s): 200220, 62637, 5435222		
Domain	Metric	Rating	Comments
Domain 1: Test Substance			
Metric 1:	Test Substance Identity	High	Test substance was identified as trans-1,2-dichloroethylene.
Metric 2:	Test Substance Source	High	The source of the test substance was Aldrich Chemical Co., (Milwaukee, WI). The lot number was provided. Information was obtained from the cited reference: Barnes et al. 1985 (HERO 200220).
Metric 3:	Test Substance Purity	High	Purity of the test substance was 98%. Information was obtained from the cited reference: Barnes et al. 1985 (HERO 200220).
Domain 2: Test Design			
Metric 4:	Negative and Vehicle Controls	High	Negative control was appropriate (vehicle).
Metric 5:	Positive Controls	N/A	Positive control was not required in this study.
Metric 6:	Randomized Allocation of Animals	Medium	The current study did not specify whether animals were randomly distributed across groups; however, the study followed methodological details reported in HERO ID 64563. This reference indicated that the study animals were randomized (method not specified).
Domain 3: Exposure Characterization			
Metric 7:	Preparation and Storage of Test Substance	Medium	DCE was prepared on the day of administration and maintained in dark glassware at 4oC until use. The test substance is volatile, it was not specified whether bottles were sealed to prevent volatilization.
Metric 8:	Consistency of Exposure Administration	High	Exposures were administered consistently across groups; the gavage volume (0.01 mL/g) was reported.
Metric 9:	Reporting of Doses/Concentrations	Medium	Doses are reported as mg/kg without ambiguity and were based on LD50 values. The study did not specify whether the test solutions for the gavage study were analytically verified.
Metric 10:	Exposure Frequency and Duration	High	Exposure frequency and duration were reported and appropriate.
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The number of dose groups and spacing were appropriate (range of response obtained and doses were justified).
Metric 12:	Exposure Route and Method	High	Exposure route was appropriate.
Domain 4: Test Animals			
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Study Citation:	Shopp, G. M., Sanders, V. M., White, K. L., Munson, A. E. (1985). Humoral and cell-mediated immune status of mice exposed to trans-1,2-dichloroethylene. Drug and Chemical Toxicology 8(5):393-407.			
Health Outcome(s):	Immune/Hematological			
Reported Health Effect(s):	Immune/Hematological: Cellular and humoral response			
Duration:	Short-term (>1-30 days) 14 day- gavage			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	5435222; Linked HERO ID(s): 200220, 62637, 5435222			
Domain	Metric	Rating	Comments	
	Metric 13: Test Animal Characteristics	Medium	Test animal characteristics were not provided in the current study; however, some animal details were reported in White et al. 1985 (HERO 64563). The test animals were obtained from Charles River Breeding Laboratories, and the animal age was specified. Starting body weights were not provided.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Medium	Husbandry conditions were not reported in this reference, but some methodological details are provided in White et al. 1985 (HERO 64563). The reference stated that food and water were available ad libitum and acceptable room temperature, and humidity targets were used. The photoperiod was 12 hrs. The number of animals per cage was not specified.	
	Metric 15: Number of Animals per Group	Low	The total number of animals exposed /group was not reported. Different sets of animals were used for humoral and cell-mediated tests.	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	High	Outcome assessment methods were described in detail in White et al. 1985 (HERO 64563), with some details also provided in HERO IDs 200220 and 62637. The outcome assessment methods were appropriate for a range-finding study.	
	Metric 17: Consistency of Outcome Assessment	High	Details of outcome assessment are provided in the cited reference (White et al. 1985). It appeared that outcomes were assessed consistently across groups.	
	Metric 18: Sampling Adequacy	High	The number of animals sampled was adequate.	
	Metric 19: Blinding of Assessors	N/A	Blinding was not necessary for this study.	
	Metric 20: Negative Control Response	High	The negative control response was appropriate.	
Domain 6: Confounding / Variable Control				
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	The study did not report all information to determine confounding; the reported information did not identify differences.	
	Metric 22: Health Outcomes Unrelated to Exposure	Medium	Insufficient information was provided to either support or dismiss differences in groups in health outcomes or attrition.	
	Metric 23: Data Presentation and Analysis	High	Statistical analysis was performed and was appropriate. If a one-way analysis of variance of the means showed treatment effects, the authors performed a Duncan's multiple range test. Significance was set at 0.05, and means and SE values were presented.	
	Metric 24: Reporting of Data	High	Data for all endpoints were quantitatively reported as means ± SE. Statistical significance was noted. Individual animal data were not provided.	
Additional Comments:	12/23/2025: dherber@srcinc.com: Updated the following metric scores based on information in Barnes et al. 1985 (HERO 200220) and White et al. 1985 (HERO 64563): Metrics 6, 7, 9, 13, and 14. In addition, text was updated in Metrics 2, 3, 8, 15, 16, 17, and 24.			

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Study Citation:	Shopp, G. M., Sanders, V. M., White, K. L., Munson, A. E. (1985). Humoral and cell-mediated immune status of mice exposed to trans-1,2-dichloroethylene. Drug and Chemical Toxicology 8(5):393-407.
Health Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Immune/Hematological: Cellular and humoral response
Duration:	Short-term (>1-30 days) 14 day- gavage
Chemical:	trans-1,2-Dichloroethylene- Parent compound
HERO ID:	5435222; Linked HERO ID(s): 200220, 62637, 5435222

Domain	Metric	Rating	Comments
Overall Quality Determination		High	

Study Citation:	Barnes, D. W., Sanders, V. M., White, K. L., Jr, Shopp, G. M., Jr, Munson, A. E. (1985). Toxicology of trans-1,2-dichloroethylene in the mouse. Drug and Chemical Toxicology 8(5):373-392.			
Health Outcome(s):	Hepatic/Liver; Immune/Hematological; Neurological/Behavioral; Lung/Respiratory; Reproductive/Developmental; Renal/Kidney;			
Reported Health Effect(s):	Hepatic/Liver: Drinking water: Serum ALT, AST, ALP, LDH, liver weight, and hepatic microsomal activitiesGavage: Serum LDH, ALT and liver weight; Immune/Hematological: Hematology parameters, spleen and thymus weight; Neurological/Behavioral: Gavage 14-day: Brain weight; clinical signs (decreased activity, ruffled fur, ataxia, loss of righting reflex, hunch-backed appearance)Drinking water: Brain weightAcute: clinical observations (CNS effects); Lung/Respiratory: Lung weight; Reproductive/Developmental: Gavage study: Testes weightDrinking water: Testes weight; Renal/Kidney: Drinking water: Kidney weight, serum BUN, creatinine, glucose, calcium, sodium, chloride, potassiumGavage: Kidney weight, BUN;			
Duration:	Subchronic (>30-91 days) 90 day- drinking water			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	200220; Linked HERO ID(s): 200220, 62637, 5435222			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	All Outcomes: Test substance was identified as trans-1,2-dichloroethylene.	
	Metric 2: Test Substance Source	High	Hepatic/Liver: The source of the test substance was Aldrich Chemical Co., Milwaukee, WI. Lot number was included.; Immune/Hematological: The source of the test substance was Aldrich Chemical Co., Milwaukee, WI. Lot number was included.; Neurological/Behavioral: The source of the test substance was Aldrich Chemical Co., Milwaukee, WI. Lot number was included.; Lung/Respiratory: The source of the test substance was Aldrich Chemical Co., Milwaukee, WI. Lot number was included.; Reproductive/Developmental: The source of the test substance was Aldrich Chemical Co., Milwaukee, WI. Lot number was included.; Renal/Kidney: The source of the test substance was Aldrich Chemical Co., Milwaukee, WI. The lot number was included.	
	Metric 3: Test Substance Purity	High	All Outcomes: Test substance was 98% pure.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	Low	All Outcomes: Negative control group was only given deionized water. The test substance was dissolved in deionized water containing 1% emulphor.	
	Metric 5: Positive Controls	N/A	All Outcomes: Positive control was not necessary for this study.	
	Metric 6: Randomized Allocation of Animals	Medium	All Outcomes: The current study did not specify whether animals were randomly distributed across groups; however, the study followed methodological details reported in HERO ID 64563. This reference indicated that the study animals were randomized (method not specified).	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	High	All Outcomes: Preparation and storage details were described here and in HERO ID 62637. The test substance was diluted in deionized water containing 1% emulphor. The solutions were maintained at RT and stored in amber colored bottles with stainless steel spouts fitted through the corks. The solutions were changed twice weekly. This was sufficient to prevent volatilization as less than 10% of the test substance was lost between changes.	
	Metric 8: Consistency of Exposure Administration	High	All Outcomes: Details of exposure were reported and appropriate in cited reference; animals from all groups had access to water ad libitum.	

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Study Citation:	Barnes, D. W., Sanders, V. M., White, K. L., Jr, Shopp, G. M., Jr, Munson, A. E. (1985). Toxicology of trans-1,2-dichloroethylene in the mouse. Drug and Chemical Toxicology 8(5):373-392.
Health Outcome(s):	Hepatic/Liver; Immune/Hematological; Neurological/Behavioral; Lung/Respiratory; Reproductive/Developmental; Renal/Kidney;
Reported Health Effect(s):	Hepatic/Liver: Drinking water: Serum ALT, AST, ALP, LDH, liver weight, and hepatic microsomal activitiesGavage: Serum LDH, ALT and liver weight; Immune/Hematological: Hematology parameters, spleen and thymus weight; Neurological/Behavioral: Gavage 14-day: Brain weight; clinical signs (decreased activity, ruffled fur, ataxia, loss of righting reflex, hunch-backed appearance)Drinking water: Brain weightAcute: clinical observations (CNS effects); Lung/Respiratory: Lung weight; Reproductive/Developmental: Gavage study: Testes weightDrinking water: Testes weight; Renal/Kidney: Drinking water: Kidney weight, serum BUN, creatinine, glucose, calcium, sodium, chloride, potassiumGavage: Kidney weight, BUN;
Duration:	Subchronic (>30-91 days) 90 day- drinking water
Chemical:	trans-1,2-Dichloroethylene- Parent compound
HERO ID:	200220; Linked HERO ID(s): 200220, 62637, 5435222

Domain	Metric	Rating	Comments
	Metric 9: Reporting of Doses/Concentrations	Medium	All Outcomes: Doses are reported as mg/kg-day without ambiguity as time-weighted averages based on water intake and body weights. HERO ID 62637 indicated that test solutions were analytically measured using gas chromatography. It was reported that "less than 10% of DCE was lost during the three or four days between bottle changes." It is unclear whether the reported doses reflect the 10% loss.
	Metric 10: Exposure Frequency and Duration	High	All Outcomes: Exposure duration was appropriate for study.
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: There were minor limitations with the number of exposure groups (full range of responses were not obtained).
	Metric 12: Exposure Route and Method	High	All Outcomes: Exposure route was appropriate. Concentration in drinking water was measured between bottle exchanges.
Domain 4: Test Animals			
	Metric 13: Test Animal Characteristics	Medium	All Outcomes: Test animal characteristics were not provided in the current study; however, some animal details were reported in White et al. 1985 (HERO 64563). The test animals were obtained from Charles River Breeding Laboratories and the animal age was specified. Starting body weights were not provided.
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Medium	All Outcomes: Husbandry conditions were not reported in this reference, but some methodological details are provided in White et al. 1985 (HERO 64563). The reference stated that food and water were available ad libitum and acceptable room temperature, and humidity targets were used. The photoperiod was 12 hrs. The number of animals per cage was not specified.
	Metric 15: Number of Animals per Group	Medium	All Outcomes: The number of animals treated in each group was reported to be 140/sex for test substance and 260/sex for negative control. Six different sets of animals were used for evaluating different endpoints.
Domain 5: Outcome Assessment			
	Metric 16: Outcome Assessment Methodology	High	All Outcomes: Outcome assessment methods were described in detail in White et al. 1985 (HERO 64563), with some details also provided in this study. The methods were sensitive to the outcomes of interest.
	Metric 17: Consistency of Outcome Assessment	Medium	All Outcomes: Outcome assessment methods were described in White et al. (HERO 64563) and appeared to be consistent across study groups.
	Metric 18: Sampling Adequacy	Medium	All Outcomes: The number of animals sampled were reported and sufficient for conducting statistical analysis, but sample sizes were reported as a range that was different for each endpoint (numbers ranged from 7-24 animals/group).

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Study Citation:	Barnes, D. W., Sanders, V. M., White, K. L., Jr, Shopp, G. M., Jr, Munson, A. E. (1985). Toxicology of trans-1,2-dichloroethylene in the mouse. Drug and Chemical Toxicology 8(5):373-392.
Health Outcome(s):	Hepatic/Liver; Immune/Hematological; Neurological/Behavioral; Lung/Respiratory; Reproductive/Developmental; Renal/Kidney;
Reported Health Effect(s):	Hepatic/Liver: Drinking water: Serum ALT, AST, ALP, LDH, liver weight, and hepatic microsomal activitiesGavage: Serum LDH, ALT and liver weight; Immune/Hematological: Hematology parameters, spleen and thymus weight; Neurological/Behavioral: Gavage 14-day: Brain weight; clinical signs (decreased activity, ruffled fur, ataxia, loss of righting reflex, hunch-backed appearance)Drinking water: Brain weightAcute: clinical observations (CNS effects); Lung/Respiratory: Lung weight; Reproductive/Developmental: Gavage study: Testes weightDrinking water: Testes weight; Renal/Kidney: Drinking water: Kidney weight, serum BUN, creatinine, glucose, calcium, sodium, chloride, potassiumGavage: Kidney weight, BUN;
Duration:	Subchronic (>30-91 days) 90 day- drinking water
Chemical:	trans-1,2-Dichloroethylene- Parent compound
HERO ID:	200220; Linked HERO ID(s): 200220, 62637, 5435222

Domain	Metric	Rating	Comments
	Metric 19: Blinding of Assessors	N/A	All Outcomes: Blinding was not necessary for this study.
	Metric 20: Negative Control Response	High	All Outcomes: Negative control response was appropriate.

Domain 6: Confounding / Variable Control

Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: Study did not report all information to determine confounding, reported information did not identify differences between groups.
Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: No information was provided to either to support or dismiss differences in groups in health outcomes or attrition.
Metric 23:	Data Presentation and Analysis	High	All Outcomes: Statistical analysis was appropriate.
Metric 24:	Reporting of Data	High	All Outcomes: Data for all endpoints were quantitatively reported as means $\pm$ SE. Statistical significance was noted. Individual animal data were not provided.

Additional Comments: Re-Review QC: Deborah Herber; dherber@srcinc.comAdditional details were added to comments based on information provided in the study cited for methods (White et al.64563). Scores for the following metrics were changed: 6, 7, 8, 10, 11, 13, 14, 16, 18; 24 for gross necropsy. Gross necropsy form 2b was added.Form 2d was revised.

Overall Quality Determination

High

Study Citation:	Barnes, D. W., Sanders, V. M., White, K. L., Jr, Shopp, G. M., Jr, Munson, A. E. (1985). Toxicology of trans-1,2-dichloroethylene in the mouse. Drug and Chemical Toxicology 8(5):373-392.
Health Outcome(s):	Gross necropsy (Gross necropsy)
Reported Health Effect(s):	Gross necropsy (Gross necropsy): Drinking water: gross necropsy
Duration:	Subchronic (>30-91 days) 90 day- drinking water
Chemical:	trans-1,2-Dichloroethylene- Parent compound
HERO ID:	200220; Linked HERO ID(s): 200220, 62637, 5435222

Domain	Metric	Rating	Comments
Domain 1: Test Substance			
	Metric 1: Test Substance Identity	High	Test substance was identified as trans-1,2-dichloroethylene.
	Metric 2: Test Substance Source	High	The source of the test substance was Aldrich Chemical Co., Milwaukee, WI. Lot number was included.
	Metric 3: Test Substance Purity	High	Test substance was 98% pure.
Domain 2: Test Design			
	Metric 4: Negative and Vehicle Controls	Low	Negative control group was only given deionized water. The test substance was dissolved in deionized water containing 1% emulphor.
	Metric 5: Positive Controls	N/A	Positive control was not necessary for this study.
	Metric 6: Randomized Allocation of Animals	Medium	The current study did not specify whether animals were randomly distributed across groups; however, the study followed methodological details reported in HERO ID 64563. This reference indicated that the study animals were randomized (method not specified).
Domain 3: Exposure Characterization			
	Metric 7: Preparation and Storage of Test Substance	High	Preparation and storage details were described here and in HERO ID 62637. The test substance was diluted in deionized water containing 1% emulphor. The solutions were maintained at RT and stored in amber colored bottles with stainless steel spouts fitted through the corks. The solutions were changed twice weekly. This was sufficient to prevent volatilization as less than 10% of the test substance was lost between changes.
	Metric 8: Consistency of Exposure Administration	High	Details of exposure were reported and appropriate in cited reference; animals from all groups had access to water ad libitum.
	Metric 9: Reporting of Doses/Concentrations	Medium	Doses are reported as mg/kg-day without ambiguity as time-weighted averages based on water intake and body weights. HERO ID 62637 indicated that test solutions were analytically measured using gas chromatography. It was reported that "less than 10% of DCE was lost during the three or four days between bottle changes." It is unclear whether the reported doses reflect the 10% loss.
	Metric 10: Exposure Frequency and Duration	High	Exposure duration was appropriate for study.
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	There were minor limitations with the number of exposure groups (full range of responses were not obtained).
	Metric 12: Exposure Route and Method	High	Exposure route was appropriate. Concentration in drinking water was measured between bottle exchanges.
Domain 4: Test Animals			

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Study Citation:	Barnes, D. W., Sanders, V. M., White, K. L., Jr, Shopp, G. M., Jr, Munson, A. E. (1985). Toxicology of trans-1,2-dichloroethylene in the mouse. Drug and Chemical Toxicology 8(5):373-392.
Health Outcome(s):	Gross necropsy (Gross necropsy)
Reported Health Effect(s):	Gross necropsy (Gross necropsy): Drinking water: gross necropsy
Duration:	Subchronic (>30-91 days) 90 day- drinking water
Chemical:	trans-1,2-Dichloroethylene- Parent compound
HERO ID:	200220; Linked HERO ID(s): 200220, 62637, 5435222

Domain	Metric	Rating	Comments
	Metric 13: Test Animal Characteristics	Medium	Test animal characteristics were not provided in the current study; however, some animal details were reported in White et al. 1985 (HERO 64563). The test animals were obtained from Charles River Breeding Laboratories and the animal age was specified. Starting body weights were not provided.
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Medium	Husbandry conditions were not reported in this reference, but some methodological details are provided in White et al. 1985 (HERO 64563). The reference stated that food and water were available ad libitum and acceptable room temperature, and humidity targets were used. The photoperiod was 12 hrs. The number of animals per cage was not specified.
	Metric 15: Number of Animals per Group	Medium	The number of animals treated in each group was reported to be 140/sex for test substance and 260/sex for negative control. Six different sets of animals were used for evaluating different endpoints.
Domain 5: Outcome Assessment			
	Metric 16: Outcome Assessment Methodology	High	Outcome assessment methods were described in detail in White et al. 1985 (HERO 64563), with some details also provided in this study. The methods were sensitive to the outcomes of interest.
	Metric 17: Consistency of Outcome Assessment	Medium	Outcome assessment methods were described in White et al. (HERO 64563) and appeared to be consistent across study groups.
	Metric 18: Sampling Adequacy	Medium	The number of animals sampled were reported and sufficient for conducting statistical analysis, but sample sizes were reported as a range that was different for each endpoint (numbers ranged from 7-24 animals/group).
	Metric 19: Blinding of Assessors	N/A	Blinding was not necessary for this study.
	Metric 20: Negative Control Response	High	Negative control response was appropriate.
Domain 6: Confounding / Variable Control			
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	Study did not report all information to determine confounding, reported information did not identify differences between groups.
	Metric 22: Health Outcomes Unrelated to Exposure	Medium	No information was provided to either to support or dismiss differences in groups in health outcomes or attrition.
	Metric 23: Data Presentation and Analysis	High	Statistical analysis was appropriate.
	Metric 24: Reporting of Data	Medium	Gross necropsy findings were reported as negative in text.
Additional Comments: None			

Overall Quality Determination**High**

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Study Citation:	Barnes, D. W., Sanders, V. M., White, K. L., Jr, Shopp, G. M., Jr, Munson, A. E. (1985). Toxicology of trans-1,2-dichloroethylene in the mouse. Drug and Chemical Toxicology 8(5):373-392.
Health Outcome(s):	Gross necropsy (Gross necropsy)
Reported Health Effect(s):	Gross necropsy (Gross necropsy): Drinking water: gross necropsy
Duration:	Subchronic (>30-91 days) 90 day- drinking water
Chemical:	trans-1,2-Dichloroethylene- Parent compound
HERO ID:	200220; Linked HERO ID(s): 200220, 62637, 5435222

Domain	Metric	Rating	Comments
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Study Citation:	Barnes, D. W., Sanders, V. M., White, K. L., Jr, Shopp, G. M., Jr, Munson, A. E. (1985). Toxicology of trans-1,2-dichloroethylene in the mouse. Drug and Chemical Toxicology 8(5):373-392.
Health Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Nutritional/Metabolic: Body weightWater consumption (drinking water study)
Duration:	Subchronic (>30-91 days) 90 day- drinking water
Chemical:	trans-1,2-Dichloroethylene- Parent compound
HERO ID:	200220; Linked HERO ID(s): 200220, 62637, 5435222

Domain	Metric	Rating	Comments
Domain 1: Test Substance			
	Metric 1: Test Substance Identity	High	Test substance was identified as trans-1,2-dichloroethylene.
	Metric 2: Test Substance Source	High	The source of the test substance was Aldrich Chemical Co., Milwaukee, WI. Lot number was included.
	Metric 3: Test Substance Purity	High	Test substance was 98% pure.
Domain 2: Test Design			
	Metric 4: Negative and Vehicle Controls	Low	Negative control group was only given deionized water. The test substance was dissolved in deionized water containing 1% emulphor.
	Metric 5: Positive Controls	N/A	Positive control was not necessary for this study.
	Metric 6: Randomized Allocation of Animals	Medium	The current study did not specify whether animals were randomly distributed across groups; however, the study followed methodological details reported in HERO ID 64563. This reference indicated that the study animals were randomized (method not specified).
Domain 3: Exposure Characterization			
	Metric 7: Preparation and Storage of Test Substance	High	Preparation and storage details were described here and in HERO ID 62637. The test substance was diluted in deionized water containing 1% emulphor. The solutions were maintained at RT and stored in amber colored bottles with stainless steel spouts fitted through the corks. The solutions were changed twice weekly. This was sufficient to prevent volatilization as less than 10% of the test substance was lost between changes.
	Metric 8: Consistency of Exposure Administration	High	Details of exposure were reported and appropriate in cited reference; animals from all groups had access to water ad libitum.
	Metric 9: Reporting of Doses/Concentrations	Medium	Doses are reported as mg/kg-day without ambiguity as time-weighted averages based on water intake and body weights. HERO ID 62637 indicated that test solutions were analytically measured using gas chromatography. It was reported that "less than 10% of DCE was lost during the three or four days between bottle changes." It is unclear whether the reported doses reflect the 10% loss.
	Metric 10: Exposure Frequency and Duration	High	Exposure duration was appropriate for study.
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	There were minor limitations with the number of exposure groups (full range of responses were not obtained).
	Metric 12: Exposure Route and Method	High	Exposure route was appropriate. Concentration in drinking water was measured between bottle exchanges.
Domain 4: Test Animals			

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Study Citation:	Barnes, D. W., Sanders, V. M., White, K. L., Jr, Shopp, G. M., Jr, Munson, A. E. (1985). Toxicology of trans-1,2-dichloroethylene in the mouse. Drug and Chemical Toxicology 8(5):373-392.			
Health Outcome(s):	Nutritional/Metabolic			
Reported Health Effect(s):	Nutritional/Metabolic: Body weightWater consumption (drinking water study)			
Duration:	Subchronic (>30-91 days) 90 day- drinking water			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	200220; Linked HERO ID(s): 200220, 62637, 5435222			
Domain	Metric	Rating	Comments	
	Metric 13: Test Animal Characteristics	Medium	Test animal characteristics were not provided in the current study; however, some animal details were reported in White et al. 1985 (HERO 64563). The test animals were obtained from Charles River Breeding Laboratories and the animal age was specified. Starting body weights were not provided.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Medium	Husbandry conditions were not reported in this reference, but some methodological details are provided in White et al. 1985 (HERO 64563). The reference stated that food and water were available ad libitum and acceptable room temperature, and humidity targets were used. The photoperiod was 12 hrs. The number of animals per cage was not specified.	
	Metric 15: Number of Animals per Group	Medium	The number of animals treated in each group was reported to be 140/sex for test substance and 260/sex for negative control. Six different sets of animals were used for evaluating different endpoints.	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	Medium	Outcome assessment methods were described in detail in White et al. 1985 (HERO 64563), with some details also provided in this study. The methods partially addressed outcome of interest (body weight); only terminal body weights were measured.	
	Metric 17: Consistency of Outcome Assessment	Medium	Outcome assessment methods were described in White et al. (HERO 64563) and appeared to be consistent across study groups.	
	Metric 18: Sampling Adequacy	Medium	The number of animals sampled were reported and sufficient for conducting statistical analysis, but sample sizes were reported as a range that was different for each endpoint (numbers ranged from 7-24 animals/group).	
	Metric 19: Blinding of Assessors	N/A	Blinding was not necessary for this study.	
	Metric 20: Negative Control Response	High	Negative control response was appropriate.	
Domain 6: Confounding / Variable Control				
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	Study did not report all information to determine confounding, reported information did not identify differences between groups.	
	Metric 22: Health Outcomes Unrelated to Exposure	Medium	No information was provided to either to support or dismiss differences in groups in health outcomes or attrition.	
	Metric 23: Data Presentation and Analysis	High	Statistical analysis was appropriate.	
	Metric 24: Reporting of Data	High	Data for all endpoints were quantitatively reported as means ± SE. Statistical significance was noted. Individual animal data were not provided.	
Additional Comments:	None			

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Study Citation:	Barnes, D. W., Sanders, V. M., White, K. L., Jr, Shopp, G. M., Jr, Munson, A. E. (1985). Toxicology of trans-1,2-dichloroethylene in the mouse. Drug and Chemical Toxicology 8(5):373-392.
Health Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Nutritional/Metabolic: Body weightWater consumption (drinking water study)
Duration:	Subchronic (>30-91 days) 90 day- drinking water
Chemical:	trans-1,2-Dichloroethylene- Parent compound
HERO ID:	200220; Linked HERO ID(s): 200220, 62637, 5435222

Domain	Metric	Rating	Comments
Overall Quality Determination		High	

Study Citation:	DuPont, (1998). trans-1,2-Dichloroethylene: 90-day inhalation toxicity study in rats.		
Health Outcome(s):	Nutritional/Metabolic; Renal/Kidney; Gastrointestinal; Cardiovascular; Neurological/Behavioral; Ocular/Sensory; Musculoskeletal; Skin/Connective Tissue; Endocrine (Endocrine);		
Reported Health Effect(s):	Nutritional/Metabolic: Body weights and food consumption; Renal/Kidney: Clinical chemistry parameters, urinalysis parameters. kidney weight and histology (kidney and urinary bladder); Gastrointestinal: Histology (stomach, duodenum, jejunum, ileum, cecum, colon, rectum, salivary glands); Cardiovascular: Serum lipids and histology (heart, aorta); Neurological/Behavioral: Brain weight and histology (brain, spinal cord, sciatic nerve); Ocular/Sensory: Ophthalmological evaluations and histology (eye and lacrimal glands); Musculoskeletal: Histology (skeletal muscle, femur, sternum); Skin/Connective Tissue: Skin histology; Endocrine (Endocrine): Adrenal gland weights and histology (adrenal glands, pituitary, pancreas, parathyroid); also serum chemistry (minerals).;		
Duration:	Subchronic (>30-91 days) 90 days		
Chemical:	trans-1,2-Dichloroethylene- Parent compound		
HERO ID:	4154576		
Domain	Metric	Rating	Comments
Domain 1: Test Substance			
	Metric 1: Test Substance Identity	High	All Outcomes: The test substance was identified definitively as 1,2-trans-dichloroethylene.
	Metric 2: Test Substance Source	High	All Outcomes: The test substance was supplied by the sponsor; however, it was analytically verified by the performing laboratory.
	Metric 3: Test Substance Purity	High	All Outcomes: The test substance was >99% pure.
Domain 2: Test Design			
	Metric 4: Negative and Vehicle Controls	High	All Outcomes: A concurrent control group was used. Control animals were exposed to nitrogen and filtered/conditioned air from the same sources as used for the test chambers at approximately the same flow rates as those used in the exposure chambers. The test substance was not detected in the control chamber.
	Metric 5: Positive Controls	N/A	All Outcomes: A positive control is not required by study type/guideline.
	Metric 6: Randomized Allocation of Animals	Medium	All Outcomes: Allocation was performed with an unbiased method that ensured similar baseline characteristics across groups. Specifically, rats were divided into groups with the aid of a computerized, stratified, randomization program so that mean body weights for each group/sex were similar.
Domain 3: Exposure Characterization			
	Metric 7: Preparation and Storage of Test Substance	High	All Outcomes: The study indicated that the test substance appeared stable under the conditions of the study (this based on analytical verification of the test substance). The chamber distribution of the test substance was determined prior to exposures at the high concentration; this analysis showed that distribution of the vapor was homogeneous (within 2% at different positions within the breathing zone; see Appendix A). The vapor generation method (elevated temperature) and equipment was reported.
	Metric 8: Consistency of Exposure Administration	High	All Outcomes: Exposures were administered consistently across groups (no indication of any deviation in the administration of exposures was reported).
	Metric 9: Reporting of Doses/Concentrations	High	All Outcomes: Analytical, nominal, and target concentrations were reported. Mean analytical concentrations over the course of 67 exposures were the same as targeted concentrations (based on 2 significant figures); daily mean concentrations were within 20% of nominal concentrations as determined from the amounts of the test substance used and the chamber airflows.

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Study Citation:	DuPont, (1998). trans-1,2-Dichloroethylene: 90-day inhalation toxicity study in rats.		
Health Outcome(s):	Nutritional/Metabolic; Renal/Kidney; Gastrointestinal; Cardiovascular; Neurological/Behavioral; Ocular/Sensory; Musculoskeletal; Skin/Connective Tissue; Endocrine (Endocrine);		
Reported Health Effect(s):	Nutritional/Metabolic: Body weights and food consumption; Renal/Kidney: Clinical chemistry parameters, urinalysis parameters. kidney weight and histology (kidney and urinary bladder); Gastrointestinal: Histology (stomach, duodenum, jejunum, ileum, cecum, colon, rectum, salivary glands); Cardiovascular: Serum lipids and histology (heart, aorta); Neurological/Behavioral: Brain weight and histology (brain, spinal cord, sciatic nerve); Ocular/Sensory: Ophthalmological evaluations and histology (eye and lacrimal glands); Musculoskeletal: Histology (skeletal muscle, femur, sternum); Skin/Connective Tissue: Skin histology; Endocrine (Endocrine): Adrenal gland weights and histology (adrenal glands, pituitary, pancreas, parathyroid); also serum chemistry (minerals).;		
Duration:	Subchronic (>30-91 days) 90 days		
Chemical:	trans-1,2-Dichloroethylene- Parent compound		
HERO ID:	4154576		
Domain	Metric	Rating	Comments
	Metric 10: Exposure Frequency and Duration	High	Nutritional/Metabolic: The exposure frequency and duration were clearly reported (i.e. 6 hours/day, 5 days/week for 90 days) and was appropriate for the study type.; Renal/Kidney: The exposure frequency and duration were clearly reported (i.e., 6 hours/day, 5 days/week for 90 days) and was appropriate for the study type.; Gastrointestinal: The exposure frequency and duration were clearly reported (i.e. 6 hours/day, 5 days/week for 90 days) and was appropriate for the study type.; Cardiovascular: The exposure frequency and duration were clearly reported (i.e. 6 hours/day, 5 days/week for 90 days) and was appropriate for the study type.; Neurological/Behavioral: The exposure frequency and duration were clearly reported (i.e. 6 hours/day, 5 days/week for 90 days) and was appropriate for the study type.; Ocular/Sensory: The exposure frequency and duration were clearly reported (i.e. 6 hours/day, 5 days/week for 90 days) and was appropriate for the study type.; Musculoskeletal: The exposure frequency and duration were clearly reported (i.e. 6 hours/day, 5 days/week for 90 days) and was appropriate for the study type.; Skin/Connective Tissue: The exposure frequency and duration were clearly reported (i.e. 6 hours/day, 5 days/week for 90 days) and was appropriate for the study type.; Endocrine (Endocrine): The exposure frequency and duration were clearly reported (i.e. 6 hours/day, 5 days/week for 90 days) and was appropriate for the study type.
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	Medium	All Outcomes: Based on the study results (no LOAEL was identified), it was unclear whether the highest tested concentration was high enough. The applicable guideline for this study type indicates that the high concentration should result in toxicity. The study did not indicate that 4000 ppm (about 16 mg/L, based on a MW for trans-1,2-dichloroethylene of 96.95 g/mol) was the highest attainable concentration, and this concentration was lower than the maximum concentration that should be considered based on the applicable guideline (20 mg/L). A rationale for the selection of concentrations used in the study was not explicitly specified; however, the conclusions section of the study stated that effects were observed in previous studies at concentrations lower than those used in this study (i.e., 3000 ppm).
	Metric 12: Exposure Route and Method	High	All Outcomes: A dynamic whole-body chamber was used with at least 12 air changes/hour. Rats were in pretest for about 1 week prior to study initiation and housed individually once exposures were initiated.

Domain 4: Test Animals

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Health Outcome(s):	Nutritional/Metabolic; Renal/Kidney; Gastrointestinal; Cardiovascular; Neurological/Behavioral; Ocular/Sensory; Musculoskeletal; Skin/Connective Tissue; Endocrine (Endocrine);			
Reported Health Effect(s):	Nutritional/Metabolic: Body weights and food consumption; Renal/Kidney: Clinical chemistry parameters, urinalysis parameters. kidney weight and histology (kidney and urinary bladder); Gastrointestinal: Histology (stomach, duodenum, jejunum, ileum, cecum, colon, rectum, salivary glands); Cardiovascular: Serum lipids and histology (heart, aorta); Neurological/Behavioral: Brain weight and histology (brain, spinal cord, sciatic nerve); Ocular/Sensory: Ophthalmological evaluations and histology (eye and lacrimal glands); Musculoskeletal: Histology (skeletal muscle, femur, sternum); Skin/Connective Tissue: Skin histology; Endocrine (Endocrine): Adrenal gland weights and histology (adrenal glands, pituitary, pancreas, parathyroid); also serum chemistry (minerals).;			
Duration:	Subchronic (>30-91 days) 90 days			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	4154576			
Domain	Metric	Rating	Comments	
	Metric 13: Test Animal Characteristics	High	All Outcomes: The preferred species for this study type was used (i.e. rats). The species and strain (CrI:CD(SD)BR rat), sex (both males and females), age (5 weeks on the day of arrival; about 7 weeks old at study initiation), body weights on day 1 (233-246 g for males and 169-173 g for females), and source (Charles River Laboratories) were specified.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: Animal husbandry conditions were adequately reported. Animals were generally maintained on a 12 hour light/12 hour dark cycle, the temperature was maintained at 23 +/- 1C, and relative humidity was 50 +/- 10%; these fall within the windows specified by the applicable study guideline. Food and water availability was ad libitum except during exposures. There was no indication that there was variability among exposure groups with respect to animal husbandry conditions.	
	Metric 15: Number of Animals per Group	Medium	All Outcomes: The number of animals per group was reported and appropriate. Studies of this type typically require a minimum of 10 animals/sex/group (and 5 animals/sex/group to evaluate recovery). In this study, there were 15 animals/sex/group; 10/sex/group were sacrificed after 90 days and 5 sex/group were maintained for a 1-month recovery period. Two different sets of animals were used; one set for standard toxicological evaluations, and one set for the evaluation of liver cell proliferation.	
Domain 5: Outcome Assessment				
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Health Outcome(s):	Nutritional/Metabolic; Renal/Kidney; Gastrointestinal; Cardiovascular; Neurological/Behavioral; Ocular/Sensory; Musculoskeletal; Skin/Connective Tissue; Endocrine (Endocrine);
Reported Health Effect(s):	Nutritional/Metabolic: Body weights and food consumption; Renal/Kidney: Clinical chemistry parameters, urinalysis parameters. kidney weight and histology (kidney and urinary bladder); Gastrointestinal: Histology (stomach, duodenum, jejunum, ileum, cecum, colon, rectum, salivary glands); Cardiovascular: Serum lipids and histology (heart, aorta); Neurological/Behavioral: Brain weight and histology (brain, spinal cord, sciatic nerve); Ocular/Sensory: Ophthalmological evaluations and histology (eye and lacrimal glands); Musculoskeletal: Histology (skeletal muscle, femur, sternum); Skin/Connective Tissue: Skin histology; Endocrine (Endocrine): Adrenal gland weights and histology (adrenal glands, pituitary, pancreas, parathyroid); also serum chemistry (minerals).;
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Chemical:	trans-1,2-Dichloroethylene- Parent compound
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Domain	Metric	Rating	Comments
Metric 16:	Outcome Assessment Methodology	High	Nutritional/Metabolic: Body weights and food consumption measurements (weekly in all animals, and weekly in animals designated for standard toxicological evaluations, respectively) addressed the intended outcomes of interest. Although the most recent version of the applicable guideline (2018) suggests that body weights should be recorded twice weekly for at least the first 4 weeks of the study, weekly body weight measurements, in this case, appeared to be sensitive for the outcome of interest.; Renal/Kidney: Clinical chemistry parameters (including the individual parameters evaluated and the time points at which they were evaluated in animals designated for standard toxicological evaluations) were appropriate for the outcome of interest as per the applicable study guideline. Urinalysis parameters (optional as per the guideline) were appropriate. Kidney weights and gross and microscopic evaluations of the kidney and urinary bladder were also considered a sensitive measure of renal toxicity.; Gastrointestinal: Gross and microscopic evaluations of gastrointestinal (GI) tract tissues were considered a sensitive measure of toxicity.; Cardiovascular: Clinical chemistry parameters (including the serum lipids evaluated and the time points at which they were evaluated in animals designated for standard toxicological evaluations) were appropriate for the outcome of interest as per the applicable study guideline. Gross and microscopic evaluations of the heart and aorta were also considered a sensitive measure of toxicity. As per the guideline applicable to this study type, heart weights should have been recorded.; Neurological/Behavioral: Gross and microscopic evaluations of the brain (4 sections), sciatic nerve, and spinal cord (3 levels) bladder were considered a sensitive measure of toxicity and appropriate based on the applicable guideline.; Ocular/Sensory: Gross and microscopic evaluations of the eye and lacrimal glands were considered a sensitive measure of toxicity. The study did not explicitly indicate that the retina, optic nerve, and eyelids were included in the evaluation of the eyes (endpoints indicated as up to the discretion of the study director in the applicable guideline).; Musculoskeletal: Gross and microscopic evaluations of the femur (including joint), skeletal muscle, and sternum were considered a sensitive measure of toxicity; these evaluations were appropriate based on the applicable guideline.; Skin/Connective Tissue: Gross and microscopic evaluations of skin were considered a sensitive measure of toxicity; this analysis was consistent with the applicable guideline.; Endocrine (Endocrine): The outcome assessment and methodology (clinical chemistry measurements of minerals, adrenal gland weight, and histology of various endocrine tissues) addressed the outcome of interest. The timing of these assessments and the tissues that were evaluated were appropriate based on the applicable guideline.

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Reported Health Effect(s):	Nutritional/Metabolic: Body weights and food consumption; Renal/Kidney: Clinical chemistry parameters, urinalysis parameters. kidney weight and histology (kidney and urinary bladder); Gastrointestinal: Histology (stomach, duodenum, jejunum, ileum, cecum, colon, rectum, salivary glands); Cardiovascular: Serum lipids and histology (heart, aorta); Neurological/Behavioral: Brain weight and histology (brain, spinal cord, sciatic nerve); Ocular/Sensory: Ophthalmological evaluations and histology (eye and lacrimal glands); Musculoskeletal: Histology (skeletal muscle, femur, sternum); Skin/Connective Tissue: Skin histology; Endocrine (Endocrine): Adrenal gland weights and histology (adrenal glands, pituitary, pancreas, parathyroid); also serum chemistry (minerals).;
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Domain	Metric	Rating	Comments
Metric 17:	Consistency of Outcome Assessment	High	Nutritional/Metabolic: Body weights and food consumption were measured consistently across groups within the same set of animals.; Renal/Kidney: Renal endpoints were evaluated consistently across groups within the same set of animals.; Gastrointestinal: GI endpoints were evaluated consistently across groups within the same set of animals.; Cardiovascular: Cardiovascular endpoints were evaluated consistently across groups within the same set of animals.; Neurological/Behavioral: Neurological endpoints were evaluated consistently across groups within the same set of animals.; Ocular/Sensory: Ocular endpoints were evaluated consistently across groups within the same set of animals.; Musculoskeletal: Musculoskeletal endpoints were evaluated consistently across groups within the same set of animals.; Skin/Connective Tissue: Skin was evaluated consistently across groups within the same set of animals.; Endocrine (Endocrine): Endocrine-related endpoints and clinical pathology parameters were evaluated consistently across groups within the same set of animals.

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Health Outcome(s):	Nutritional/Metabolic; Renal/Kidney; Gastrointestinal; Cardiovascular; Neurological/Behavioral; Ocular/Sensory; Musculoskeletal; Skin/Connective Tissue; Endocrine (Endocrine);
Reported Health Effect(s):	Nutritional/Metabolic: Body weights and food consumption; Renal/Kidney: Clinical chemistry parameters, urinalysis parameters. kidney weight and histology (kidney and urinary bladder); Gastrointestinal: Histology (stomach, duodenum, jejunum, ileum, cecum, colon, rectum, salivary glands); Cardiovascular: Serum lipids and histology (heart, aorta); Neurological/Behavioral: Brain weight and histology (brain, spinal cord, sciatic nerve); Ocular/Sensory: Ophthalmological evaluations and histology (eye and lacrimal glands); Musculoskeletal: Histology (skeletal muscle, femur, sternum); Skin/Connective Tissue: Skin histology; Endocrine (Endocrine): Adrenal gland weights and histology (adrenal glands, pituitary, pancreas, parathyroid); also serum chemistry (minerals).;
Duration:	Subchronic (>30-91 days) 90 days
Chemical:	trans-1,2-Dichloroethylene- Parent compound
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Domain	Metric	Rating	Comments
Metric 18:	Sampling Adequacy	High	Nutritional/Metabolic: Body weights were recorded individually (in all animals), and food consumption was measured by group (animals designated for standard toxicological evaluations).; Renal/Kidney: Clinical pathology and urinalysis (10 animals/sex/group), and kidney weights and histology (10 animals/sex/group after 90 days and the remaining 5 animals/sex/group after the one-month recovery period) were assessed in animals designated for standard toxicological evaluations.;; Gastrointestinal: Histology (10 animals/sex/group after 90 days and the remaining 5 animals/sex/group after the one-month recovery period) were assessed in animals designated for standard toxicological evaluations (high-concentration animals and controls).; Cardiovascular: Clinical pathology (10 animals/sex/group) and histology (10 animals/sex/group after 90 days and the remaining 5 animals/sex/group after the one-month recovery period) were assessed in animals designated for standard toxicological evaluations. Microscopic pathology was assessed in high-concentration animals and controls.;; Neurological/Behavioral: Histology (10 animals/sex/group after 90 days and the remaining 5 animals/sex/group after the one-month recovery period) were assessed in animals designated for standard toxicological evaluations (high-concentration animals and controls).; Ocular/Sensory: Ophthalmological examinations were performed on all rats received for the study prior to selection and grouping, and in all rats designated for standard toxicological evaluations after 90 days exposure. Histology (10 animals/sex/group after 90 days and the remaining 5 animals/sex/group after the one-month recovery period) were assessed in animals designated for standard toxicological evaluations (high-concentration animals and controls).; Musculoskeletal: Histology (10 animals/sex/group after 90 days and the remaining 5 animals/sex/group after the one-month recovery period) was assessed in animals designated for standard toxicological evaluations (high-concentration and control animals).; Skin/Connective Tissue: Histology (10 animals/sex/group after 90 days and the remaining 5 animals/sex/group after the one-month recovery period) was assessed in animals designated for standard toxicological evaluations (high-concentration and control groups).; Endocrine (Endocrine): Clinical pathology measurements (10 animals/sex/group) and adrenal weights and histology of endocrine tissues (10 animals/sex/group after 90 days and the remaining 5 animals/sex/group after the one-month recovery period) were assessed in animals designated for standard toxicological evaluations. Microscopic pathology was assessed in high-concentration animals and controls.

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Reported Health Effect(s):	Nutritional/Metabolic: Body weights and food consumption; Renal/Kidney: Clinical chemistry parameters, urinalysis parameters. kidney weight and histology (kidney and urinary bladder); Gastrointestinal: Histology (stomach, duodenum, jejunum, ileum, cecum, colon, rectum, salivary glands); Cardiovascular: Serum lipids and histology (heart, aorta); Neurological/Behavioral: Brain weight and histology (brain, spinal cord, sciatic nerve); Ocular/Sensory: Ophthalmological evaluations and histology (eye and lacrimal glands); Musculoskeletal: Histology (skeletal muscle, femur, sternum); Skin/Connective Tissue: Skin histology; Endocrine (Endocrine): Adrenal gland weights and histology (adrenal glands, pituitary, pancreas, parathyroid); also serum chemistry (minerals).;		
Duration:	Subchronic (>30-91 days) 90 days		
Chemical:	trans-1,2-Dichloroethylene- Parent compound		
HERO ID:	4154576		
Domain	Metric	Rating	Comments
	Metric 19: Blinding of Assessors	N/A	Nutritional/Metabolic: Blinding is not required for these endpoints.; Renal/Kidney: Blinding was not required for these endpoints.; Gastrointestinal: Blinding was not required for these endpoints.; Cardiovascular: Blinding was not required for these endpoints.; Neurological/Behavioral: Blinding was not required for these endpoints.; Ocular/Sensory: Blinding was not required for these endpoints.; Musculoskeletal: Blinding was not required for these endpoints.; Skin/Connective Tissue: Blinding was not required for these endpoints.; Endocrine (Endocrine): Blinding was not required for these endpoints.
	Metric 20: Negative Control Response	High	Nutritional/Metabolic: Body weights and food consumption values appeared reasonable in the control groups (i.e., control animals gained weight over the course of the study and daily food consumption rates appeared appropriate).; Renal/Kidney: In animals designated for standard toxicological evaluations, clinical chemistry and urinalysis parameters were generally within expected ranges for control animals; the incidence of gross and/or microscopic changes in the kidneys and/or urinary bladder of control animals was low and/or considered spontaneous and incidental.; Gastrointestinal: In animals designated for standard toxicological evaluations, the incidence of gross and/or microscopic changes in the GI tract of control animals was low and/or considered spontaneous and incidental.; Cardiovascular: In animals designated for standard toxicological evaluations, clinical chemistry parameters were generally within expected ranges for control animals; the incidence of gross and/or microscopic changes of control animals was low and/or considered spontaneous and incidental.; Neurological/Behavioral: In animals designated for standard toxicological evaluations, the incidence of gross and/or microscopic changes in control animals was low and/or considered spontaneous and incidental.; Ocular/Sensory: An ophthalmological abnormality was observed in only one of the control animals (a female); this effect was consistent with trauma. The incidence of gross and/or microscopic changes in control animals was low and/or considered spontaneous and incidental.; Musculoskeletal: The incidence of gross and/or microscopic changes in control animals was low and/or considered spontaneous and incidental.; Skin/Connective Tissue: The incidence of gross and/or microscopic changes in control animals was low and/or considered spontaneous and incidental.; Endocrine (Endocrine): Clinical pathology parameters (serum mineral levels) in controls were within expected ranges; the incidence of gross and/or microscopic changes in endocrine tissues of control animals was low and/or considered spontaneous and incidental.

Domain 6: Confounding / Variable Control

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Health Outcome(s):	Nutritional/Metabolic; Renal/Kidney; Gastrointestinal; Cardiovascular; Neurological/Behavioral; Ocular/Sensory; Musculoskeletal; Skin/Connective Tissue; Endocrine (Endocrine);
Reported Health Effect(s):	Nutritional/Metabolic: Body weights and food consumption; Renal/Kidney: Clinical chemistry parameters, urinalysis parameters. kidney weight and histology (kidney and urinary bladder); Gastrointestinal: Histology (stomach, duodenum, jejunum, ileum, cecum, colon, rectum, salivary glands); Cardiovascular: Serum lipids and histology (heart, aorta); Neurological/Behavioral: Brain weight and histology (brain, spinal cord, sciatic nerve); Ocular/Sensory: Ophthalmological evaluations and histology (eye and lacrimal glands); Musculoskeletal: Histology (skeletal muscle, femur, sternum); Skin/Connective Tissue: Skin histology; Endocrine (Endocrine): Adrenal gland weights and histology (adrenal glands, pituitary, pancreas, parathyroid); also serum chemistry (minerals).;
Duration:	Subchronic (>30-91 days) 90 days
Chemical:	trans-1,2-Dichloroethylene- Parent compound
HERO ID:	4154576

Domain	Metric	Rating	Comments
Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Nutritional/Metabolic: Reported information did not identify differences among study groups; it is unlikely that these factors impacted nutritional/metabolic status because body weights and food consumption were similar across groups.; Renal/Kidney: Reported information did not identify differences among groups; it is unlikely that these factors impacted renal endpoints because clinical chemistry and urinalysis parameters, kidney weights, and the incidence of gross and microscopic findings were similar across groups.; Gastrointestinal: Reported information did not identify differences among groups; it is unlikely that these factors impacted GI endpoints because the incidence of gross and microscopic findings was similar across groups.; Cardiovascular: Reported information did not identify differences among groups; it is unlikely that these factors impacted cardiovascular endpoints because clinical chemistry parameters and the incidence of gross and microscopic findings were similar across groups.; Neurological/Behavioral: Reported information did not identify differences among groups; it is unlikely that these factors impacted neurological endpoints because the incidence of gross and microscopic findings was similar across groups.; Ocular/Sensory: Reported information did not identify differences among groups; it is unlikely that these factors impacted ocular endpoints because the incidence of gross and microscopic findings was similar across groups.; Musculoskeletal: Reported information did not identify differences among groups; it is unlikely that these factors impacted musculoskeletal endpoints because the incidence of gross and microscopic findings was similar across groups.; Skin/Connective Tissue: Reported information did not identify differences among groups; it is unlikely that these factors impacted the skin because the incidence of gross and microscopic findings was similar across groups.; Endocrine (Endocrine): Reported information did not identify differences among groups; it is unlikely that these factors impacted endocrine endpoints because adrenal gland weights and the incidence of gross and microscopic findings were similar across groups.

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Reported Health Effect(s):	Nutritional/Metabolic: Body weights and food consumption; Renal/Kidney: Clinical chemistry parameters, urinalysis parameters. kidney weight and histology (kidney and urinary bladder); Gastrointestinal: Histology (stomach, duodenum, jejunum, ileum, cecum, colon, rectum, salivary glands); Cardiovascular: Serum lipids and histology (heart, aorta); Neurological/Behavioral: Brain weight and histology (brain, spinal cord, sciatic nerve); Ocular/Sensory: Ophthalmological evaluations and histology (eye and lacrimal glands); Musculoskeletal: Histology (skeletal muscle, femur, sternum); Skin/Connective Tissue: Skin histology; Endocrine (Endocrine): Adrenal gland weights and histology (adrenal glands, pituitary, pancreas, parathyroid); also serum chemistry (minerals).;
Duration:	Subchronic (>30-91 days) 90 days
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Domain	Metric	Rating	Comments
Metric 22:	Health Outcomes Unrelated to Exposure	Medium	Nutritional/Metabolic: There was no information regarding health outcomes unrelated to exposure; however, there was no significant mortality, and nutritional/metabolic endpoints were not likely impacted.; Renal/Kidney: There was no information regarding health outcomes unrelated to exposure; however, there was no significant mortality, and renal endpoints were not likely impacted.; Gastrointestinal: There was no information regarding health outcomes unrelated to exposure; however, there was no significant mortality, and GI endpoints were not likely impacted.; Cardiovascular: There was no information regarding health outcomes unrelated to exposure; however, there was no significant mortality, and cardiovascular endpoints were not likely impacted.; Neurological/Behavioral: There was no information regarding health outcomes unrelated to exposure; however, there was no significant mortality, and neurological endpoints were not likely impacted.; Ocular/Sensory: There was no information regarding health outcomes unrelated to exposure; however, there was no significant mortality, and ocular endpoints were not likely impacted.; Musculoskeletal: There was no information regarding health outcomes unrelated to exposure; however, there was no significant mortality, and musculoskeletal endpoints were not likely impacted.; Skin/Connective Tissue: There was no information regarding health outcomes unrelated to exposure; however, there was no significant mortality, and skin was not likely impacted.; Endocrine (Endocrine): There was no information regarding health outcomes unrelated to exposure; however, there was no significant mortality, and endocrine endpoints were not likely impacted.

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Reported Health Effect(s):	Nutritional/Metabolic: Body weights and food consumption; Renal/Kidney: Clinical chemistry parameters, urinalysis parameters. kidney weight and histology (kidney and urinary bladder); Gastrointestinal: Histology (stomach, duodenum, jejunum, ileum, cecum, colon, rectum, salivary glands); Cardiovascular: Serum lipids and histology (heart, aorta); Neurological/Behavioral: Brain weight and histology (brain, spinal cord, sciatic nerve); Ocular/Sensory: Ophthalmological evaluations and histology (eye and lacrimal glands); Musculoskeletal: Histology (skeletal muscle, femur, sternum); Skin/Connective Tissue: Skin histology; Endocrine (Endocrine): Adrenal gland weights and histology (adrenal glands, pituitary, pancreas, parathyroid); also serum chemistry (minerals).;		
Duration:	Subchronic (>30-91 days) 90 days		
Chemical:	trans-1,2-Dichloroethylene- Parent compound		
HERO ID:	4154576		
Domain	Metric	Rating	Comments
Metric 23:	Data Presentation and Analysis	High	Nutritional/Metabolic: Body weight data were analyzed using one-way ANOVA and/or Dunnett's test (for pairwise comparisons between exposed groups and controls). Food consumption was measured by group (there was no measure of variance or individual values) and therefore, could not be analyzed statistically.; Renal/Kidney: Statistical methods were described. For clinical chemistry and urinalysis parameters, ANOVA and Bartlett's test were used at each sampling time, and Dunnett's test was used for pairwise comparisons. When Bartlett's was significant, Kruskal-Wallis was used and the Mann-Whitney U test was used to compare means among exposed groups and controls. Kidney weights were analyzed with ANOVA. When the F-statistic for differences among groups was significant, Dunnett's test was used for pairwise comparisons. Bartlett's test was used to test for homogeneity of variances. Incidence data were not analyzed statistically; however, data enabling independent analyses were provided.; Gastrointestinal: Incidence data were not analyzed statistically; however, data enabling independent analyses were provided.; Cardiovascular: Statistical methods were described. For clinical chemistry parameters, ANOVA and Bartlett's test were used at each sampling time, and Dunnett's test was used for pairwise comparisons. When Bartlett's was significant, Kruskal-Wallis was used and the Mann-Whitney U test was used to compare means among exposed groups and controls. Incidence data were not analyzed statistically; however, data enabling independent analyses were provided.; Neurological/Behavioral: Incidence data were not analyzed statistically; however, data enabling independent analyses were provided.; Ocular/Sensory: Incidence data were not analyzed statistically; however, data enabling independent analyses were provided (see Appendix F).; Musculoskeletal: Incidence data were not analyzed statistically; however, data enabling independent analyses were provided.; Skin/Connective Tissue: Incidence data were not analyzed statistically; however, data enabling independent analyses were provided.; Endocrine (Endocrine): Statistical methods were described. Clinical pathology was analyzed using ANOVA and Bartlett's test for each sampling time; Dunnett's test was used for pairwise comparisons. When Bartlett's test was significant, the Kruskal-Wallis and Mann-Whitney U tests were used. Adrenal gland weights were analyzed with ANOVA; when the F-statistic was significant, Dunnett's test was used for pairwise comparisons. Bartlett's test was used to determine homogeneity of variances. Incidence data were not analyzed statistically; however, data enabling independent analyses were provided.

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Reported Health Effect(s):	Nutritional/Metabolic: Body weights and food consumption; Renal/Kidney: Clinical chemistry parameters, urinalysis parameters. kidney weight and histology (kidney and urinary bladder); Gastrointestinal: Histology (stomach, duodenum, jejunum, ileum, cecum, colon, rectum, salivary glands); Cardiovascular: Serum lipids and histology (heart, aorta); Neurological/Behavioral: Brain weight and histology (brain, spinal cord, sciatic nerve); Ocular/Sensory: Ophthalmological evaluations and histology (eye and lacrimal glands); Musculoskeletal: Histology (skeletal muscle, femur, sternum); Skin/Connective Tissue: Skin histology; Endocrine (Endocrine): Adrenal gland weights and histology (adrenal glands, pituitary, pancreas, parathyroid); also serum chemistry (minerals).;
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HERO ID:	4154576

Domain	Metric	Rating	Comments
Metric 24:	Reporting of Data	High	Nutritional/Metabolic: Body weight and food consumption data were reported for each exposure group and sex.; Renal/Kidney: Data for renal endpoints were provided for each exposure group and sex.; Gastrointestinal: Data for GI endpoints were provided for each exposure group and sex.; Cardiovascular: Data for cardiovascular endpoints were provided for each exposure group and sex.; Neurological/Behavioral: Data for neurological endpoints were provided for each exposure group and sex.; Ocular/Sensory: Data for ocular endpoints were provided for each exposure group and sex.; Musculoskeletal: Data for musculoskeletal endpoints were provided for each exposure group and sex.; Skin/Connective Tissue: Data were provided for each exposure group and sex.; Endocrine (Endocrine): Data for other/endocrine endpoints were provided for each exposure group and sex.

Additional Comments: None

Overall Quality Determination**High**

Study Citation:	DuPont, (1998). trans-1,2-Dichloroethylene: 90-day inhalation toxicity study in rats.			
Health Outcome(s):	Mortality; Hepatic/Liver;			
Reported Health Effect(s):	Mortality; Mortality; Hepatic/Liver: Clinical chemistry parameters, liver weight and histology, hepatic cell proliferation;			
Duration:	Subchronic (>30-91 days) 90 days			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	4154576			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
Metric 1:	Test Substance Identity	High	All Outcomes: The test substance was identified definitively as 1,2-trans-dichloroethylene.	
Metric 2:	Test Substance Source	High	All Outcomes: The test substance was supplied by the sponsor; however, it was analytically verified by the performing laboratory.	
Metric 3:	Test Substance Purity	High	All Outcomes: The test substance was >99% pure.	
Domain 2: Test Design				
Metric 4:	Negative and Vehicle Controls	High	All Outcomes: A concurrent control group was used. Control animals were exposed to nitrogen and filtered/conditioned air from the same sources as used for the test chambers at approximately the same flow rates as those used in the exposure chambers. The test substance was not detected in the control chamber.	
Metric 5:	Positive Controls	N/A	All Outcomes: A positive control is not required by study type/guideline.	
Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: Allocation was performed with an unbiased method that ensured similar baseline characteristics across groups. Specifically, rats were divided into groups with the aid of a computerized, stratified, randomization program so that mean body weights for each group/sex were similar.	
Domain 3: Exposure Characterization				
Metric 7:	Preparation and Storage of Test Substance	High	All Outcomes: The study indicated that the test substance appeared stable under the conditions of the study (this based on analytical verification of the test substance). The chamber distribution of the test substance was determined prior to exposures at the high concentration; this analysis showed that distribution of the vapor was homogeneous (within 2% at different positions within the breathing zone; see Appendix A). The vapor generation method (elevated temperature) and equipment was reported.	
Metric 8:	Consistency of Exposure Administration	High	All Outcomes: Exposures were administered consistently across groups (no indication of any deviation in the administration of exposures was reported).	
Metric 9:	Reporting of Doses/Concentrations	High	All Outcomes: Analytical, nominal, and target concentrations were reported. Mean analytical concentrations over the course of 67 exposures were the same as targeted concentrations (based on 2 significant figures); daily mean concentrations were within 20% of nominal concentrations as determined from the amounts of the test substance used and the chamber airflows.	
Metric 10:	Exposure Frequency and Duration	High	All Outcomes: The exposure frequency and duration were clearly reported (i.e. 6 hours/day, 5 days/week for 90 days) and was appropriate for the study type.	
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Study Citation:	DuPont, (1998). trans-1,2-Dichloroethylene: 90-day inhalation toxicity study in rats.			
Health Outcome(s):	Mortality; Hepatic/Liver;			
Reported Health Effect(s):	Mortality; Mortality; Hepatic/Liver: Clinical chemistry parameters, liver weight and histology, hepatic cell proliferation;			
Duration:	Subchronic (>30-91 days) 90 days			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	4154576			
Domain	Metric	Rating	Comments	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	Medium	All Outcomes: Based on the study results (no LOAEL was identified), it was unclear whether the highest tested concentration was high enough. The applicable guideline for this study type indicates that the high concentration should result in toxicity. The study did not indicate that 4000 ppm (about 16 mg/L, based on a MW for trans-1,2-dichloroethylene of 96.95 g/mol) was the highest attainable concentration, and this concentration was lower than the maximum concentration that should be considered based on the applicable guideline (20 mg/L). A rationale for the selection of concentrations used in the study was not explicitly specified; however, the conclusions section of the study stated that effects were observed in previous studies at concentrations lower than those used in this study (i.e., 3000 ppm).	
	Metric 12: Exposure Route and Method	High	All Outcomes: A dynamic whole-body chamber was used with at least 12 air changes/hour. Rats were in pretest for about 1 week prior to study initiation and housed individually once exposures were initiated.	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	High	All Outcomes: The preferred species for this study type was used (i.e. rats). The species and strain (CrI:CD(SD)BR rat), sex (both males and females), age (5 weeks on the day of arrival; about 7 weeks old at study initiation), body weights on day 1 (233-246 g for males and 169-173 g for females), and source (Charles River Laboratories) were specified.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: Animal husbandry conditions were adequately reported. Animals were generally maintained on a 12 hour light/12 hour dark cycle, the temperature was maintained at 23 +/- 1C, and relative humidity was 50 +/- 10%; these fall within the windows specified by the applicable study guideline. Food and water availability was ad libitum except during exposures. There was no indication that there was variability among exposure groups with respect to animal husbandry conditions.	
	Metric 15: Number of Animals per Group	Medium	All Outcomes: The number of animals per group was reported and appropriate. Studies of this type typically require a minimum of 10 animals/sex/group (and 5 animals/sex/group to evaluate recovery). In this study, there were 15 animals/sex/group; 10/sex/group were sacrificed after 90 days and 5 sex/group were maintained for a 1-month recovery period. Two different sets of animals were used; one set for standard toxicological evaluations, and one set for the evaluation of liver cell proliferation.	
Domain 5: Outcome Assessment				
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Study Citation: DuPont, (1998). trans-1,2-Dichloroethylene: 90-day inhalation toxicity study in rats. Health Outcome(s): Mortality; Hepatic/Liver; Reported Health Effect(s): Mortality; Mortality; Hepatic/Liver: Clinical chemistry parameters, liver weight and histology, hepatic cell proliferation; Duration: Subchronic (>30-91 days) 90 days Chemical: trans-1,2-Dichloroethylene- Parent compound HERO ID: 4154576				
Domain		Metric	Rating	Comments
	Metric 16:	Outcome Assessment Methodology	High	Mortality: The study indicated that animals were observed for clinical signs (and presumably mortality) once per week before exposure and after each exposure; group observations were made during exposure (in the set of animals designated for toxicological evaluations). The guideline for this study type indicates that animals should be clinically observed before, during, and after each exposure; based on the study protocol, mortality would have been observed at these timepoints.; Hepatic/Liver: Endpoints evaluated (serum chemistry, liver weight, liver histology, and liver cell proliferation) addressed the intended outcome of interest and appeared appropriate.
	Metric 17:	Consistency of Outcome Assessment	High	Mortality: Mortality was consistently assessed across groups within the same set of animals.; Hepatic/Liver: Liver endpoints were evaluated consistently across groups within the same set of animals.
	Metric 18:	Sampling Adequacy	Medium	Mortality: Mortality was assessed in all animals. However, the animal that was sacrificed moribund should have been examined microscopically, as per the applicable guideline. The study indicated that the animal was not subjected to necropsy because it was designated for liver cell proliferation evaluation.; Hepatic/Liver: Clinical pathology (10 animals/sex/group), and liver weights and histology (10 animals/sex/group after 90 days and the remaining 5 animals/sex/group after the one-month recovery period) were assessed in animals designated for standard toxicological evaluations. Five animals/sex/group were evaluated at each time point (7 days and 90 days) for liver cell proliferation; the number of animals evaluated may have been too low to detect an effect.
	Metric 19:	Blinding of Assessors	N/A	Mortality: Blinding is not required for this endpoint.; Hepatic/Liver: Blinding was not required for these endpoints.
	Metric 20:	Negative Control Response	High	Mortality: None of the control animals died or and only one was sacrificed moribund during the conduct of the study.; Hepatic/Liver: Clinical chemistry parameters (in animals designated for standard toxicological evaluations) and BrdU labeling (in animals designated for liver cell proliferation) were generally within expected ranges for control animals; the incidence of gross and/or microscopic changes in the livers of control animals (designated for standard toxicological evaluations) was low and/or considered spontaneous and incidental.
Domain 6: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Mortality: Reported information did not identify differences among study groups; it is unlikely that these factors impacted the study results because the incidence of mortality in the study was minimal (one high-concentration female designated for liver cell proliferation evaluation was sacrificed moribund).; Hepatic/Liver: Reported information did not identify differences among groups; it is unlikely that these factors impacted liver endpoints because clinical chemistry, liver cell proliferation, liver weight, and the incidence of gross and microscopic findings were similar across groups.
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Study Citation: DuPont, (1998). trans-1,2-Dichloroethylene: 90-day inhalation toxicity study in rats.				
Health Outcome(s): Mortality; Hepatic/Liver;				
Reported Health Effect(s): Mortality; Mortality; Hepatic/Liver: Clinical chemistry parameters, liver weight and histology, hepatic cell proliferation;				
Duration: Subchronic (>30-91 days) 90 days				
Chemical: trans-1,2-Dichloroethylene- Parent compound				
HERO ID: 4154576				
Domain		Metric	Rating	Comments
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	Mortality: There were only minor differences among study groups with respect to mortality (one high-concentration female was sacrificed compared to no animals in any of the other 15 exposure groups).; Hepatic/Liver: There was no information regarding health outcomes unrelated to exposure; however, there was no significant mortality, and liver endpoints were not likely impacted.
	Metric 23:	Data Presentation and Analysis	High	Mortality: Statistical analysis was not performed; however, data are available enabling independent statistical analysis.; Hepatic/Liver: Statistical methods were described. For clinical chemistry parameters, ANOVA and Bartlett's test were used at each sampling time, and Dunnett's test was used for pairwise comparisons. When Bartlett's was significant, Kruskal-Wallis was used and the Mann-Whitney U test was used to compare means among exposed groups and controls. Liver weights were analyzed with ANOVA; when the F-statistic was significant, Dunnett's test was used for pairwise comparisons. Bartlett's test was used to determine homogeneity of variances. Cell proliferation data were analyzed with ANOVA and Bartlett's test for homogeneity of variances. Incidence data were not analyzed statistically; however, data enabling independent analyses were provided.
	Metric 24:	Reporting of Data	High	Mortality: Mortality was reported for all exposure groups.; Hepatic/Liver: Data for liver endpoints were provided for each exposures group and sex.
Additional Comments: None				
Overall Quality Determination			High	

Study Citation:	DuPont, (1998). trans-1,2-Dichloroethylene: 90-day inhalation toxicity study in rats.			
Health Outcome(s):	Immune/Hematological; Lung/Respiratory; Thyroid; Reproductive/Developmental;			
Reported Health Effect(s):	Immune/Hematological: Hematological parameters and histology (spleen, thymus, bone marrow, mesenteric and mandibular lymph nodes); Lung/Respiratory: Lung weights and histology (lungs, pharynx, larynx, trachea, esophagus, nose - 4 sections); Thyroid: Thyroid histology; Reproductive/Developmental: Testes and ovaries weights, histology of reproductive organs (mammary gland in females, ovaries, uterus, vagina, prostate, seminal vesicles, testes, and epididymides);			
Duration:	Subchronic (>30-91 days) 90 days			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	4154576			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1:	Test Substance Identity	High	All Outcomes: The test substance was identified definitively as 1,2-trans-dichloroethylene.
	Metric 2:	Test Substance Source	High	All Outcomes: The test substance was supplied by the sponsor; however, it was analytically verified by the performing laboratory.
	Metric 3:	Test Substance Purity	High	All Outcomes: The test substance was >99% pure.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: A concurrent control group was used. Control animals were exposed to nitrogen and filtered/conditioned air from the same sources as used for the test chambers at approximately the same flow rates as those used in the exposure chambers. The test substance was not detected in the control chamber.
	Metric 5:	Positive Controls	N/A	All Outcomes: A positive control is not required by study type/guideline.
	Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: Allocation was performed with an unbiased method that ensured similar baseline characteristics across groups. Specifically, rats were divided into groups with the aid of a computerized, stratified, randomization program so that mean body weights for each group/sex were similar.
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and Storage of Test Substance	High	All Outcomes: The study indicated that the test substance appeared stable under the conditions of the study (this based on analytical verification of the test substance). The chamber distribution of the test substance was determined prior to exposures at the high concentration; this analysis showed that distribution of the vapor was homogeneous (within 2% at different positions within the breathing zone; see Appendix A). The vapor generation method (elevated temperature) and equipment was reported.
	Metric 8:	Consistency of Exposure Administration	High	All Outcomes: Exposures were administered consistently across groups (no indication of any deviation in the administration of exposures was reported).
	Metric 9:	Reporting of Doses/Concentrations	High	All Outcomes: Analytical, nominal, and target concentrations were reported. Mean analytical concentrations over the course of 67 exposures were the same as targeted concentrations (based on 2 significant figures); daily mean concentrations were within 20% of nominal concentrations as determined from the amounts of the test substance used and the chamber airflows.
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: The exposure frequency and duration were clearly reported (i.e. 6 hours/day, 5 days/week for 90 days) and was appropriate for the study type.
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Study Citation:	DuPont, (1998). trans-1,2-Dichloroethylene: 90-day inhalation toxicity study in rats.			
Health Outcome(s):	Immune/Hematological; Lung/Respiratory; Thyroid; Reproductive/Developmental;			
Reported Health Effect(s):	Immune/Hematological: Hematological parameters and histology (spleen, thymus, bone marrow, mesenteric and mandibular lymph nodes); Lung/Respiratory: Lung weights and histology (lungs, pharynx, larynx, trachea, esophagus, nose - 4 sections); Thyroid: Thyroid histology; Reproductive/Developmental: Testes and ovaries weights, histology of reproductive organs (mammary gland in females, ovaries, uterus, vagina, prostate, seminal vesicles, testes, and epididymides);			
Duration:	Subchronic (>30-91 days) 90 days			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	4154576			
Domain	Metric	Rating	Comments	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	Medium	All Outcomes: Based on the study results (no LOAEL was identified), it was unclear whether the highest tested concentration was high enough. The applicable guideline for this study type indicates taht the high concentration should result in toxicity. The study did not indicate that 4000 ppm (about 16 mg/L, based on a MW for trans-1,2-dichloroethylene of 96.95 g/mol) was the highest attainable concentration, and this concentration was lower than the maximum concentration that should be considered based on the applicable guideline (20 mg/L). A rationale for the selection of concentrations used in the study was not explicitly specified; however, the conclusions section of the study stated that effects were observed in previous studies at concentrations lower than those used in this study (i.e., 3000 ppm).	
	Metric 12: Exposure Route and Method	High	All Outcomes: A dynamic whole-body chamber was used with at least 12 air changes/hour. Rats were in pretest for about 1 week prior to study initiation and housed individually once exposures were initiated.	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	High	All Outcomes: The preferred species for this study type was used (i.e. rats). The species and strain (CrI:CD(SD)BR rat), sex (both males and females), age (5 weeks on the day of arrival; about 7 weeks old at study initiation), body weights on day 1 (233-246 g for males and 169-173 g for females), and source (Charles River Laboratories) were specified.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: Animal husbandry conditions were adequately reported. Animals were generally maintained on a 12 hour light/12 hour dark cycle, the temperature was maintained at 23 +/- 1C, and relative humidity was 50 +/- 10%; these fall within the windows specified by the applicable study guideline. Food and water availability was ad libitum except during exposures. There was no indication that there was variability among exposure groups with respect to animal husbandry conditions.	
	Metric 15: Number of Animals per Group	Medium	All Outcomes: The number of animals per group was reported and appropriate. Studies of this type typically require a minimum of 10 animals/sex/group (and 5 animals/sex/group to evaluate recovery). In this study, there were 15 animals/sex/group; 10/sex/group were sacrificed after 90 days and 5 sex/group were maintained for a 1-month recovery period. Two different sets of animals were used; one set for standard toxicological evaluations, and one set for the evaluation of liver cell proliferation.	

Domain 5: Outcome Assessment

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Study Citation:	DuPont, (1998). trans-1,2-Dichloroethylene: 90-day inhalation toxicity study in rats.			
Health Outcome(s):	Immune/Hematological; Lung/Respiratory; Thyroid; Reproductive/Developmental;			
Reported Health Effect(s):	Immune/Hematological: Hematological parameters and histology (spleen, thymus, bone marrow, mesenteric and mandibular lymph nodes); Lung/Respiratory: Lung weights and histology (lungs, pharynx, larynx, trachea, esophagus, nose - 4 sections); Thyroid: Thyroid histology; Reproductive/Developmental: Testes and ovaries weights, histology of reproductive organs (mammary gland in females, ovaries, uterus, vagina, prostate, seminal vesicles, testes, and epididymides); Subchronic (>30-91 days) 90 days			
Duration:	Subchronic (>30-91 days) 90 days			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	4154576			
Domain	Metric	Rating	Comments	
	Metric 16: Outcome Assessment Methodology	Medium	Immune/Hematological: Hematological parameters (including the individual parameters evaluated and the time points at which they were evaluated in animals designated for standard toxicological evaluations) were appropriate for the outcome of interest as per the applicable study guideline. Gross and microscopic evaluations (spleen, thymus, lymph nodes) were also a sensitive measure of toxicity. However, spleen and thymus weights were not recorded (but are specified per guideline).; Lung/Respiratory: The outcome assessment and methodology (measurements of lung weight and histology of various respiratory tract tissues) mostly addressed the outcome of interest. The timing of these assessments and the tissues that were evaluated were appropriate. However, BALF evaluations were not performed (as specified by guideline).; Thyroid: Gross and microscopic evaluations of the thyroid were considered a sensitive measure of toxicity. However, thyroid weight is recommended by the applicable guideline; thyroid weights were not recorded.; Reproductive/Developmental: The outcome assessment and methodology (measurements of testes and ovaries weights and histology of various tissues of the reproductive tract) were considered appropriate for the study type. Additional assessments of reproductive toxicity (sperm counts, fertility, etc.) might be more sensitive measures but were not the focus of the study. The tissues evaluated were appropriate as per the applicable guideline with the following exceptions: epididymides weight was not recorded and the mammary gland was not evaluated in males.	
	Metric 17: Consistency of Outcome Assessment	High	Immune/Hematological: Hematological/immune endpoints were evaluated consistently across groups within the same set of animals.; Lung/Respiratory: Respiratory/lung endpoints were evaluated consistently across groups within the same set of animals.; Thyroid: The thyroid was evaluated consistently across groups within the same set of animals.; Reproductive/Developmental: Reproductive endpoints were evaluated consistently across groups within the same set of animals.	
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Study Citation:	DuPont, (1998). trans-1,2-Dichloroethylene: 90-day inhalation toxicity study in rats.			
Health Outcome(s):	Immune/Hematological; Lung/Respiratory; Thyroid; Reproductive/Developmental;			
Reported Health Effect(s):	Immune/Hematological: Hematological parameters and histology (spleen, thymus, bone marrow, mesenteric and mandibular lymph nodes); Lung/Respiratory: Lung weights and histology (lungs, pharynx, larynx, trachea, esophagus, nose - 4 sections); Thyroid: Thyroid histology; Reproductive/Developmental: Testes and ovaries weights, histology of reproductive organs (mammary gland in females, ovaries, uterus, vagina, prostate, seminal vesicles, testes, and epididymides); Subchronic (>30-91 days) 90 days			
Duration:	trans-1,2-Dichloroethylene- Parent compound			
Chemical:	4154576			
HERO ID:				
Domain	Metric	Rating	Comments	
	Metric 18: Sampling Adequacy	High	Immune/Hematological: Hematology (10 animals/sex/group), and histology (10 animals/sex/group after 90 days and the remaining 5 animals/sex/group after the one-month recovery period) were assessed in animals designated for standard toxicological evaluations. Tissues were examined microscopically in high-concentration animals and controls.; Lung/Respiratory: Lung weights and histology (10 animals/sex/group after 90 days and the remaining 5 animals/sex/group after the one-month recovery period) were assessed in animals designated for standard toxicological evaluations. Microscopic pathology was assessed in high-concentration animals and controls.; Thyroid: Histology (10 animals/sex/group after 90 days and the remaining 5 animals/sex/group after the one-month recovery period) was assessed in animals designated for standard toxicological evaluations (high-concentration and control groups).; Reproductive/Developmental: Reproductive organ weights and histology (10 animals/sex/group after 90 days and the remaining 5 animals/sex/group after the one-month recovery period) were assessed in animals designated for standard toxicological evaluations. Microscopic pathology was assessed in high-concentration animals and controls.	
	Metric 19: Blinding of Assessors	N/A	All Outcomes: Blinding was not required for these endpoints.	
	Metric 20: Negative Control Response	High	Immune/Hematological: In animals designated for standard toxicological evaluations, hematology parameters were generally within expected ranges for control animals; the incidence of gross and/or microscopic changes in control animals was low and/or considered spontaneous and incidental.; Lung/Respiratory: In animals designated for standard toxicological evaluations, the incidence of gross and/or microscopic changes in the respiratory tract tissues of control animals was low and/or considered spontaneous and incidental.; Thyroid: The incidence of gross and/or microscopic changes in control animals was low and/or considered spontaneous and incidental.; Reproductive/Developmental: In animals designated for standard toxicological evaluations, the incidence of gross and/or microscopic changes in the reproductive tract tissues of control animals was low and/or considered spontaneous and incidental.	

Domain 6: Confounding / Variable Control

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Study Citation:	DuPont, (1998). trans-1,2-Dichloroethylene: 90-day inhalation toxicity study in rats.			
Health Outcome(s):	Immune/Hematological; Lung/Respiratory; Thyroid; Reproductive/Developmental;			
Reported Health Effect(s):	Immune/Hematological: Hematological parameters and histology (spleen, thymus, bone marrow, mesenteric and mandibular lymph nodes); Lung/Respiratory: Lung weights and histology (lungs, pharynx, larynx, trachea, esophagus, nose - 4 sections); Thyroid: Thyroid histology; Reproductive/Developmental: Testes and ovaries weights, histology of reproductive organs (mammary gland in females, ovaries, uterus, vagina, prostate, seminal vesicles, testes, and epididymides); Subchronic (>30-91 days) 90 days			
Duration:	trans-1,2-Dichloroethylene- Parent compound			
Chemical:	4154576			
HERO ID:				
Domain	Metric	Rating	Comments	
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	Immune/Hematological: Reported information did not identify differences among groups; it is unlikely that these factors impacted hematological/immune endpoints because hematology parameters and the incidence of gross and microscopic findings were similar across groups.; Lung/Respiratory: Reported information did not identify differences among groups; it is unlikely that these factors impacted respiratory/lung endpoints because lung weights and the incidence of gross and microscopic findings were similar across groups.; Thyroid: Reported information did not identify differences among groups; it is unlikely that these factors impacted the thyroid because the incidence of gross and microscopic findings was similar across groups.; Reproductive/Developmental: Reported information did not identify differences among groups; it is unlikely that these factors impacted reproductive endpoints because reproductive organ weights and the incidence of gross and microscopic findings were similar across groups.	
	Metric 22: Health Outcomes Unrelated to Exposure	Medium	Immune/Hematological: There was no information regarding health outcomes unrelated to exposure; however, there was no significant mortality, and hematological/immune endpoints were not likely impacted.; Lung/Respiratory: There was no information regarding health outcomes unrelated to exposure; however, there was no significant mortality, and respiratory/lung endpoints were not likely impacted.; Thyroid: There was no information regarding health outcomes unrelated to exposure; however, there was no significant mortality, and the thyroid was not likely impacted.; Reproductive/Developmental: There was no information regarding health outcomes unrelated to exposure; however, there was no significant mortality, and reproductive endpoints were not likely impacted.	
	Metric 23: Data Presentation and Analysis	High	Immune/Hematological: Statistical methods were described. For hematology parameters, ANOVA and Bartlett's test were used at each sampling time, and Dunnett's test was used for pairwise comparisons. When Bartlett's was significant, Kruskal-Wallis was used and the Mann-Whitney U test was used to compare means among exposed groups and controls. Incidence data were not analyzed statistically; however, data enabling independent analyses were provided.; Lung/Respiratory: Statistical methods were described. Lung weights were analyzed with ANOVA; when the F-statistic was significant, Dunnett's test was used for pairwise comparisons. Bartlett's test was used to determine homogeneity of variances. Incidence data were not analyzed statistically; however, data enabling independent analyses were provided.; Thyroid: Incidence data were not analyzed statistically; however, data enabling independent analyses were provided.; Reproductive/Developmental: Statistical methods were described. Reproductive organ weights were analyzed with ANOVA; when the F-statistic was significant, Dunnett's test was used for pairwise comparisons. Bartlett's test was used to determine homogeneity of variances. Incidence data were not analyzed statistically; however, data enabling independent analyses were provided.	

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Study Citation:	DuPont, (1998). trans-1,2-Dichloroethylene: 90-day inhalation toxicity study in rats.		
Health Outcome(s):	Immune/Hematological; Lung/Respiratory; Thyroid; Reproductive/Developmental;		
Reported Health Effect(s):	Immune/Hematological: Hematological parameters and histology (spleen, thymus, bone marrow, mesenteric and mandibular lymph nodes); Lung/Respiratory: Lung weights and histology (lungs, pharynx, larynx, trachea, esophagus, nose - 4 sections); Thyroid: Thyroid histology; Reproductive/Developmental: Testes and ovaries weights, histology of reproductive organs (mammary gland in females, ovaries, uterus, vagina, prostate, seminal vesicles, testes, and epididymides);		
Duration:	Subchronic (>30-91 days) 90 days		
Chemical:	trans-1,2-Dichloroethylene- Parent compound		
HERO ID:	4154576		
Domain	Metric	Rating	Comments
	Metric 24: Reporting of Data	High	Immune/Hematological: Data for hematological/immune endpoints were provided for each exposure group and sex.; Lung/Respiratory: Data for respiratory endpoints were provided for each exposure group and sex.; Thyroid: Data were provided for each exposure group and sex.; Reproductive/Developmental: Data for reproductive endpoints were provided for each exposure group and sex.
Additional Comments:	The applicable study guideline indicates that spleen and thymus weights should be recorded, but they were not. The most recent version of the guideline was adopted in 2018; the study was conducted in 1998. It is unclear if spleen and thymus weights were required as per the guideline that was used when the study was conducted.		

Overall Quality Determination**High**

Study Citation:	DuPont, (1998). trans-1,2-Dichloroethylene: 90-day inhalation toxicity study in rats.			
Health Outcome(s):	Cancer/Carcinogenesis			
Reported Health Effect(s):	Cancer/Carcinogenesis: Tumor incidence (any)			
Duration:	Subchronic (>30-91 days) 90 days			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	4154576			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	The test substance was identified definitively as 1,2-trans-dichloroethylene.	
	Metric 2: Test Substance Source	High	The test substance was supplied by the sponsor; however, it was analytically verified by the performing laboratory.	
	Metric 3: Test Substance Purity	High	The test substance was >99% pure.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	A concurrent control group was used. Control animals were exposed to nitrogen and filtered/conditioned air from the same sources as used for the test chambers at approximately the same flow rates as those used in the exposure chambers. The test substance was not detected in the control chamber.	
	Metric 5: Positive Controls	N/A	A positive control is not required by study type/guideline.	
	Metric 6: Randomized Allocation of Animals	Medium	Allocation was performed with an unbiased method that ensured similar baseline characteristics across groups. Specifically, rats were divided into groups with the aid of a computerized, stratified, randomization program so that mean body weights for each group/sex were similar.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	High	The study indicated that the test substance appeared stable under the conditions of the study (this based on analytical verification of the test substance). The chamber distribution of the test substance was determined prior to exposures at the high concentration; this analysis showed that distribution of the vapor was homogeneous (within 2% at different positions within the breathing zone; see Appendix A). The vapor generation method (elevated temperature) and equipment was reported.	
	Metric 8: Consistency of Exposure Administration	High	Exposures were administered consistently across groups (no indication of any deviation in the administration of exposures was reported).	
	Metric 9: Reporting of Doses/Concentrations	High	Analytical, nominal, and target concentrations were reported. Mean analytical concentrations over the course of 67 exposures were the same as targeted concentrations (based on 2 significant figures); daily mean concentrations were within 20% of nominal concentrations as determined from the amounts of the test substance used and the chamber airflows.	
	Metric 10: Exposure Frequency and Duration	Uninformative	The exposure frequency and duration were clearly reported (i.e. 6 hours/day, 5 days/week for 90 days) and but was not appropriate for the study type (detection of cancer; study is not long enough).	
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Study Citation:	DuPont, (1998). trans-1,2-Dichloroethylene: 90-day inhalation toxicity study in rats.			
Health Outcome(s):	Cancer/Carcinogenesis			
Reported Health Effect(s):	Cancer/Carcinogenesis: Tumor incidence (any)			
Duration:	Subchronic (>30-91 days) 90 days			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	4154576			
Domain	Metric	Rating	Comments	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	Medium	Based on the study results (no LOAEL was identified), it was unclear whether the highest tested concentration was high enough. The applicable guideline for this study type indicates taht the high concentration should result in toxicity. The study did not indicate that 4000 ppm (about 16 mg/L, based on a MW for trans-1,2-dichloroethylene of 96.95 g/mol) was the highest attainable concentration, and this concentration was lower than the maximum concentration that should be considered based on the applicable guideline (20 mg/L). A rationale for the selection of concentrations used in the study was not explicitly specified; however, the conclusions section of the study stated that effects were observed in previous studies at concentrations lower than those used in this study (i.e., 3000 ppm).	
	Metric 12: Exposure Route and Method	High	A dynamic whole-body chamber was used with at least 12 air changes/hour. Rats were in pretest for about 1 week prior to study initiation and housed individually once exposures were initiated.	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	High	The preferred species for this study type was used (i.e. rats). The species and strain (CrI:CD(SD)BR rat), sex (both males and females), age (5 weeks on the day of arrival; about 7 weeks old at study initiation), body weights on day 1 (233-246 g for males and 169-173 g for females), and source (Charles River Laboratories) were specified.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	High	Animal husbandry conditions were adequately reported. Animals were generally maintained on a 12 hour light/12 hour dark cycle, the temperature was maintained at 23 +/- 1C, and relative humidity was 50 +/- 10%; these fall within the windows specified by the applicable study guideline. Food and water availability was ad libitum except during exposures. There was no indication that there was variability among exposure groups with respect to animal husbandry conditions.	
	Metric 15: Number of Animals per Group	Medium	The number of animals per group was reported and appropriate. Studies of this type typically require a minimum of 10 animals/sex/group (and 5 animals/sex/group to evaluate recovery). In this study, there were 15 animals/sex/group; 10/sex/group were sacrificed after 90 days and 5 sex/group were maintained for a 1-month recovery period. Two different sets of animals were used; one set for standard toxicological evaluations, and one set for the evaluation of liver cell proliferation.	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	Medium	The study partially addressed the outcome of interest. Tumor incidence was recorded during gross and/or microscopic examinations (but was not the purpose of the study; incidence was reported as discovered, presumably incidentally).	
	Metric 17: Consistency of Outcome Assessment	High	Tumor incidence was evaluated consistently among groups within the same set of animals.	
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Study Citation:	DuPont, (1998). trans-1,2-Dichloroethylene: 90-day inhalation toxicity study in rats.			
Health Outcome(s):	Cancer/Carcinogenesis			
Reported Health Effect(s):	Cancer/Carcinogenesis: Tumor incidence (any)			
Duration:	Subchronic (>30-91 days) 90 days			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	4154576			
Domain	Metric	Rating	Comments	
	Metric 18: Sampling Adequacy	High	Tumors were evaluated in all animals at the time of sacrifice (10 sex/group after 90 days and 5 sex/group after the recovery period).	
	Metric 19: Blinding of Assessors	N/A	Blinding was not required for this endpoint.	
	Metric 20: Negative Control Response	High	The tumor incidence in controls was zero.	
Domain 6: Confounding / Variable Control				
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	Reported information did not identify differences among groups; it is unlikely that these factors impacted carcinogenicity; the incidence of gross and microscopic findings were similar across groups.	
	Metric 22: Health Outcomes Unrelated to Exposure	Medium	There was no information regarding health outcomes unrelated to exposure; however, there was no significant mortality, and carcinogenicity was not likely impacted.	
	Metric 23: Data Presentation and Analysis	High	Statistical analyses of tumor incidence was not performed, but data were available enabling independent analysis, and it was clear that there were no differences among groups (incidence = 0).	
	Metric 24: Reporting of Data	High	Data were reported for each exposure group and sex.	
Additional Comments:	None			

Overall Quality Determination**Uninformative**

Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.			
Health Outcome(s):	Lung/Respiratory			
Reported Health Effect(s):	Lung/Respiratory: Lungs: gross pathology (acute oral and i.p studies); histopathology (inhalation – all durations)			
Duration:	Subchronic (>30-91 days) 8hrs/day, 5 days/week for 8 weeks			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740886			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	The test substance was identified by a definitive name, trans-1,2-dichloroethylene.	
	Metric 2: Test Substance Source	Low	The test substance was obtained from a commercial source (Merck). A batch or lot number was not reported, so this metric is rated Low.	
	Metric 3: Test Substance Purity	Low	Purity or grade of the test substance was not reported.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	It was specified that control animals were treated identically to the treated animals except that no test substance was added to the air (sham-exposed). This was also apparent from Table III, which showed controls for every exposure paradigm.	
	Metric 5: Positive Controls	N/A	No positive controls are required for this study type.	
	Metric 6: Randomized Allocation of Animals	Low	The method of allocation of test animals was not reported.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Medium	Test substance preparation and generation of the vapor for inhalation exposures were reported with adequate detail. Test substance storage was not reported; therefore, this metric is rated as Medium.	
	Metric 8: Consistency of Exposure Administration	High	Exposures occurred daily between 8 am-4pm.	
	Metric 9: Reporting of Doses/Concentrations	Medium	Target concentrations were reported without ambiguity. Analytical concentrations (gas chromatography) were not specified but were reported to be within 3% of target concentrations. Therefore, the lack of reporting analytical concentrations is not expected to have substantially impacted results.	
	Metric 10: Exposure Frequency and Duration	Medium	Inhalation exposures were administered for 8 hours per day, which differs from the typical 6 hours per day. However, this difference is not expected to have substantially impacted results.	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	Only a single concentration is tested. However, the aim of the study was to evaluate the effects of this concentration (200 ppm, the TLV/MAC in many countries at the time of the study) across multiple timepoints, rather than multiple concentrations at one time-point. Therefore, this is not considered to have significantly impacted results or to have significantly hampered conclusions.	
	Metric 12: Exposure Route and Method	Medium	The route and exposure method were suited to the test substance. Air changes/hour was specified to be > 10. Whole-body exposure chambers were utilized. The test substance may condense at the higher concentrations tested for the acute exposures.	
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Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.			
Health Outcome(s):	Lung/Respiratory			
Reported Health Effect(s):	Lung/Respiratory: Lungs: gross pathology (acute oral and i.p studies); histopathology (inhalation – all durations)			
Duration:	Subchronic (>30-91 days) 8hrs/day, 5 days/week for 8 weeks			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740886			
Domain	Metric	Rating	Comments	
Domain 4: Test Animals				
Metric 13:	Test Animal Characteristics	High	Test animal species, strain, sex, and starting body weight were reported. The age of the test animals was specified to be "mature." The test animals were obtained from a commercial source and were appropriate for the study type.	
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Most husbandry conditions were reported. Light-dark cycle was not reported.	
Metric 15:	Number of Animals per Group	Low	6 animals/group (female only) were utilized for all treatment and control groups. This is lower than typical for a sub-chronic study but was sufficient to conduct statistical analysis.	
Domain 5: Outcome Assessment				
Metric 16:	Outcome Assessment Methodology	High	Histopathology was considered to be adequate to assess the outcome of interest. Organ weights were not measured.	
Metric 17:	Consistency of Outcome Assessment	High	Outcomes appeared to be assessed consistently across study groups. A protocol for histopathology was provided.	
Metric 18:	Sampling Adequacy	High	All 6 animals/group appear to have been sampled for histopathology based on Table III.	
Metric 19:	Blinding of Assessors	N/A	Blinding is not required for initial histopathology.	
Metric 20:	Negative Control Response	High	Negative control responses were adequate	
Domain 6: Confounding / Variable Control				
Metric 21:	Confounding Variables in Test Design and Procedures	High	No confounding variables were reported or identified.	
Metric 22:	Health Outcomes Unrelated to Exposure	High	No effects unrelated to exposure were reported or identified.	
Metric 23:	Data Presentation and Analysis	High	Statistical analysis was not performed, but sufficient data were provided to allow for independent analysis.	
Metric 24:	Reporting of Data	High	Data were adequately reported as incidences including level of severity.	
Additional Comments:	None			
Overall Quality Determination		High		

Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.			
Health Outcome(s):	Musculoskeletal			
Reported Health Effect(s):	Musculoskeletal: Histopathology (quadriceps muscle; inhalation, all durations)			
Duration:	Subchronic (>30-91 days) 8hrs/day, 5 days/week for 8 weeks			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740886			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	The test substance was identified by a definitive name, trans-1,2-dichloroethylene.	
	Metric 2: Test Substance Source	Low	The test substance was obtained from a commercial source (Merck). A batch or lot number was not reported, so this metric is rated Low.	
	Metric 3: Test Substance Purity	Low	Purity or grade of the test substance was not reported.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	It was specified that control animals were treated identically to the treated animals except that no test substance was added to the air (sham-exposed). This was also apparent from Table III, which showed controls for every exposure paradigm.	
	Metric 5: Positive Controls	N/A	No positive controls are required for this study type.	
	Metric 6: Randomized Allocation of Animals	Low	The method of allocation of test animals was not reported.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Medium	Test substance preparation and generation of the vapor for inhalation exposures were reported with adequate detail. Test substance storage was not reported; therefore, this metric is rated as Medium.	
	Metric 8: Consistency of Exposure Administration	High	Exposures occurred daily between 8 am-4pm.	
	Metric 9: Reporting of Doses/Concentrations	Medium	Target concentrations were reported without ambiguity. Analytical concentrations (gas chromatography) were not specified but were reported to be within 3% of target concentrations. Therefore, the lack of reporting analytical concentrations is not expected to have substantially impacted results.	
	Metric 10: Exposure Frequency and Duration	Medium	Inhalation exposures were administered for 8 hours per day, which differs from the typical 6 hours per day. However, this difference is not expected to have substantially impacted results.	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	Only a single concentration is tested. However, the aim of the study was to evaluate the effects of this concentration (200 ppm, the TLV/MAC in many countries at the time of the study) across multiple timepoints, rather than multiple concentrations at one time-point. Therefore, this is not considered to have significantly impacted results or to have significantly hampered conclusions.	
	Metric 12: Exposure Route and Method	Medium	The route and exposure method were suited to the test substance. Air changes/hour was specified to be > 10. Whole-body exposure chambers were utilized. The test substance may condense at the higher concentrations tested for the acute exposures.	
Domain 4: Test Animals				
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Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.			
Health Outcome(s):	Musculoskeletal			
Reported Health Effect(s):	Musculoskeletal: Histopathology (quadriceps muscle; inhalation, all durations)			
Duration:	Subchronic (>30-91 days) 8hrs/day, 5 days/week for 8 weeks			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740886			
Domain	Metric	Rating	Comments	
	Metric 13: Test Animal Characteristics	High	Test animal species, strain, sex, and starting body weight were reported. The age of the test animals was specified to be "mature." The test animals were obtained from a commercial source and were appropriate for the study type.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Medium	Most husbandry conditions were reported. Light-dark cycle was not reported.	
	Metric 15: Number of Animals per Group	Low	6 animals/group (female only) were utilized for all treatment and control groups. This is lower than typical for a sub-chronic study but was sufficient to conduct statistical analysis.	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	High	Histopathology was considered to be adequate to assess the outcome of interest. Organ weights were not measured.	
	Metric 17: Consistency of Outcome Assessment	High	Outcomes appeared to be assessed consistently across study groups. A protocol for histopathology was provided.	
	Metric 18: Sampling Adequacy	High	All 6 animals/group appear to have been sampled for histopathology based on Table III. Table III reports histopathology results for the lung and liver, but it is assumed that histopathology for all organs specified was carried out on these animals.	
	Metric 19: Blinding of Assessors	N/A	Blinding is not required for initial histopathology.	
	Metric 20: Negative Control Response	Low	Only data for organs with evidence of lesions were reported.	
Domain 6: Confounding / Variable Control				
	Metric 21: Confounding Variables in Test Design and Procedures	High	No confounding variables were reported or identified.	
	Metric 22: Health Outcomes Unrelated to Exposure	High	No effects unrelated to exposure were reported or identified.	
	Metric 23: Data Presentation and Analysis	N/A	Statistical analysis was not necessary given the supposed negative findings.	
	Metric 24: Reporting of Data	High	Negative data were qualitatively reported	
Additional Comments:	None			
Overall Quality Determination		High		

Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.			
Health Outcome(s):	Cardiovascular			
Reported Health Effect(s):	Cardiovascular: Heart (gross pathology in acute oral and i.p studies); histopathology (inhalation – acute)			
Duration:	Subchronic (>30-91 days) 8hrs/day, 5 days/week for 8 weeks			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740886			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	The test substance was identified by a definitive name, trans-1,2-dichloroethylene.	
	Metric 2: Test Substance Source	Low	The test substance was obtained from a commercial source (Merck). A batch or lot number was not reported, so this metric is rated Low.	
	Metric 3: Test Substance Purity	Low	Purity or grade of the test substance was not reported.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	It was specified that control animals were treated identically to the treated animals except that no test substance was added to the air (sham-exposed). This was also apparent from Table III, which showed controls for every exposure paradigm.	
	Metric 5: Positive Controls	N/A	No positive controls are required for this study type.	
	Metric 6: Randomized Allocation of Animals	Low	The method of allocation of test animals was not reported.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Medium	Test substance preparation and generation of the vapor for inhalation exposures were reported with adequate detail. Test substance storage was not reported; therefore, this metric is rated as Medium.	
	Metric 8: Consistency of Exposure Administration	High	Exposures occurred daily between 8 am-4pm.	
	Metric 9: Reporting of Doses/Concentrations	Medium	Target concentrations were reported without ambiguity. Analytical concentrations (gas chromatography) were not specified but were reported to be within 3% of target concentrations. Therefore, the lack of reporting analytical concentrations is not expected to have substantially impacted results.	
	Metric 10: Exposure Frequency and Duration	Medium	Inhalation exposures were administered for 8 hours per day, which differs from the typical 6 hours per day. However, this difference is not expected to have substantially impacted results.	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	Only a single concentration is tested. However, the aim of the study was to evaluate the effects of this concentration (200 ppm, the TLV/MAC in many countries at the time of the study) across multiple timepoints, rather than multiple concentrations at one time-point. Therefore, this is not considered to have significantly impacted results or to have significantly hampered conclusions.	
	Metric 12: Exposure Route and Method	Medium	The route and exposure method were suited to the test substance. Air changes/hour was specified to be > 10. Whole-body exposure chambers were utilized. The test substance may condense at the higher concentrations tested for the acute exposures.	
Domain 4: Test Animals				
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Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.			
Health Outcome(s):	Cardiovascular			
Reported Health Effect(s):	Cardiovascular: Heart (gross pathology in acute oral and i.p studies); histopathology (inhalation – acute)			
Duration:	Subchronic (>30-91 days) 8hrs/day, 5 days/week for 8 weeks			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740886			
Domain	Metric	Rating	Comments	
	Metric 13: Test Animal Characteristics	High	Test animal species, strain, sex, and starting body weight were reported. The age of the test animals was specified to be "mature." The test animals were obtained from a commercial source and were appropriate for the study type.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Medium	Most husbandry conditions were reported. Light-dark cycle was not reported.	
	Metric 15: Number of Animals per Group	Low	6 animals/group (female only) were utilized for all treatment and control groups. This is lower than typical for a sub-chronic study but was sufficient to conduct statistical analysis.	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	High	Histopathology was considered to be adequate to assess the outcome of interest. Organ weights were not measured.	
	Metric 17: Consistency of Outcome Assessment	High	Outcomes appeared to be assessed consistently across study groups. A protocol for histopathology was provided.	
	Metric 18: Sampling Adequacy	High	All 6 animals/group appear to have been sampled for histopathology based on Table III. Table III reports histopathology results for the lung and liver, but it is assumed that histopathology for all organs specified was carried out on these animals.	
	Metric 19: Blinding of Assessors	N/A	Blinding is not required for initial histopathology.	
	Metric 20: Negative Control Response	Low	Only data for organs with evidence of lesions were reported.	
Domain 6: Confounding / Variable Control				
	Metric 21: Confounding Variables in Test Design and Procedures	High	No confounding variables were reported or identified.	
	Metric 22: Health Outcomes Unrelated to Exposure	High	No effects unrelated to exposure were reported or identified.	
	Metric 23: Data Presentation and Analysis	N/A	Statistical analysis was not necessary given the supposed negative findings.	
	Metric 24: Reporting of Data	Uninformative	Heart histopathology data were only reported for the 3000 ppm acute inhalation exposure and corresponding control. Negative findings were not described qualitatively; therefore, the results for this outcome for this exposure duration were not reported.	
Additional Comments: None				
Overall Quality Determination		Uninformative		

Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.			
Health Outcome(s):	Renal/Kidney; Hepatic/Liver; Immune/Hematological;			
Reported Health Effect(s):	Renal/Kidney: Gross pathology of the kidney and bladder and hematuria (acute oral and i.p studies); histopathology (inhalation – all durations; no effects); serum chemistry (electrolytes, BUN, uric acid – inhalation acute durations); Hepatic/Liver: Gross pathology of the liver (acute oral and i.p studies); histopathology of the liver (inhalation – all durations); serum chemistry (cholesterol, bilirubin, total protein, alkaline phosphatase, GOT, GPT, albumin, glucose; in inhalation acute studies and possibly 16-week duration); bile accumulation (acute inhalation); Immune/Hematological: Histopathology (spleen; inhalation – all durations; no effects); hematology (WBC count, RBC count, Hgb, packed cell volume, MCV, MCH, MCHC; inhalation studies – acute duration);			
Duration:	Subchronic (>30-91 days) 8hrs/day, 5 days/week for 8 weeks			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740886			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	All Outcomes: The test substance was identified by a definitive name, trans-1,2-dichloroethylene.	
	Metric 2: Test Substance Source	Low	All Outcomes: The test substance was obtained from a commercial source (Merck). A batch or lot number was not reported, so this metric is rated Low.	
	Metric 3: Test Substance Purity	Low	All Outcomes: Purity or grade of the test substance was not reported.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	All Outcomes: It was specified that control animals were treated identically to the treated animals except that no test substance was added to the air (sham-exposed). This was also apparent from Table III, which showed controls for every exposure paradigm.	
	Metric 5: Positive Controls	N/A	All Outcomes: No positive controls are required for this study type.	
	Metric 6: Randomized Allocation of Animals	Low	All Outcomes: The method of allocation of test animals was not reported.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Medium	All Outcomes: Test substance preparation and generation of the vapor for inhalation exposures were reported with adequate detail. Test substance storage was not reported; therefore, this metric is rated as Medium.	
	Metric 8: Consistency of Exposure Administration	High	All Outcomes: Exposures occurred daily between 8 am-4pm.	
	Metric 9: Reporting of Doses/Concentrations	Medium	All Outcomes: Target concentrations were reported without ambiguity. Analytical concentrations (gas chromatography) were not specified but were reported to be within 3% of target concentrations. Therefore, the lack of reporting analytical concentrations is not expected to have substantially impacted results.	
	Metric 10: Exposure Frequency and Duration	Medium	All Outcomes: Inhalation exposures were administered for 8 hours per day, which differs from the typical 6 hours per day. However, this difference is not expected to have substantially impacted results.	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: Only a single concentration is tested. However, the aim of the study was to evaluate the effects of this concentration (200 ppm, the TLV/MAC in many countries at the time of the study) across multiple timepoints, rather than multiple concentrations at one timepoint. Therefore, this is not considered to have significantly impacted results or to have significantly hampered conclusions.	

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Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.			
Health Outcome(s):	Renal/Kidney; Hepatic/Liver; Immune/Hematological;			
Reported Health Effect(s):	Renal/Kidney: Gross pathology of the kidney and bladder and hematuria (acute oral and i.p studies); histopathology (inhalation – all durations; no effects); serum chemistry (electrolytes, BUN, uric acid – inhalation acute durations); Hepatic/Liver: Gross pathology of the liver (acute oral and i.p studies); histopathology of the liver (inhalation – all durations); serum chemistry (cholesterol, bilirubin, total protein, alkaline phosphatase, GOT, GPT, albumin, glucose; in inhalation acute studies and possibly 16-week duration); bile accumulation (acute inhalation); Immune/Hematological: Histopathology (spleen; inhalation – all durations; no effects); hematology (WBC count, RBC count, Hgb, packed cell volume, MCV, MCH, MCHC; inhalation studies – acute duration);			
Duration:	Subchronic (>30-91 days) 8hrs/day, 5 days/week for 8 weeks			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740886			
Domain		Metric	Rating	Comments
	Metric 12:	Exposure Route and Method	Medium	All Outcomes: The route and exposure method were suited to the test substance. Air changes/hour was specified to be > 10. Whole-body exposure chambers were utilized. The test substance may condense at the higher concentrations tested for the acute exposures.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	High	All Outcomes: Test animal species, strain, sex, and starting body weight were reported. The age of the test animals was specified to be "mature." The test animals were obtained from a commercial source and were appropriate for the study type.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	All Outcomes: Most husbandry conditions were reported. Light-dark cycle was not reported.
	Metric 15:	Number of Animals per Group	Low	All Outcomes: 6 animals/group (female only) were utilized for all treatment and control groups. This is lower than typical for a sub-chronic study but was sufficient to conduct statistical analysis.
Domain 5: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	Medium	Renal/Kidney: Histopathology was considered to be adequate to assess the outcome of interest; however, clinical chemistry and organ weights were not measured and these endpoints are typically included in repeat dose experiments.; Hepatic/Liver: Histopathology was considered to be adequate to assess the outcome of interest; however, clinical chemistry and organ weights were not measured and these endpoints are typically included in repeat dose experiments.; Immune/Hematological: Histopathology was considered to be adequate to assess the outcome of interest; however, hematology and organ weights were not measured and these endpoints are typically included in repeat dose experiments.
	Metric 17:	Consistency of Outcome Assessment	High	All Outcomes: Outcomes appeared to be assessed consistently across study groups. A protocol for histopathology was provided.
	Metric 18:	Sampling Adequacy	High	All Outcomes: All 6 animals/group appear to have been sampled for histopathology based on Table III.
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding is not required for initial histopathology.
	Metric 20:	Negative Control Response	High	All Outcomes: Negative control responses were adequate
Domain 6: Confounding / Variable Control				
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Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.			
Health Outcome(s):	Renal/Kidney; Hepatic/Liver; Immune/Hematological;			
Reported Health Effect(s):	Renal/Kidney: Gross pathology of the kidney and bladder and hematuria (acute oral and i.p studies); histopathology (inhalation – all durations; no effects); serum chemistry (electrolytes, BUN, uric acid – inhalation acute durations); Hepatic/Liver: Gross pathology of the liver (acute oral and i.p studies); histopathology of the liver (inhalation – all durations); serum chemistry (cholesterol, bilirubin, total protein, alkaline phosphatase, GOT, GPT, albumin, glucose; in inhalation acute studies and possibly 16-week duration); bile accumulation (acute inhalation); Immune/Hematological: Histopathology (spleen; inhalation – all durations; no effects); hematology (WBC count, RBC count, Hgb, packed cell volume, MCV, MCH, MCHC; inhalation studies – acute duration);			
Duration:	Subchronic (>30-91 days) 8hrs/day, 5 days/week for 8 weeks			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740886			
Domain	Metric	Rating	Comments	
	Metric 21: Confounding Variables in Test Design and Procedures	High	All Outcomes: No confounding variables were reported or identified.	
	Metric 22: Health Outcomes Unrelated to Exposure	High	All Outcomes: No effects unrelated to exposure were reported or identified.	
	Metric 23: Data Presentation and Analysis	High	All Outcomes: Statistical analysis was not performed, but sufficient data were provided to allow for independent analysis.	
	Metric 24: Reporting of Data	High	All Outcomes: Data were adequately reported as incidences including level of severity.	
Additional Comments:	None			
Overall Quality Determination		High		

Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.			
Health Outcome(s):	Neurological/Behavioral			
Reported Health Effect(s):	Neurological/Behavioral: Neurological/behavioral clinical signs (acute oral and ip and inhalation – all durations); histopathology brain and peripheral nerves (inhalation – all durations, no effects)			
Duration:	Subchronic (>30-91 days) 8hrs/day, 5 days/week for 8 weeks			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740886			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	The test substance was identified by a definitive name, trans-1,2-dichloroethylene.	
	Metric 2: Test Substance Source	Low	The test substance was obtained from a commercial source (Merck). A batch or lot number was not reported, so this metric is rated Low.	
	Metric 3: Test Substance Purity	Low	Purity or grade of the test substance was not reported.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	It was specified that control animals were treated identically to the treated animals except that no test substance was added to the air (sham-exposed). This was also apparent from Table III, which showed controls for every exposure paradigm.	
	Metric 5: Positive Controls	N/A	No positive controls are required for this study type.	
	Metric 6: Randomized Allocation of Animals	Low	The method of allocation of test animals was not reported.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Medium	Test substance preparation and generation of the vapor for inhalation exposures were reported with adequate detail. Test substance storage was not reported; therefore, this metric is rated as Medium.	
	Metric 8: Consistency of Exposure	High	Exposures consistently occurred from 8:00 am to 4:00 pm.	
	Metric 9: Administration Reporting of Doses/Concentrations	Medium	Target concentrations were reported without ambiguity. Analytical concentrations (gas chromatography) were not specified but were reported to be within 3% of target concentrations. Therefore, the lack of reporting analytical concentrations is not expected to have substantially impacted results.	
	Metric 10: Exposure Frequency and Duration	Medium	Inhalation exposures were administered for 8 hours per day, which differs from the typical 6 hours per day. However, this difference is not expected to have substantially impacted results.	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	Only a single concentration is tested. However, the aim of the study was to evaluate the effects of this concentration (200 ppm, the TLV/MAC in many countries at the time of the study) across multiple timepoints, rather than multiple concentrations at one time-point. Therefore, this is not considered to have significantly impacted results or to have significantly hampered conclusions.	
	Metric 12: Exposure Route and Method	Medium	The route and exposure method were suited to the test substance. Air changes/hour was specified to be > 10. Whole-body exposure chambers were utilized. The test substance may condense at the higher concentrations tested for the acute exposures.	
Domain 4: Test Animals				
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Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.			
Health Outcome(s):	Neurological/Behavioral			
Reported Health Effect(s):	Neurological/Behavioral: Neurological/behavioral clinical signs (acute oral and ip and inhalation – all durations); histopathology brain and peripheral nerves (inhalation – all durations, no effects)			
Duration:	Subchronic (>30-91 days) 8hrs/day, 5 days/week for 8 weeks			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740886			
Domain	Metric	Rating	Comments	
	Metric 13: Test Animal Characteristics	High	Test animal species, strain, sex, and starting body weight were reported. The age of the test animals was specified to be "mature." The test animals were obtained from a commercial source and were appropriate for the study type.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Medium	Most husbandry conditions were reported. Light-dark cycle was not reported.	
	Metric 15: Number of Animals per Group	Low	6 animals/group (female only) were utilized for all treatment and control groups. This is lower than typical for a subchronic study but was sufficient to conduct statistical analysis.	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	Medium	Histopathology (brain, sciatic nerve) and clinical signs were considered to be adequate to assess the outcome of interest. The study authors were specifically interested in acute neurotoxicity (CNS depression), which was the basis of the TLV-MAC (200 ppm) that was the focus of the study. This would be appropriately addressed by noting clinical signs of toxicity during exposure administration. A protocol for animal observations (frequency/duration) was not provided.	
	Metric 17: Consistency of Outcome Assessment	Medium	Outcomes appeared to be assessed consistently across study groups. A protocol for histopathology was provided, but not for clinical observations.	
	Metric 18: Sampling Adequacy	High	It is unclear whether all 6 animals/group were sampled for clinical signs. All 6 animals/group appear to have been sampled for histopathology based on Table III. Table III reports histopathology results for the lung and liver, but it is assumed that histopathology for all organs specified was carried out on these animals.	
	Metric 19: Blinding of Assessors	N/A	Blinding is not required for initial histopathology. Blinding was not specified for clinical observations.	
	Metric 20: Negative Control Response	High	Negative controls responded appropriately.	
Domain 6: Confounding / Variable Control				
	Metric 21: Confounding Variables in Test Design and Procedures	High	No confounding variables were reported or identified.	
	Metric 22: Health Outcomes Unrelated to Exposure	High	No effects unrelated to exposure were reported or identified.	
	Metric 23: Data Presentation and Analysis	N/A	Statistical analysis was not necessary given the negative findings (qualitatively described).	
	Metric 24: Reporting of Data	High	Negative data were qualitatively described.	
Additional Comments:	None			

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Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Neurological/Behavioral: Neurological/behavioral clinical signs (acute oral and ip and inhalation – all durations); histopathology brain and peripheral nerves (inhalation – all durations, no effects)
Duration:	Subchronic (>30-91 days) 8hrs/day, 5 days/week for 8 weeks
Chemical:	trans-1,2-Dichloroethylene- Parent compound
HERO ID:	1740886

Domain	Metric	Rating	Comments
Overall Quality Determination		High	

Study Citation:	Hayes, J. R., Condie Jr., L. W., Egle Jr., J. L., Borzelleca, J. F. (1987). The acute and subchronic toxicity in rats of trans-1,2-dichloroethylene in drinking water. Journal of the American College of Toxicology 6(4):471-478.
Health Outcome(s):	Hepatic/Liver; Nutritional/Metabolic; Mortality;
Reported Health Effect(s):	Hepatic/Liver: No changes in mean or relative (to body weight or brain weight) liver weights, and no treatment-related effects on serum chemistry parameters or treatment-related lesions liver in the 90-day study. For serum chemistry measurements, serum was analyzed for SGPT (ALT), SGOT (AST), ALP, 5' nucleotidase, BUN, protein, glucose, cholesterol, bilirubin, creatinine, calcium, phosphorus, albumin, chloride, and globulin.; Nutritional/Metabolic: No effects on fluid consumption and or mean body weights in the 90-day study.; Mortality: Mortality and LD50 in the acute oral toxicity study. No test substance-related mortalities in the 90-day study.;
Duration:	Subchronic (>30-91 days) 90 days
Chemical:	trans-1,2-Dichloroethylene- Parent compound
HERO ID:	1740814

Domain	Metric	Rating	Comments
Domain 1: Test Substance			
	Metric 1: Test Substance Identity	High	All Outcomes: The test substance was identified as trans-1,2-dichloroethylene (CASN 156-60-5).
	Metric 2: Test Substance Source	High	All Outcomes: The test substance was obtained from Aldrich Chemical Company (Milwaukee, WI). Lot number 5201 J.J.
	Metric 3: Test Substance Purity	High	All Outcomes: Purity was reported to be 98%.
Domain 2: Test Design			
	Metric 4: Negative and Vehicle Controls	High	All Outcomes: Appropriate concurrent negative control groups were included.
	Metric 5: Positive Controls	N/A	All Outcomes: Not applicable for this study type.
	Metric 6: Randomized Allocation of Animals	Medium	All Outcomes: Study authors state that animals were randomly assigned into five treatment groups.
Domain 3: Exposure Characterization			
	Metric 7: Preparation and Storage of Test Substance	High	Hepatic/Liver: Test substance preparation/administration and storage conditions were reported in detail and were appropriate for the test substance.; Nutritional/Metabolic: Test substance preparation/administration and storage conditions were reported in detail (test substance and were appropriate for the test substance.; Mortality: Test substance preparation/administration and storage conditions were reported in detail and were appropriate for the test substance.
	Metric 8: Consistency of Exposure Administration	High	All Outcomes: Test substance was administered in drinking water, which was provided to all animals ad libitum. Drinking water intake was monitored and did not vary across treatment groups.

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Study Citation:	Hayes, J. R., Condie Jr., L. W., Egle Jr., J. L., Borzelleca, J. F. (1987). The acute and subchronic toxicity in rats of trans-1,2-dichloroethylene in drinking water. Journal of the American College of Toxicology 6(4):471-478.
Health Outcome(s):	Hepatic/Liver; Nutritional/Metabolic; Mortality;
Reported Health Effect(s):	Hepatic/Liver: No changes in mean or relative (to body weight or brain weight) liver weights, and no treatment-related effects on serum chemistry parameters or treatment-related lesions liver in the 90-day study. For serum chemistry measurements, serum was analyzed for SGPT (ALT), SGOT (AST), ALP, 5'nucleotidase, BUN, protein, glucose, cholesterol, bilirubin, creatinine, calcium, phosphorus, albumin, chloride, and globulin.; Nutritional/Metabolic: No effects on fluid consumption and or mean body weights in the 90-day study.; Mortality: Mortality and LD50 in the acute oral toxicity study. No test substance-related mortalities in the 90-day study.;
Duration:	Subchronic (>30-91 days) 90 days
Chemical:	trans-1,2-Dichloroethylene- Parent compound
HERO ID:	1740814

Domain	Metric	Rating	Comments
	Metric 9: Reporting of Doses/Concentrations	Low	Hepatic/Liver: A stability study was conducted to evaluate the loss of trans 1,2 DCE from drinking water. Based on the rate of loss of the test substance, average daily drinking water concentrations were calculated, which were then used to estimate the mean dose of consumed test substance in units of mg/kg-d based on animal body weight and drinking water intake. However, drinking water concentrations were not analytically verified and there is some uncertainty due to the volatile nature of the test substance.; Nutritional/Metabolic: A stability study was conducted to evaluate the loss of trans 1,2 DCE from drinking water. Based on the rate of loss of the test substance, average daily drinking water concentrations were calculated, which were then used to estimate the mean dose of consumed test substance in units of mg/kg-d based on animal body weight and drinking water intake. However, drinking water concentrations were not analytically verified and there is some uncertainty due to the volatile nature of the test substance.; Mortality: A stability study was conducted to evaluate the loss of trans 1,2 DCE from drinking water. Based on the rate of loss of the test substance, average daily drinking water concentrations were calculated, which were then used to estimate the mean dose of consumed test substance in units of mg/kg-d based on animal body weight and drinking water intake. However, results of the stability study were not reported and drinking water concentrations were not analytically verified.
	Metric 10: Exposure Frequency and Duration	High	All Outcomes: Rats were exposed continuously via drinking water for 90 days. This exposure duration is appropriate.
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	Low	All Outcomes: Male (0, 402, 1314, 3114 mg/kg-d) and female (0, 353, 1257, 2809 mg/kg-d) rats were administered 3 dose levels of the test substance via drinking water. No effects were reported in male rats, while the only effect reported in females was a slight increase in kidney weight. It is unclear if the highest dose tested was high enough to observe an adverse effect.
	Metric 12: Exposure Route and Method	Low	All Outcomes: Animals were administered the test substance via drinking water. Studies were conducted to evaluate the stability of the test substance in water over a 4-day period, however, the stability results are not reported or described. Loss of the test substance due to instability may have been partially mitigated, as test solutions were prepared twice weekly and water bottles were changed twice weekly. However, there is uncertainty as the results of the stability studies were not provided, so its unclear if preparing test substance twice weekly was sufficient or if solutions should have been prepare more frequently (i.e., daily) or if another exposure method may have been more appropriate.

Domain 4: Test Animals

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Study Citation:	Hayes, J. R., Condie Jr., L. W., Egle Jr., J. L., Borzelleca, J. F. (1987). The acute and subchronic toxicity in rats of trans-1,2-dichloroethylene in drinking water. Journal of the American College of Toxicology 6(4):471-478.			
Health Outcome(s):	Hepatic/Liver; Nutritional/Metabolic; Mortality;			
Reported Health Effect(s):	Hepatic/Liver: No changes in mean or relative (to body weight or brain weight) liver weights, and no treatment-related effects on serum chemistry parameters or treatment-related lesions liver in the 90-day study. For serum chemistry measurements, serum was analyzed for SGPT (ALT), SGOT (AST), ALP, 5'nucleotidase, BUN, protein, glucose, cholesterol, bilirubin, creatinine, calcium, phosphorus, albumin, chloride, and globulin.; Nutritional/Metabolic: No effects on fluid consumption and or mean body weights in the 90-day study.; Mortality: Mortality and LD50 in the acute oral toxicity study. No test substance-related mortalities in the 90-day study.;			
Duration:	Subchronic (>30-91 days) 90 days			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740814			
Domain	Metric	Rating	Comments	
	Metric 13: Test Animal Characteristics	Medium	All Outcomes: The test animal species, strain, sex, and age were reported, and the test animal was obtained from a commercial source. Animal starting body weight was not reported.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: All husbandry conditions were reported and were adequate.	
	Metric 15: Number of Animals per Group	Medium	All Outcomes: 20 males and females were included in each exposure group.	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	High	Hepatic/Liver: The outcome assessment methodology addressed the intended outcomes of interest and the methodology was sensitive and appropriate. Livers were weighed and histologic examinations were conducted. Serum chemistry parameters were measured.; Nutritional/Metabolic: The outcome assessment methodology was sensitive and addressed the intended outcome(s) of interest. Animals were weighed on the 1st day of exposure and weekly thereafter.; Mortality: The outcome assessment methodology was sensitive and addressed the intended outcome(s) of interest. Animals were observed twice daily.	
	Metric 17: Consistency of Outcome Assessment	High	Hepatic/Liver: Details of the outcome assessment protocol were reported and outcomes were assessed consistently across study groups (e.g., at the same time after initial exposure) using the same protocol in all study groups.; Nutritional/Metabolic: Details of the outcome assessment protocol were reported and outcomes were assessed consistently across study groups.; Mortality: Details of the outcome assessment protocol were reported and outcomes were assessed consistently across study groups (i.e., all animals were observed twice daily, separated by an interval of at least 5 hours).	
	Metric 18: Sampling Adequacy	High	All Outcomes: Reported information indicates the study used adequate sampling for the outcome(s) of interest.	
	Metric 19: Blinding of Assessors	N/A	All Outcomes: Not necessary for this study type.	
	Metric 20: Negative Control Response	High	All Outcomes: The biological responses of the negative control group(s) were adequate.	
Domain 6: Confounding / Variable Control				
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	All Outcomes: Although the study did not report all information to determine confounding, reported information did not identify differences among study groups with regard to terminal body weight and water intake. Food consumption was not reported.	
	Metric 22: Health Outcomes Unrelated to Exposure	High	All Outcomes: Details regarding animal attrition and health outcomes unrelated to exposure were reported for each study group and there were no differences among groups that could influence the outcome assessment.	

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Study Citation:	Hayes, J. R., Condie Jr., L. W., Egle Jr., J. L., Borzelleca, J. F. (1987). The acute and subchronic toxicity in rats of trans-1,2-dichloroethylene in drinking water. Journal of the American College of Toxicology 6(4):471-478.
Health Outcome(s):	Hepatic/Liver; Nutritional/Metabolic; Mortality;
Reported Health Effect(s):	Hepatic/Liver: No changes in mean or relative (to body weight or brain weight) liver weights, and no treatment-related effects on serum chemistry parameters or treatment-related lesions liver in the 90-day study. For serum chemistry measurements, serum was analyzed for SGPT (ALT), SGOT (AST), ALP, 5'nucleotidase, BUN, protein, glucose, cholesterol, bilirubin, creatinine, calcium, phosphorus, albumin, chloride, and globulin.; Nutritional/Metabolic: No effects on fluid consumption and or mean body weights in the 90-day study.; Mortality: Mortality and LD50 in the acute oral toxicity study. No test substance-related mortalities in the 90-day study.;
Duration:	Subchronic (>30-91 days) 90 days
Chemical:	trans-1,2-Dichloroethylene- Parent compound
HERO ID:	1740814

Domain	Metric	Rating	Comments
	Metric 23: Data Presentation and Analysis	High	Hepatic/Liver: Statistical methods were clearly described and were appropriate.; Nutritional/Metabolic: Statistical methods were clearly described and were appropriate for the dataset(s).; Mortality: Statistical methods were clearly described and were appropriate for the dataset(s).
	Metric 24: Reporting of Data	High	Hepatic/Liver: Organ weight and histopathology incidence data were adequately reported. Serum chemistry data were not reported, but study authors clearly state that no significant effects were observed.; Nutritional/Metabolic: Terminal body weight and water intake data is reported as mean +/- SEM.; Mortality: Survival data is reported for all exposure groups and by sex.

Additional Comments: None

Overall Quality Determination**Medium**

Study Citation:	Hayes, J. R., Condie Jr., L. W., Egle Jr., J. L., Borzelleca, J. F. (1987). The acute and subchronic toxicity in rats of trans-1,2-dichloroethylene in drinking water. Journal of the American College of Toxicology 6(4):471-478.
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Renal/Kidney: Dose-dependent increases in mean and relative (to brain weight) kidney weight in females only, with no treatment-related effects on serum chemistry parameters or treatment-related lesions in the kidneys in the 90-day study. No changes in relative-to-body weight kidney weight were observed in females and no changes in mean or relative kidney weights were observed in males. For serum chemistry measurements, serum was analyzed for SGPT (ALT), SGOT (AST), ALP, 5'nucleotidase, BUN, protein, glucose, cholesterol, bilirubin, creatinine, calcium, phosphorus, albumin, chloride, and globulin. No adverse, treatment-related effects on urinary parameters in the 90-day study. Urinary parameters measured included pH, bilirubin, glucose, protein, ketones, and blood.
Duration:	Subchronic (>30-91 days) 90 days
Chemical:	trans-1,2-Dichloroethylene- Parent compound
HERO ID:	1740814

Domain	Metric	Rating	Comments
Domain 1: Test Substance			
	Metric 1: Test Substance Identity	High	The test substance was identified as trans-1,2-dichloroethylene (CASN 156-60-5).
	Metric 2: Test Substance Source	High	The test substance was obtained from Aldrich Chemical Company (Milwaukee, WI). Lot number 5201 J.J.
	Metric 3: Test Substance Purity	High	Purity was reported to be 98%.
Domain 2: Test Design			
	Metric 4: Negative and Vehicle Controls	High	Appropriate concurrent negative control groups were included.
	Metric 5: Positive Controls	N/A	Not applicable for this study type.
	Metric 6: Randomized Allocation of Animals	Medium	Study authors state that animals were randomly assigned into five treatment groups.
Domain 3: Exposure Characterization			
	Metric 7: Preparation and Storage of Test Substance	High	Test substance preparation/administration and storage conditions were reported in detail and were appropriate for the test substance.
	Metric 8: Consistency of Exposure Administration	High	Test substance was administered in drinking water, which was provided to all animals ad libitum. Drinking water intake was monitored and did not vary across treatment groups.
	Metric 9: Reporting of Doses/Concentrations	Low	A stability study was conducted to evaluate the loss of trans 1,2 DCE from drinking water. Based on the rate of loss of the test substance, average daily drinking water concentrations were calculated, which were then used to estimate the mean dose of consumed test substance in units of mg/kg-d based on animal body weight and drinking water intake. However, drinking water concentrations were not analytically verified and there is some uncertainty due to the volatile nature of the test substance.
	Metric 10: Exposure Frequency and Duration	High	Rats were exposed continuously via drinking water for 90 days. This exposure duration is appropriate.
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	Low	Male (0, 402, 1314, 3114 mg/kg-d) and female (0, 353, 1257, 2809 mg/kg-d) rats were administered 3 dose levels of the test substance via drinking water. No effects were reported in male rats, while the only effect reported in females was a slight increase in kidney weight. It is unclear if the highest dose tested was high enough to observe an adverse effect.

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Study Citation:	Hayes, J. R., Condie Jr., L. W., Egle Jr., J. L., Borzelleca, J. F. (1987). The acute and subchronic toxicity in rats of trans-1,2-dichloroethylene in drinking water. Journal of the American College of Toxicology 6(4):471-478.			
Health Outcome(s):	Renal/Kidney			
Reported Health Effect(s):	Renal/Kidney: Dose-dependent increases in mean and relative (to brain weight) kidney weight in females only, with no treatment-related effects on serum chemistry parameters or treatment-related lesions in the kidneys in the 90-day study. No changes in relative-to-body weight kidney weight were observed in females and no changes in mean or relative kidney weights were observed in males. For serum chemistry measurements, serum was analyzed for SGPT (ALT), SGOT (AST), ALP, 5'nucleotidase, BUN, protein, glucose, cholesterol, bilirubin, creatinine, calcium, phosphorus, albumin, chloride, and globulin. No adverse, treatment-related effects on urinary parameters in the 90-day study. Urinary parameters measured included pH, bilirubin, glucose, protein, ketones, and blood.			
Duration:	Subchronic (>30-91 days) 90 days			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740814			
Domain	Metric	Rating	Comments	
	Metric 12: Exposure Route and Method	Low	Animals were administered the test substance via drinking water. Studies were conducted to evaluate the stability of the test substance in water over a 4-day period, however, the stability results are not reported or described. Loss of the test substance due to instability may have been partially mitigated, as test solutions were prepared twice weekly and water bottles were changed twice weekly. However, there is uncertainty as the results of the stability studies were not provided, so its unclear if preparing test substance twice weekly was sufficient or if solutions should have been prepare more frequently (i.e., daily) or if another exposure method may have been more appropriate.	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	Medium	The test animal species, strain, sex, and age were reported, and the test animal was obtained from a commercial source. Animal starting body weight was not reported.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were reported and were adequate.	
	Metric 15: Number of Animals per Group	Medium	20 males and females were included in each exposure group.	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	High	The outcome assessment methodology addressed the intended outcome of interest and the assessment methodology was sensitive and appropriate for the outcome of interest.	
	Metric 17: Consistency of Outcome Assessment	High	Details of the outcome assessment protocol were reported and outcomes were assessed consistently across study groups.	
	Metric 18: Sampling Adequacy	High	Reported information indicates the study used adequate sampling for the outcome(s) of interest.	
	Metric 19: Blinding of Assessors	N/A	Not necessary for this study type.	
	Metric 20: Negative Control Response	Medium	The biological responses of the negative control group(s) were adequate for most outcomes. However, the incidence of basophilic cortical tubules was elevated in control males, which may impact results.	
Domain 6: Confounding / Variable Control				
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	Although the study did not report all information to determine confounding, reported information did not identify differences among study groups with regard to terminal body weight and water intake. Food consumption was not reported.	
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Study Citation:	Hayes, J. R., Condie Jr., L. W., Egle Jr., J. L., Borzelleca, J. F. (1987). The acute and subchronic toxicity in rats of trans-1,2-dichloroethylene in drinking water. Journal of the American College of Toxicology 6(4):471-478.
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Renal/Kidney: Dose-dependent increases in mean and relative (to brain weight) kidney weight in females only, with no treatment-related effects on serum chemistry parameters or treatment-related lesions in the kidneys in the 90-day study. No changes in relative-to-body weight kidney weight were observed in females and no changes in mean or relative kidney weights were observed in males. For serum chemistry measurements, serum was analyzed for SGPT (ALT), SGOT (AST), ALP, 5' nucleotidase, BUN, protein, glucose, cholesterol, bilirubin, creatinine, calcium, phosphorus, albumin, chloride, and globulin. No adverse, treatment-related effects on urinary parameters in the 90-day study. Urinary parameters measured included pH, bilirubin, glucose, protein, ketones, and blood.
Duration:	Subchronic (>30-91 days) 90 days
Chemical:	trans-1,2-Dichloroethylene- Parent compound
HERO ID:	1740814

Domain	Metric	Rating	Comments
	Metric 22: Health Outcomes Unrelated to Exposure	High	Details regarding animal attrition and health outcomes unrelated to exposure were reported for each study group and there were no differences among groups that could influence the outcome assessment.
	Metric 23: Data Presentation and Analysis	High	Statistical methods were clearly described and were appropriate for the dataset(s).
	Metric 24: Reporting of Data	High	Organ weight and histopathology incidence data were adequately reported. Serum chemistry data were not reported, but study authors clearly state that no significant effects were observed.

Additional Comments: None

Overall Quality Determination**Medium**

Study Citation:	Hayes, J. R., Condie Jr., L. W., Egle Jr., J. L., Borzelleca, J. F. (1987). The acute and subchronic toxicity in rats of trans-1,2-dichloroethylene in drinking water. Journal of the American College of Toxicology 6(4):471-478.			
Health Outcome(s):	Lung/Respiratory; Reproductive/Developmental;			
Reported Health Effect(s):	Lung/Respiratory: No changes in mean or relative (to body weight or brain weight) lung weights in the 90-day study.; Reproductive/Developmental: No changes in mean or relative (to body weight or brain weight) testes weights in males or ovaries weights in females, and no treatment-related histopathological changes in these organs, in the 90-day study.;			
Duration:	Subchronic (>30-91 days) 90 days			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740814			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
Metric 1:	Test Substance Identity	High	All Outcomes: The test substance was identified as trans-1,2-dichloroethylene (CASN 156-60-5).	
Metric 2:	Test Substance Source	High	All Outcomes: The test substance was obtained from Aldrich Chemical Company (Milwaukee, WI). Lot number 5201 J.J.	
Metric 3:	Test Substance Purity	High	All Outcomes: Purity was reported to be 98%.	
Domain 2: Test Design				
Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Appropriate concurrent negative control groups were included.	
Metric 5:	Positive Controls	N/A	All Outcomes: Not applicable for this study type.	
Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: Study authors state that animals were randomly assigned into five treatment groups.	
Domain 3: Exposure Characterization				
Metric 7:	Preparation and Storage of Test Substance	High	All Outcomes: Test substance preparation/administration and storage conditions were reported in detail and were appropriate for the test substance.	
Metric 8:	Consistency of Exposure Administration	High	All Outcomes: Test substance was administered in drinking water, which was provided to all animals ad libitum. Drinking water intake was monitored and did not vary across treatment groups.	
Metric 9:	Reporting of Doses/Concentrations	Low	All Outcomes: A stability study was conducted to evaluate the loss of trans 1,2 DCE from drinking water. Based on the rate of loss of the test substance, average daily drinking water concentrations were calculated, which were then used to estimate the mean dose of consumed test substance in units of mg/kg-d based on animal body weight and drinking water intake. However, drinking water concentrations were not analytically verified and there is some uncertainty due to the volatile nature of the test substance.	
Metric 10:	Exposure Frequency and Duration	High	All Outcomes: Rats were exposed continuously via drinking water for 90 days. This exposure duration is appropriate.	
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	All Outcomes: Male (0, 402, 1314, 3114 mg/kg-d) and female (0, 353, 1257, 2809 mg/kg-d) rats were administered 3 dose levels of the test substance via drinking water. No effects were reported in male rats, while the only effect reported in females was a slight increase in kidney weight. It is unclear if the highest dose tested was high enough to observe an adverse effect.	
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Study Citation:	Hayes, J. R., Condie Jr., L. W., Egle Jr., J. L., Borzelleca, J. F. (1987). The acute and subchronic toxicity in rats of trans-1,2-dichloroethylene in drinking water. Journal of the American College of Toxicology 6(4):471-478.			
Health Outcome(s):	Lung/Respiratory; Reproductive/Developmental;			
Reported Health Effect(s):	Lung/Respiratory: No changes in mean or relative (to body weight or brain weight) lung weights in the 90-day study.; Reproductive/Developmental: No changes in mean or relative (to body weight or brain weight) testes weights in males or ovaries weights in females, and no treatment-related histopathological changes in these organs, in the 90-day study.;			
Duration:	Subchronic (>30-91 days) 90 days			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740814			
Domain	Metric	Rating	Comments	
	Metric 12:	Exposure Route and Method	Low	All Outcomes: Animals were administered the test substance via drinking water. Studies were conducted to evaluate the stability of the test substance in water over a 4-day period, however, the stability results are not reported or described. Loss of the test substance due to instability may have been partially mitigated, as test solutions were prepared twice weekly and water bottles were changed twice weekly. However, there is uncertainty as the results of the stability studies were not provided, so its unclear if preparing test substance twice weekly was sufficient or if solutions should have been prepare more frequently (i.e., daily) or if another exposure method may have been more appropriate.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Medium	All Outcomes: The test animal species, strain, sex, and age were reported, and the test animal was obtained from a commercial source. Animal starting body weight was not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: All husbandry conditions were reported and were adequate.
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: 20 males and females were included in each exposure group.
Domain 5: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	Medium	Lung/Respiratory: The outcome assessment methodology partially addressed the intended outcomes(s) of interest. Lung weight was evaluated, however, histopathologic examinations of the lung were not conducted.; Reproductive/Developmental: The outcome assessment methodology partially addressed the intended outcomes(s) of interest (ovary and testes weight and histologic examinations of these organs were conducted in the absence of more functional measures of reproduction).
	Metric 17:	Consistency of Outcome Assessment	High	Lung/Respiratory: Details of the outcome assessment protocol were reported and outcomes were assessed consistently across study groups (e.g., at the same time after initial exposure) using the same protocol in all study groups.; Reproductive/Developmental: Details of the outcome assessment protocol were reported and outcomes were assessed consistently across study groups.
	Metric 18:	Sampling Adequacy	High	All Outcomes: Reported information indicates the study used adequate sampling for the outcome(s) of interest.
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Not necessary for this study type.
	Metric 20:	Negative Control Response	High	All Outcomes: The biological responses of the negative control group(s) were adequate.
Domain 6: Confounding / Variable Control				
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Study Citation:	Hayes, J. R., Condie Jr., L. W., Egle Jr., J. L., Borzelleca, J. F. (1987). The acute and subchronic toxicity in rats of trans-1,2-dichloroethylene in drinking water. Journal of the American College of Toxicology 6(4):471-478.			
Health Outcome(s):	Lung/Respiratory; Reproductive/Developmental;			
Reported Health Effect(s):	Lung/Respiratory: No changes in mean or relative (to body weight or brain weight) lung weights in the 90-day study.; Reproductive/Developmental: No changes in mean or relative (to body weight or brain weight) testes weights in males or ovaries weights in females, and no treatment-related histopathological changes in these organs, in the 90-day study.;			
Duration:	Subchronic (>30-91 days) 90 days			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740814			
Domain	Metric	Rating	Comments	
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	All Outcomes: Although the study did not report all information to determine confounding, reported information did not identify differences among study groups with regard to terminal body weight and water intake. Food consumption was not reported.	
	Metric 22: Health Outcomes Unrelated to Exposure	High	All Outcomes: Details regarding animal attrition and health outcomes unrelated to exposure were reported for each study group and there were no differences among groups that could influence the outcome assessment.	
	Metric 23: Data Presentation and Analysis	High	All Outcomes: Statistical methods were clearly described and were appropriate for the dataset(s).	
	Metric 24: Reporting of Data	High	Lung/Respiratory: Organ weight data were adequately reported as mean +/- SEM and is broken out by exposure group and sex.; Reproductive/Developmental: Organ weight and histopathology incidence data were adequately reported.	

Additional Comments: None

Overall Quality Determination**Medium**

Study Citation:	Hayes, J. R., Condie Jr., L. W., Egle Jr., J. L., Borzelleca, J. F. (1987). The acute and subchronic toxicity in rats of trans-1,2-dichloroethylene in drinking water. Journal of the American College of Toxicology 6(4):471-478.			
Health Outcome(s):	Neurological/Behavioral			
Reported Health Effect(s):	Neurological/Behavioral: Neurological effects (depression, ataxia, and depressed respiration) were reported in the acute oral toxicity study. No effects on mean or relative (to body weight) brain weight and no effects on general appearance or signs of intoxication (i.e., potential evidence of neurotoxicity) were reported in the 90-day study.			
Duration:	Subchronic (>30-91 days) 90 days			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740814			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	The test substance was identified as trans-1,2-dichloroethylene (CASN 156-60-5).	
	Metric 2: Test Substance Source	High	The test substance was obtained from Aldrich Chemical Company (Milwaukee, WI). Lot number 5201 J.J.	
	Metric 3: Test Substance Purity	High	Purity was reported to be 98%.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	Appropriate concurrent negative control groups were included.	
	Metric 5: Positive Controls	N/A	Not applicable for this study type.	
	Metric 6: Randomized Allocation of Animals	Medium	Study authors state that animals were randomly assigned into five treatment groups.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	High	Test substance preparation/administration and storage conditions were reported in detail and were appropriate for the test substance.	
	Metric 8: Consistency of Exposure Administration	High	Test substance was administered in drinking water, which was provided to all animals ad libitum. Drinking water intake was monitored and did not vary across treatment groups.	
	Metric 9: Reporting of Doses/Concentrations	Low	A stability study was conducted to evaluate the loss of trans 1,2 DCE from drinking water. Based on the rate of loss of the test substance, average daily drinking water concentrations were calculated, which were then used to estimate the mean dose of consumed test substance in units of mg/kg-d based on animal body weight and drinking water intake. However, drinking water concentrations were not analytically verified and there is some uncertainty due to the volatile nature of the test substance.	
	Metric 10: Exposure Frequency and Duration	High	Rats were exposed continuously via drinking water for 90 days. This exposure duration is appropriate.	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	Low	Male (0, 402, 1314, 3114 mg/kg-d) and female (0, 353, 1257, 2809 mg/kg-d) rats were administered 3 dose levels of the test substance via drinking water. No effects were reported in male rats, while the only effect reported in females was a slight increase in kidney weight. It is unclear if the highest dose tested was high enough to observe an adverse effect.	
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Study Citation:	Hayes, J. R., Condie Jr., L. W., Egle Jr., J. L., Borzelleca, J. F. (1987). The acute and subchronic toxicity in rats of trans-1,2-dichloroethylene in drinking water. Journal of the American College of Toxicology 6(4):471-478.			
Health Outcome(s):	Neurological/Behavioral			
Reported Health Effect(s):	Neurological/Behavioral: Neurological effects (depression, ataxia, and depressed respiration) were reported in the acute oral toxicity study. No effects on mean or relative (to body weight) brain weight and no effects on general appearance or signs of intoxication (i.e., potential evidence of neurotoxicity) were reported in the 90-day study.			
Duration:	Subchronic (>30-91 days) 90 days			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740814			
Domain		Metric	Rating	Comments
	Metric 12:	Exposure Route and Method	Low	Animals were administered the test substance via drinking water. Studies were conducted to evaluate the stability of the test substance in water over a 4-day period, however, the stability results are not reported or described. Loss of the test substance due to instability may have been partially mitigated, as test solutions were prepared twice weekly and water bottles were changed twice weekly. However, there is uncertainty as the results of the stability studies were not provided, so its unclear if preparing test substance twice weekly was sufficient or if solutions should have been prepare more frequently (i.e., daily) or if another exposure method may have been more appropriate.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Medium	The test animal species, strain, sex, and age were reported, and the test animal was obtained from a commercial source. Animal starting body weight was not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were reported and were adequate.
	Metric 15:	Number of Animals per Group	Medium	20 males and females were included in each exposure group.
Domain 5: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	Medium	The outcome assessment methodology partially addressed the intended outcomes(s) of interest (brain weight was recorded and animals were monitored twice daily for clinical signs, however, other measures were not included (e.g., a FOB or brain histopathology).
	Metric 17:	Consistency of Outcome Assessment	High	Details of the outcome assessment protocol were reported and outcomes were assessed consistently across study groups.
	Metric 18:	Sampling Adequacy	High	Reported information indicates the study used adequate sampling for the outcome(s) of interest.
	Metric 19:	Blinding of Assessors	N/A	Not necessary for this study type.
	Metric 20:	Negative Control Response	High	The biological responses of the negative control group(s) were adequate.
Domain 6: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Although the study did not report all information to determine confounding, reported information did not identify differences among study groups with regard to terminal body weight and water intake. Food consumption was not reported.
	Metric 22:	Health Outcomes Unrelated to Exposure	High	Details regarding animal attrition and health outcomes unrelated to exposure were reported for each study group and there were no differences among groups that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	High	Statistical methods were clearly described and were appropriate for the dataset(s).
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Study Citation:	Hayes, J. R., Condie Jr., L. W., Egle Jr., J. L., Borzelleca, J. F. (1987). The acute and subchronic toxicity in rats of trans-1,2-dichloroethylene in drinking water. Journal of the American College of Toxicology 6(4):471-478.			
Health Outcome(s):	Neurological/Behavioral			
Reported Health Effect(s):	Neurological/Behavioral: Neurological effects (depression, ataxia, and depressed respiration) were reported in the acute oral toxicity study. No effects on mean or relative (to body weight) brain weight and no effects on general appearance or signs of intoxication (i.e., potential evidence of neurotoxicity) were reported in the 90-day study.			
Duration:	Subchronic (>30-91 days) 90 days			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740814			
Domain	Metric	Rating	Comments	
Metric 24:	Reporting of Data	Medium	Organ weight data was adequately reported (i.e., mean +/- SEM) for all exposure groups by sex. Clinical observation data is not sufficiently reported. In the discussion section, study authors state that "general behavior" was not adversely effected, but no further description is provided.	

Additional Comments: None

Overall Quality Determination**Medium**

Study Citation:	Hayes, J. R., Condie Jr., L. W., Egle Jr., J. L., Borzelleca, J. F. (1987). The acute and subchronic toxicity in rats of trans-1,2-dichloroethylene in drinking water. Journal of the American College of Toxicology 6(4):471-478.			
Health Outcome(s):	Immune/Hematological			
Reported Health Effect(s):	Immune/Hematological: No adverse, treatment-related effects on hematological/immunity parameters, and no changes in absolute or relative (to body weight or brain weight) spleen or thymus weights, in the 90-day study. For hematology/immunity parameters, whole blood was examined for hemoglobin, hematocrit, erythrocytes, leukocytes, and platelets, differential leukocyte counts, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, fibrinogen, and prothrombin times.			
Duration:	Subchronic (>30-91 days) 90 days			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740814			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	The test substance was identified as trans-1,2-dichloroethylene (CASN 156-60-5).	
	Metric 2: Test Substance Source	High	The test substance was obtained from Aldrich Chemical Company (Milwaukee, WI). Lot number 5201 J.J.	
	Metric 3: Test Substance Purity	High	Purity was reported to be 98%.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	Appropriate concurrent negative control groups were included.	
	Metric 5: Positive Controls	N/A	Not applicable for this study type.	
	Metric 6: Randomized Allocation of Animals	Medium	Study authors state that animals were randomly assigned into five treatment groups.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	High	Test substance preparation/administration and storage conditions were reported in detail and were appropriate for the test substance.	
	Metric 8: Consistency of Exposure Administration	High	Test substance was administered in drinking water, which was provided to all animals ad libitum. Drinking water intake was monitored and did not vary across treatment groups.	
	Metric 9: Reporting of Doses/Concentrations	Low	A stability study was conducted to evaluate the loss of trans 1,2 DCE from drinking water. Based on the rate of loss of the test substance, average daily drinking water concentrations were calculated, which were then used to estimate the mean dose of consumed test substance in units of mg/kg-d based on animal body weight and drinking water intake. However, drinking water concentrations were not analytically verified and there is some uncertainty due to the volatile nature of the test substance.	
	Metric 10: Exposure Frequency and Duration	High	Rats were exposed continuously via drinking water for 90 days. This exposure duration is appropriate.	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	Low	Male (0, 402, 1314, 3114 mg/kg-d) and female (0, 353, 1257, 2809 mg/kg-d) rats were administered 3 dose levels of the test substance via drinking water. No effects were reported in male rats, while the only effect reported in females was a slight increase in kidney weight. It is unclear if the highest dose tested was high enough to observe an adverse effect.	
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Study Citation:	Hayes, J. R., Condie Jr., L. W., Egle Jr., J. L., Borzelleca, J. F. (1987). The acute and subchronic toxicity in rats of trans-1,2-dichloroethylene in drinking water. Journal of the American College of Toxicology 6(4):471-478.			
Health Outcome(s):	Immune/Hematological			
Reported Health Effect(s):	Immune/Hematological: No adverse, treatment-related effects on hematological/immunity parameters, and no changes in absolute or relative (to body weight or brain weight) spleen or thymus weights, in the 90-day study. For hematology/immunity parameters, whole blood was examined for hemoglobin, hematocrit, erythrocytes, leukocytes, and platelets, differential leukocyte counts, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, fibrinogen, and prothrombin times.			
Duration:	Subchronic (>30-91 days) 90 days			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740814			
Domain		Metric	Rating	Comments
	Metric 12:	Exposure Route and Method	Low	Animals were administered the test substance via drinking water. Studies were conducted to evaluate the stability of the test substance in water over a 4-day period, however, the stability results are not reported or described. Loss of the test substance due to instability may have been partially mitigated, as test solutions were prepared twice weekly and water bottles were changed twice weekly. However, there is uncertainty as the results of the stability studies were not provided, so its unclear if preparing test substance twice weekly was sufficient or if solutions should have been prepare more frequently (i.e., daily) or if another exposure method may have been more appropriate.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Medium	The test animal species, strain, sex, and age were reported, and the test animal was obtained from a commercial source. Animal starting body weight was not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were reported and were adequate.
	Metric 15:	Number of Animals per Group	Medium	20 males and females were included in each exposure group.
Domain 5: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	Medium	The outcome assessment methodology partially addressed the intended outcomes(s) of interest (hematological parameters were measured, and spleen and thymus weight were recorded, however, no histopathologic examination was conducted).
	Metric 17:	Consistency of Outcome Assessment	High	Details of the outcome assessment protocol were reported and outcomes were assessed consistently across study groups (e.g., at the same time after initial exposure) using the same protocol in all study groups.
	Metric 18:	Sampling Adequacy	High	Reported information indicates the study used adequate sampling for the outcome(s) of interest.
	Metric 19:	Blinding of Assessors	N/A	Not necessary for this study type.
	Metric 20:	Negative Control Response	Medium	There were minor uncertainties or limitations regarding the biological responses of the negative control groups (e.g., negative control data for hematological parameters was not reported, so the biological response could not be evaluated).
Domain 6: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Although the study did not report all information to determine confounding, reported information did not identify differences among study groups with regard to terminal body weight and water intake. Food consumption was not reported.
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Study Citation:	Hayes, J. R., Condie Jr., L. W., Egle Jr., J. L., Borzelleca, J. F. (1987). The acute and subchronic toxicity in rats of trans-1,2-dichloroethylene in drinking water. Journal of the American College of Toxicology 6(4):471-478.
Health Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Immune/Hematological: No adverse, treatment-related effects on hematological/immunity parameters, and no changes in absolute or relative (to body weight or brain weight) spleen or thymus weights, in the 90-day study. For hematology/immunity parameters, whole blood was examined for hemoglobin, hematocrit, erythrocytes, leukocytes, and platelets, differential leukocyte counts, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, fibrinogen, and prothrombin times.
Duration:	Subchronic (>30-91 days) 90 days
Chemical:	trans-1,2-Dichloroethylene- Parent compound
HERO ID:	1740814

Domain	Metric	Rating	Comments
	Metric 22: Health Outcomes Unrelated to Exposure	High	Details regarding animal attrition and health outcomes unrelated to exposure were reported for each study group and there were no differences among groups that could influence the outcome assessment.
	Metric 23: Data Presentation and Analysis	High	Statistical methods were clearly described and were appropriate for the dataset(s).
	Metric 24: Reporting of Data	High	Organ weight data (mean +/- SEM) was adequately reported for all treatment groups by sex. Hematology data was not reported, however, study authors clearly indicate that there were no significant effects on any parameter.

Additional Comments: None

Overall Quality Determination**Medium**

Study Citation:	Shopp, G. M., Sanders, V. M., White, K. L., Munson, A. E. (1985). Humoral and cell-mediated immune status of mice exposed to trans-1,2-dichloroethylene. Drug and Chemical Toxicology 8(5):393-407.			
Health Outcome(s):	Immune/Hematological			
Reported Health Effect(s):	Immune/Hematological: Cellular and humoral response			
Duration:	Subchronic (>30-91 days) 90 day- drinking water			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	5435222; Linked HERO ID(s): 200220, 62637, 5435222			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	Test substance was identified as trans-1,2-dichloroethylene.	
	Metric 2: Test Substance Source	High	The source of the test substance was Aldrich Chemical Co. (Milwaukee, WI). The lot number was provided. Information was obtained from the cited reference: Barnes et al. 1985 (HERO 200220).	
	Metric 3: Test Substance Purity	High	Purity of the test substance was 98%. Information was obtained from the cited reference: Barnes et al. 1985 (HERO 200220).	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	Low	Drinking water control did not contain the emulphor vehicle.	
	Metric 5: Positive Controls	N/A	Positive control was not required in this study.	
	Metric 6: Randomized Allocation of Animals	Low	The current study did not specify whether animals were randomly distributed across groups; however, the study followed methodological details reported in HERO ID 64563. This reference indicated that the study animals were randomized (method not specified).	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	High	Preparation and storage details were described in HERO ID 62637. The test substance was diluted in deionized water containing 1% emulphor. The solutions were maintained at RT and stored in amber colored bottles with stainless steel spouts fitted through the corks. The solutions were changed twice weekly. This was sufficient to prevent volatilization as less than 10% of the test substance was lost between changes.	
	Metric 8: Consistency of Exposure Administration	High	Details of exposure were reported in the cited reference and were appropriate; animals from all groups had access to water ad libitum.	
	Metric 9: Reporting of Doses/Concentrations	Medium	Doses are reported as mg/kg-day without ambiguity and were time-weighted averages based on water intake and body weights as reported in HERO 200220. HERO ID 62637 indicated that test solutions were analytically measured using gas chromatography. It was reported that "less than 10% of DCE was lost during the three or four days between bottle changes." It is unclear whether the reported doses reflect the 10% loss.	
	Metric 10: Exposure Frequency and Duration	High	Exposure frequency and duration were reported and appropriate.	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	The number of dose groups and spacing were appropriate (range of responses obtained and doses were justified).	
	Metric 12: Exposure Route and Method	High	The exposure route was appropriate. The concentration in drinking water was measured between bottle exchanges.	

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Study Citation:	Shopp, G. M., Sanders, V. M., White, K. L., Munson, A. E. (1985). Humoral and cell-mediated immune status of mice exposed to trans-1,2-dichloroethylene. Drug and Chemical Toxicology 8(5):393-407.
Health Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Immune/Hematological: Cellular and humoral response
Duration:	Subchronic (>30-91 days) 90 day- drinking water
Chemical:	trans-1,2-Dichloroethylene- Parent compound
HERO ID:	5435222; Linked HERO ID(s): 200220, 62637, 5435222

Domain	Metric	Rating	Comments
Domain 4: Test Animals			
Metric 13:	Test Animal Characteristics	Medium	Test animal characteristics were not provided in the current study; however, some animal details were reported in White et al. 1985 (HERO 64563). The test animals were obtained from Charles River Breeding Laboratories, and the animal age was specified. Starting body weights were not provided.
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Husbandry conditions were not reported in this reference, but some methodological details are provided in White et al. 1985 (HERO 64563). The reference stated that food and water were available ad libitum and acceptable room temperature, and humidity targets were used. The photoperiod was 12 hrs. The number of animals per cage was not specified.
Metric 15:	Number of Animals per Group	Low	The total number of animals exposed/group was not reported. Six different sets of animals were used for evaluating different endpoints.
Domain 5: Outcome Assessment			
Metric 16:	Outcome Assessment Methodology	High	Outcome assessment methods were described in detail in White et al. 1985 (HERO 64563), with some details also provided in HERO ID 200220. The methods were sensitive to the outcomes of interest (immune effects).
Metric 17:	Consistency of Outcome Assessment	High	Details of outcome assessment are provided in the cited reference (White et al. 1985) and were consistent across groups.
Metric 18:	Sampling Adequacy	Low	Each data table included sample sizes, reported as ranges. For some endpoints the sample sizes were small (n = 2-9)
Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary for this study.
Metric 20:	Negative Control Response	High	The negative control responses were appropriate.
Domain 6: Confounding / Variable Control			
Metric 21:	Confounding Variables in Test Design and Procedures	Medium	The study did not report all information to determine confounding; the reported information did not identify differences.
Metric 22:	Health Outcomes Unrelated to Exposure	Medium	No information was provided to either support or dismiss differences in groups in health outcomes or attrition.
Metric 23:	Data Presentation and Analysis	High	Statistical analysis was performed and was appropriate. If a one-way analysis of variance of the means showed treatment effects, the authors performed a Duncan's multiple range test. Significance was set at 0.05, and means and SE values were presented.
Metric 24:	Reporting of Data	High	Data for all endpoints were quantitatively reported as means $\pm$ SE. Statistical significance was noted. Individual animal data were not provided.

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Study Citation:	Shopp, G. M., Sanders, V. M., White, K. L., Munson, A. E. (1985). Humoral and cell-mediated immune status of mice exposed to trans-1,2-dichloroethylene. Drug and Chemical Toxicology 8(5):393-407.
Health Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Immune/Hematological: Cellular and humoral response
Duration:	Subchronic (>30-91 days) 90 day- drinking water
Chemical:	trans-1,2-Dichloroethylene- Parent compound
HERO ID:	5435222; Linked HERO ID(s): 200220, 62637, 5435222

Domain	Metric	Rating	Comments
Additional Comments:	12/23/2025: dherber@srcinc.com: Updated the following metric scores based on information in Barnes et al. 1985 (HERO 200220) and White et al. 1985 (HERO 64563): Metrics 6, 7, 9, 13, 14, and 18; in addition, text was updated in Metrics 2, 3, 8, 15, 16, 17, and 24.		

Overall Quality Determination**High**

Study Citation:	Shopp, G. M., Sanders, V. M., White, K. L., Munson, A. E. (1985). Humoral and cell-mediated immune status of mice exposed to trans-1,2-dichloroethylene. Drug and Chemical Toxicology 8(5):393-407.			
Health Outcome(s):	Nutritional/Metabolic			
Reported Health Effect(s):	Nutritional/Metabolic: Body weight			
Duration:	Subchronic (>30-91 days) 90 day- drinking water			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	5435222; Linked HERO ID(s): 200220, 62637, 5435222			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	Test substance was identified as trans-1,2-dichloroethylene.	
	Metric 2: Test Substance Source	High	The source of the test substance was Aldrich Chemical Co. (Milwaukee, WI). The lot number was provided. Information was obtained from the cited reference: Barnes et al. 1985 (HERO 200220).	
	Metric 3: Test Substance Purity	High	Purity of the test substance was 98%. Information was obtained from the cited reference: Barnes et al. 1985 (HERO 200220).	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	Low	Drinking water control did not contain the emulphor vehicle.	
	Metric 5: Positive Controls	N/A	A positive control was not required in this study.	
	Metric 6: Randomized Allocation of Animals	Low	The current study did not specify whether animals were randomly distributed across groups; however, the study followed methodological details reported in HERO ID 64563. This reference indicated that the study animals were randomized (method not specified).	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	High	Preparation and storage details were described in HERO ID 62637. The test substance was diluted in deionized water containing 1% emulphor. The solutions were maintained at RT and stored in amber colored bottles with stainless steel spouts fitted through the corks. The solutions were changed twice weekly. This was sufficient to prevent volatilization as less than 10% of the test substance was lost between changes.	
	Metric 8: Consistency of Exposure Administration	High	Details of exposure were reported and appropriate in cited reference; animals from all groups had access to water ad libitum.	
	Metric 9: Reporting of Doses/Concentrations	Medium	Doses are reported as mg/kg-day without ambiguity and were time-weighted averages based on water intake and body weights as reported in HERO 200220. HERO ID 62637 indicated that test solutions were analytically measured using gas chromatography. It was reported that "less than 10% of DCE was lost during the three or four days between bottle changes." It is unclear whether the reported dosses reflect the 10% loss.	
	Metric 10: Exposure Frequency and Duration	High	Exposure frequency and duration were reported and appropriate.	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	The number of dose groups and spacing were appropriate (range of response obtained and doses were justified).	
	Metric 12: Exposure Route and Method	High	The exposure route was appropriate. Concentration in drinking water was measured between bottle exchanges.	
Domain 4: Test Animals				
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Study Citation:	Shopp, G. M., Sanders, V. M., White, K. L., Munson, A. E. (1985). Humoral and cell-mediated immune status of mice exposed to trans-1,2-dichloroethylene. Drug and Chemical Toxicology 8(5):393-407.			
Health Outcome(s):	Nutritional/Metabolic			
Reported Health Effect(s):	Nutritional/Metabolic: Body weight			
Duration:	Subchronic (>30-91 days) 90 day- drinking water			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	5435222; Linked HERO ID(s): 200220, 62637, 5435222			
Domain	Metric	Rating	Comments	
	Metric 13: Test Animal Characteristics	Medium	Test animal characteristics were not provided in the current study; however, some animal details were reported in White et al. 1985 (HERO 64563). The test animals were obtained from Charles River Breeding Laboratories, and the animal age was specified. Starting body weights were not provided.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Medium	Husbandry conditions were not reported in this reference, but some methodological details are provided in White et al. 1985 (HERO 64563). The reference stated that food and water were available ad libitum and acceptable room temperature, and humidity targets were used. The photoperiod was 12 hrs. The number of animals per cage was not specified.	
	Metric 15: Number of Animals per Group	Low	The total number of animals exposed /group was not reported. Six different sets of animals were used for evaluating different endpoints.	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	Medium	Outcome assessment methods were described in detail in White et al. 1985 (HERO 64563), with some details also provided in HERO IDs 200220. The methods partially addressed the outcome of interest (body weight); only terminal body weights were measured.	
	Metric 17: Consistency of Outcome Assessment	High	Details of outcome assessment are provided in the cited reference (White et al. 1985) and were consistent across groups.	
	Metric 18: Sampling Adequacy	High	The sample size was adequate. Terminal body weights were reported for 7-9 animals/group, which is sufficient.	
	Metric 19: Blinding of Assessors	N/A	Blinding was not necessary for this study.	
	Metric 20: Negative Control Response	High	The negative control response was appropriate.	
Domain 6: Confounding / Variable Control				
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	The study did not report all information to determine confounding; the reported information did not identify differences.	
	Metric 22: Health Outcomes Unrelated to Exposure	Medium	No information was provided to either support or dismiss differences in groups in health outcomes or attrition.	
	Metric 23: Data Presentation and Analysis	High	Statistical analysis was performed and was appropriate. If a one-way analysis of variance of the means showed treatment effects, the authors performed a Duncan’s multiple range test. Significance was set at 0.05 and means and SE values were presented.	
	Metric 24: Reporting of Data	High	Data for all endpoints were quantitatively reported as means ± SE. Statistical significance was noted. Individual animal data were not provided.	
Additional Comments:	12/23/2025: dherber@srcinc.com: Updated the following metric scores based on information in Barnes et al. 1985 (HERO 200220) and White et al. 1985 (HERO 64563): Metric 6, 7, 9, 13, 14, and 18; in addition, text was updated in Metric 2, 3, 8, 15, 16, 17, and 24.			

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Study Citation:	Shopp, G. M., Sanders, V. M., White, K. L., Munson, A. E. (1985). Humoral and cell-mediated immune status of mice exposed to trans-1,2-dichloroethylene. Drug and Chemical Toxicology 8(5):393-407.
Health Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Nutritional/Metabolic: Body weight
Duration:	Subchronic (>30-91 days) 90 day- drinking water
Chemical:	trans-1,2-Dichloroethylene- Parent compound
HERO ID:	5435222; Linked HERO ID(s): 200220, 62637, 5435222

Domain	Metric	Rating	Comments
Overall Quality Determination		High	

Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.			
Health Outcome(s):	Lung/Respiratory			
Reported Health Effect(s):	Lung/Respiratory: Lungs: gross pathology (acute oral and i.p studies); histopathology (inhalation – all durations)			
Duration:	Chronic (>91 days) 8 hrs/day, 5 days/wk, for 16 weeks			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740886			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	The test substance was identified by a definitive name, trans-1,2-dichloroethylene.	
	Metric 2: Test Substance Source	Low	The test substance was obtained from a commercial source (Merck). A batch or lot number was not reported, so this metric is rated Low.	
	Metric 3: Test Substance Purity	Low	Purity or grade of the test substance was not reported.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	It was specified that control animals were treated identically to the treated animals except that no test substance was added to the air (sham-exposed). This was also apparent from Table III, which showed controls for every exposure paradigm.	
	Metric 5: Positive Controls	N/A	No positive controls are required for this study type.	
	Metric 6: Randomized Allocation of Animals	Low	The method of allocation of test animals was not reported.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Medium	Test substance preparation and generation of the vapor for inhalation exposures were reported with adequate detail. Test substance storage was not reported; therefore, this metric is rated as Medium.	
	Metric 8: Consistency of Exposure Administration	High	Exposures occurred daily between 8 am-4pm.	
	Metric 9: Reporting of Doses/Concentrations	Medium	Target concentrations were reported without ambiguity. Analytical concentrations (gas chromatography) were not specified but were reported to be within 3% of target concentrations. Therefore, the lack of reporting analytical concentrations is not expected to have substantially impacted results.	
	Metric 10: Exposure Frequency and Duration	Medium	Inhalation exposures were administered for 8 hours per day, which differs from the typical 6 hours per day. However, this difference is not expected to have substantially impacted results.	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	Only a single concentration is tested. However, the aim of the study was to evaluate the effects of this concentration (200 ppm, the TLV/MAC in many countries at the time of the study) across multiple timepoints, rather than multiple concentrations at one time-point. Therefore, this is not considered to have significantly impacted results or to have significantly hampered conclusions.	
	Metric 12: Exposure Route and Method	Medium	The route and exposure method were suited to the test substance. Air changes/hour was specified to be > 10. Whole-body exposure chambers were utilized. The test substance may condense at the higher concentrations tested for the acute exposures.	
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Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.			
Health Outcome(s):	Lung/Respiratory			
Reported Health Effect(s):	Lung/Respiratory: Lungs: gross pathology (acute oral and i.p studies); histopathology (inhalation – all durations)			
Duration:	Chronic (>91 days) 8 hrs/day, 5 days/wk, for 16 weeks			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740886			
Domain	Metric	Rating	Comments	
Domain 4: Test Animals				
Metric 13:	Test Animal Characteristics	High	Test animal species, strain, sex, and starting body weight were reported. The age of the test animals was specified to be "mature." The test animals were obtained from a commercial source and were appropriate for the study type.	
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Most husbandry conditions were reported. Light-dark cycle was not reported.	
Metric 15:	Number of Animals per Group	Low	6 animals/group (female only) were utilized for all treatment and control groups. This is lower than typical for chronic study but was sufficient to conduct statistical analysis.	
Domain 5: Outcome Assessment				
Metric 16:	Outcome Assessment Methodology	High	Histopathology was considered to be adequate to assess the outcome of interest. Organ weights were not measured.	
Metric 17:	Consistency of Outcome Assessment	High	Outcomes appeared to be assessed consistently across study groups. A protocol for histopathology was provided.	
Metric 18:	Sampling Adequacy	High	All 6 animals/group appear to have been sampled for histopathology based on Table III.	
Metric 19:	Blinding of Assessors	N/A	Blinding is not required for initial histopathology.	
Metric 20:	Negative Control Response	High	The negative control response was appropriate	
Domain 6: Confounding / Variable Control				
Metric 21:	Confounding Variables in Test Design and Procedures	High	No confounding variables were reported or identified.	
Metric 22:	Health Outcomes Unrelated to Exposure	High	No effects unrelated to exposure were reported or identified.	
Metric 23:	Data Presentation and Analysis	High	Statistical analysis was not performed, but sufficient data were provided to allow for independent analysis.	
Metric 24:	Reporting of Data	High	Data were adequately reported as incidences including level of severity.	
Additional Comments:	None			
Overall Quality Determination		High		

Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.			
Health Outcome(s):	Musculoskeletal			
Reported Health Effect(s):	Musculoskeletal: Histopathology (quadriceps muscle; inhalation, all durations)			
Duration:	Chronic (>91 days) 8 hrs/day, 5 days/wk, for 16 weeks			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740886			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	The test substance was identified by a definitive name, trans-1,2-dichloroethylene.	
	Metric 2: Test Substance Source	Low	The test substance was obtained from a commercial source (Merck). A batch or lot number was not reported, so this metric is rated Low.	
	Metric 3: Test Substance Purity	Low	Purity or grade of the test substance was not reported.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	It was specified that control animals were treated identically to the treated animals except that no test substance was added to the air (sham-exposed). This was also apparent from Table III, which showed controls for every exposure paradigm.	
	Metric 5: Positive Controls	N/A	No positive controls are required for this study type.	
	Metric 6: Randomized Allocation of Animals	Low	The method of allocation of test animals was not reported.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Medium	Test substance preparation and generation of the vapor for inhalation exposures were reported with adequate detail. Test substance storage was not reported; therefore, this metric is rated as Medium.	
	Metric 8: Consistency of Exposure Administration	High	Exposures occurred daily between 8 am-4pm.	
	Metric 9: Reporting of Doses/Concentrations	Medium	Target concentrations were reported without ambiguity. Analytical concentrations (gas chromatography) were not specified but were reported to be within 3% of target concentrations. Therefore, the lack of reporting analytical concentrations is not expected to have substantially impacted results.	
	Metric 10: Exposure Frequency and Duration	Medium	Inhalation exposures were administered for 8 hours per day, which differs from the typical 6 hours per day. However, this difference is not expected to have substantially impacted results.	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	Only a single concentration is tested. However, the aim of the study was to evaluate the effects of this concentration (200 ppm, the TLV/MAC in many countries at the time of the study) across multiple timepoints, rather than multiple concentrations at one time-point. Therefore, this is not considered to have significantly impacted results or to have significantly hampered conclusions.	
	Metric 12: Exposure Route and Method	Medium	The route and exposure method were suited to the test substance. Air changes/hour was specified to be > 10. Whole-body exposure chambers were utilized. The test substance may condense at the higher concentrations tested for the acute exposures.	
Domain 4: Test Animals				
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Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.			
Health Outcome(s):	Musculoskeletal			
Reported Health Effect(s):	Musculoskeletal: Histopathology (quadriceps muscle; inhalation, all durations)			
Duration:	Chronic (>91 days) 8 hrs/day, 5 days/wk, for 16 weeks			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740886			
Domain	Metric	Rating	Comments	
	Metric 13: Test Animal Characteristics	High	Test animal species, strain, sex, and starting body weight were reported. The age of the test animals was specified to be "mature." The test animals were obtained from a commercial source and were appropriate for the study type.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Medium	Most husbandry conditions were reported. Light-dark cycle was not reported.	
	Metric 15: Number of Animals per Group	Low	6 animals/group (female only) were utilized for all treatment and control groups. This is lower than typical for chronic study but was sufficient to conduct statistical analysis.	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	High	Histopathology was considered to be adequate to assess the outcome of interest. Organ weights were not measured.	
	Metric 17: Consistency of Outcome Assessment	High	Outcomes appeared to be assessed consistently across study groups. A protocol for histopathology was provided.	
	Metric 18: Sampling Adequacy	High	All 6 animals/group appear to have been sampled for histopathology based on Table III. Table III reports histopathology results for the lung and liver, but it is assumed that histopathology for all organs specified was carried out on these animals.	
	Metric 19: Blinding of Assessors	N/A	Blinding is not required for initial histopathology.	
	Metric 20: Negative Control Response	Low	Only data for organs with evidence of lesions were reported.	
Domain 6: Confounding / Variable Control				
	Metric 21: Confounding Variables in Test Design and Procedures	High	No confounding variables were reported or identified.	
	Metric 22: Health Outcomes Unrelated to Exposure	High	No effects unrelated to exposure were reported or identified.	
	Metric 23: Data Presentation and Analysis	N/A	Statistical analysis was not necessary given the supposed negative findings.	
	Metric 24: Reporting of Data	High	Negative results were qualitatively reported.	
Additional Comments: None				
Overall Quality Determination		High		

Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.			
Health Outcome(s):	Cardiovascular			
Reported Health Effect(s):	Cardiovascular: Heart (gross pathology in acute oral and i.p studies); histopathology (inhalation – acute)			
Duration:	Chronic (>91 days) 8 hrs/day, 5 days/wk, for 16 weeks			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740886			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	The test substance was identified by a definitive name, trans-1,2-dichloroethylene.	
	Metric 2: Test Substance Source	Low	The test substance was obtained from a commercial source (Merck). A batch or lot number was not reported, so this metric is rated Low.	
	Metric 3: Test Substance Purity	Low	Purity or grade of the test substance was not reported.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	It was specified that control animals were treated identically to the treated animals except that no test substance was added to the air (sham-exposed). This was also apparent from Table III, which showed controls for every exposure paradigm.	
	Metric 5: Positive Controls	N/A	No positive controls are required for this study type.	
	Metric 6: Randomized Allocation of Animals	Low	The method of allocation of test animals was not reported.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Medium	Test substance preparation and generation of the vapor for inhalation exposures were reported with adequate detail. Test substance storage was not reported; therefore, this metric is rated as Medium.	
	Metric 8: Consistency of Exposure Administration	High	Exposures occurred daily between 8 am-4pm.	
	Metric 9: Reporting of Doses/Concentrations	Medium	Target concentrations were reported without ambiguity. Analytical concentrations (gas chromatography) were not specified but were reported to be within 3% of target concentrations. Therefore, the lack of reporting analytical concentrations is not expected to have substantially impacted results.	
	Metric 10: Exposure Frequency and Duration	Medium	Inhalation exposures were administered for 8 hours per day, which differs from the typical 6 hours per day. However, this difference is not expected to have substantially impacted results.	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	Only a single concentration is tested. However, the aim of the study was to evaluate the effects of this concentration (200 ppm, the TLV/MAC in many countries at the time of the study) across multiple timepoints, rather than multiple concentrations at one time-point. Therefore, this is not considered to have significantly impacted results or to have significantly hampered conclusions.	
	Metric 12: Exposure Route and Method	Medium	The route and exposure method were suited to the test substance. Air changes/hour was specified to be > 10. Whole-body exposure chambers were utilized. The test substance may condense at the higher concentrations tested for the acute exposures.	
Domain 4: Test Animals				
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Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.			
Health Outcome(s):	Cardiovascular			
Reported Health Effect(s):	Cardiovascular: Heart (gross pathology in acute oral and i.p studies); histopathology (inhalation – acute)			
Duration:	Chronic (>91 days) 8 hrs/day, 5 days/wk, for 16 weeks			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740886			
Domain	Metric	Rating	Comments	
	Metric 13: Test Animal Characteristics	High	Test animal species, strain, sex, and starting body weight were reported. The age of the test animals was specified to be "mature." The test animals were obtained from a commercial source and were appropriate for the study type.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Medium	Most husbandry conditions were reported. Light-dark cycle was not reported.	
	Metric 15: Number of Animals per Group	Low	6 animals/group (female only) were utilized for all treatment and control groups. This is lower than typical for chronic study but was sufficient to conduct statistical analysis.	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	High	Histopathology was considered to be adequate to assess the outcome of interest. Organ weights were not measured.	
	Metric 17: Consistency of Outcome Assessment	High	Outcomes appeared to be assessed consistently across study groups. A protocol for histopathology was provided.	
	Metric 18: Sampling Adequacy	High	All 6 animals/group appear to have been sampled for histopathology based on Table III. Table III reports histopathology results for the lung and liver, but it is assumed that histopathology for all organs specified was carried out on these animals.	
	Metric 19: Blinding of Assessors	N/A	Blinding is not required for initial histopathology.	
	Metric 20: Negative Control Response	Low	Only data for organs with evidence of lesions were reported.	
Domain 6: Confounding / Variable Control				
	Metric 21: Confounding Variables in Test Design and Procedures	High	No confounding variables were reported or identified.	
	Metric 22: Health Outcomes Unrelated to Exposure	High	No effects unrelated to exposure were reported or identified.	
	Metric 23: Data Presentation and Analysis	N/A	Statistical analysis was not necessary given the supposed negative findings.	
	Metric 24: Reporting of Data	Uninformative	Heart histopathology data were only reported for the 3000 ppm acute inhalation exposure and corresponding control. Negative findings were not described qualitatively; therefore, the results for this outcome for this exposure duration were not reported.	

Additional Comments: None

Overall Quality Determination**Uninformative**

Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.			
Health Outcome(s):	Immune/Hematological; Hepatic/Liver; Renal/Kidney;			
Reported Health Effect(s):	Immune/Hematological: Histopathology (spleen; inhalation – all durations; no effects); hematology (WBC count, RBC count, Hgb, packed cell volume, MCV, MCH, MCHC; inhalation studies – acute duration); Hepatic/Liver: Gross pathology of the liver (acute oral and i.p studies); histopathology of the liver (inhalation – all durations); serum chemistry (cholesterol, bilirubin, total protein, alkaline phosphatase, GOT, GPT, albumin, glucose; in inhalation acute studies and possibly 16-week duration); bile accumulation (acute inhalation); Renal/Kidney: Gross pathology of the kidney and bladder and hematuria (acute oral and i.p studies); histopathology (inhalation – all durations; no effects); serum chemistry (electrolytes, BUN, uric acid – inhalation acute durations);			
Duration:	Chronic (>91 days) 8 hrs/day, 5 days/wk, for 16 weeks			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740886			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
Metric 1:	Test Substance Identity	High	All Outcomes: The test substance was identified by a definitive name, trans-1,2-dichloroethylene.	
Metric 2:	Test Substance Source	Low	All Outcomes: The test substance was obtained from a commercial source (Merck). A batch or lot number was not reported, so this metric is rated Low.	
Metric 3:	Test Substance Purity	Low	All Outcomes: Purity or grade of the test substance was not reported.	
Domain 2: Test Design				
Metric 4:	Negative and Vehicle Controls	High	All Outcomes: It was specified that control animals were treated identically to the treated animals except that no test substance was added to the air (sham-exposed). This was also apparent from Table III, which showed controls for every exposure paradigm.	
Metric 5:	Positive Controls	N/A	All Outcomes: No positive controls are required for this study type.	
Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: The method of allocation of test animals was not reported.	
Domain 3: Exposure Characterization				
Metric 7:	Preparation and Storage of Test Substance	Medium	All Outcomes: Test substance preparation and generation of the vapor for inhalation exposures were reported with adequate detail. Test substance storage was not reported; therefore, this metric is rated as Medium.	
Metric 8:	Consistency of Exposure Administration	High	All Outcomes: Exposures occurred daily between 8 am-4pm.	
Metric 9:	Reporting of Doses/Concentrations	Medium	All Outcomes: Target concentrations were reported without ambiguity. Analytical concentrations (gas chromatography) were not specified but were reported to be within 3% of target concentrations. Therefore, the lack of reporting analytical concentrations is not expected to have substantially impacted results.	
Metric 10:	Exposure Frequency and Duration	Medium	All Outcomes: Inhalation exposures were administered for 8 hours per day, which differs from the typical 6 hours per day. However, this difference is not expected to have substantially impacted results.	
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: Only a single concentration is tested. However, the aim of the study was to evaluate the effects of this concentration (200 ppm, the TLV/MAC in many countries at the time of the study) across multiple timepoints, rather than multiple concentrations at one timepoint. Therefore, this is not considered to have significantly impacted results or to have significantly hampered conclusions.	
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Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.			
Health Outcome(s):	Immune/Hematological; Hepatic/Liver; Renal/Kidney;			
Reported Health Effect(s):	Immune/Hematological: Histopathology (spleen; inhalation – all durations; no effects); hematology (WBC count, RBC count, Hgb, packed cell volume, MCV, MCH, MCHC; inhalation studies – acute duration); Hepatic/Liver: Gross pathology of the liver (acute oral and i.p studies); histopathology of the liver (inhalation – all durations); serum chemistry (cholesterol, bilirubin, total protein, alkaline phosphatase, GOT, GPT, albumin, glucose; in inhalation acute studies and possibly 16-week duration); bile accumulation (acute inhalation); Renal/Kidney: Gross pathology of the kidney and bladder and hematuria (acute oral and i.p studies); histopathology (inhalation – all durations; no effects); serum chemistry (electrolytes, BUN, uric acid – inhalation acute durations);			
Duration:	Chronic (>91 days) 8 hrs/day, 5 days/wk, for 16 weeks			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740886			
Domain	Metric	Rating	Comments	
	Metric 12: Exposure Route and Method	Medium	All Outcomes: The route and exposure method were suited to the test substance. Air changes/hour was specified to be > 10. Whole-body exposure chambers were utilized. The test substance may condense at the higher concentrations tested for the acute exposures.	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	High	All Outcomes: Test animal species, strain, sex, and starting body weight were reported. The age of the test animals was specified to be "mature." The test animals were obtained from a commercial source and were appropriate for the study type.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Medium	All Outcomes: Most husbandry conditions were reported. Light-dark cycle was not reported.	
	Metric 15: Number of Animals per Group	Low	All Outcomes: 6 animals/group (female only) were utilized for all treatment and control groups. This is lower than typical for chronic study but was sufficient to conduct statistical analysis.	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	Medium	Immune/Hematological: Histopathology was considered to be adequate to assess the outcome of interest; however, hematology and organ weights were not measured and these endpoints are typically included in repeat dose experiments.; Hepatic/Liver: Histopathology was considered to be adequate to assess the outcome of interest. It is unclear whether clinical chemistry was assessed at this duration. A table footnote reports a result for one endpoint (GPT). Organ weights were not measured. Clinical chemistry and organ weights are endpoints are typically included in repeat dose experiments.; Renal/Kidney: Histopathology was considered to be adequate to assess the outcome of interest; however, clinical chemistry and organ weights were not measured and these endpoints are typically included in repeat dose experiments.	
	Metric 17: Consistency of Outcome Assessment	High	All Outcomes: Outcomes appeared to be assessed consistently across study groups. A protocol for histopathology was provided.	
	Metric 18: Sampling Adequacy	High	All Outcomes: All 6 animals/group appear to have been sampled for histopathology based on Table III.	
	Metric 19: Blinding of Assessors	N/A	All Outcomes: Blinding is not required for initial histopathology.	
	Metric 20: Negative Control Response	High	All Outcomes: The negative control response was appropriate	
Domain 6: Confounding / Variable Control				
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Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.			
Health Outcome(s):	Immune/Hematological; Hepatic/Liver; Renal/Kidney;			
Reported Health Effect(s):	Immune/Hematological: Histopathology (spleen; inhalation – all durations; no effects); hematology (WBC count, RBC count, Hgb, packed cell volume, MCV, MCH, MCHC; inhalation studies – acute duration); Hepatic/Liver: Gross pathology of the liver (acute oral and i.p studies); histopathology of the liver (inhalation – all durations); serum chemistry (cholesterol, bilirubin, total protein, alkaline phosphatase, GOT, GPT, albumin, glucose; in inhalation acute studies and possibly 16-week duration); bile accumulation (acute inhalation); Renal/Kidney: Gross pathology of the kidney and bladder and hematuria (acute oral and i.p studies); histopathology (inhalation – all durations; no effects); serum chemistry (electrolytes, BUN, uric acid – inhalation acute durations);			
Duration:	Chronic (>91 days) 8 hrs/day, 5 days/wk, for 16 weeks			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740886			
Domain	Metric	Rating	Comments	
	Metric 21: Confounding Variables in Test Design and Procedures	High	All Outcomes: No confounding variables were reported or identified.	
	Metric 22: Health Outcomes Unrelated to Exposure	High	All Outcomes: No effects unrelated to exposure were reported or identified.	
	Metric 23: Data Presentation and Analysis	High	All Outcomes: Statistical analysis was not performed, but sufficient data were provided to allow for independent analysis.	
	Metric 24: Reporting of Data	High	All Outcomes: Data were adequately reported as incidences including level of severity.	
Additional Comments:	None			
Overall Quality Determination		High		

Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.			
Health Outcome(s):	Neurological/Behavioral			
Reported Health Effect(s):	Neurological/Behavioral: Neurological/behavioral clinical signs (acute oral and ip and inhalation – all durations); histopathology brain and peripheral nerves (inhalation – all durations, no effects)			
Duration:	Chronic (>91 days) 8 hrs/day, 5 days/wk, for 16 weeks			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740886			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	The test substance was identified by a definitive name, trans-1,2-dichloroethylene.	
	Metric 2: Test Substance Source	Low	The test substance was obtained from a commercial source (Merck). A batch or lot number was not reported, so this metric is rated Low.	
	Metric 3: Test Substance Purity	Low	Purity or grade of the test substance was not reported.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	It was specified that control animals were treated identically to the treated animals except that no test substance was added to the air (sham-exposed). This was also apparent from Table III, which showed controls for every exposure paradigm.	
	Metric 5: Positive Controls	N/A	No positive controls are required for this study type.	
	Metric 6: Randomized Allocation of Animals	Low	The method of allocation of test animals was not reported.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Medium	Test substance preparation and generation of the vapor for inhalation exposures were reported with adequate detail. Test substance storage was not reported; therefore, this metric is rated as Medium.	
	Metric 8: Consistency of Exposure Administration	High	Exposures consistently occurred from 8:00 am to 4:00 pm.	
	Metric 9: Reporting of Doses/Concentrations	Medium	Target concentrations were reported without ambiguity. Analytical concentrations (gas chromatography) were not specified but were reported to be within 3% of target concentrations. Therefore, the lack of reporting analytical concentrations is not expected to have substantially impacted results.	
	Metric 10: Exposure Frequency and Duration	Medium	Inhalation exposures were administered for 8 hours per day, which differs from the typical 6 hours per day. However, this difference is not expected to have substantially impacted results.	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	Only a single concentration is tested. However, the aim of the study was to evaluate the effects of this concentration (200 ppm, the TLV/MAC in many countries at the time of the study) across multiple timepoints, rather than multiple concentrations at one time-point. Therefore, this is not considered to have significantly impacted results or to have significantly hampered conclusions.	
	Metric 12: Exposure Route and Method	Medium	The route and exposure method were suited to the test substance. Air changes/hour was specified to be > 10. Whole-body exposure chambers were utilized. The test substance may condense at the higher concentrations tested for the acute exposures.	
Domain 4: Test Animals				
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Study Citation:	Freundt, K. J., Leibaldt, G. P., Lieberwirth, E. (1977). Toxicity studies on trans-1,2-dichloroethylene. Toxicology 7(2):141-153.			
Health Outcome(s):	Neurological/Behavioral			
Reported Health Effect(s):	Neurological/Behavioral: Neurological/behavioral clinical signs (acute oral and ip and inhalation – all durations); histopathology brain and peripheral nerves (inhalation – all durations, no effects)			
Duration:	Chronic (>91 days) 8 hrs/day, 5 days/wk, for 16 weeks			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1740886			
Domain	Metric	Rating	Comments	
	Metric 13: Test Animal Characteristics	High	Test animal species, strain, sex, and starting body weight were reported. The age of the test animals was specified to be "mature." The test animals were obtained from a commercial source and were appropriate for the study type.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Medium	Most husbandry conditions were reported. Light-dark cycle was not reported.	
	Metric 15: Number of Animals per Group	Low	6 animals/group (female only) were utilized for all treatment and control groups. This is lower than typical for a chronic study but was sufficient to conduct statistical analysis.	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	Medium	Histopathology (brain, sciatic nerve) and clinical signs were considered to be adequate to assess the outcome of interest. The study authors were specifically interested in acute neurotoxicity (CNS depression), which was the basis of the TLV-MAC (200 ppm) that was the focus of the study. This would be appropriately addressed by noting clinical signs of toxicity during exposure administration. A protocol for animal observations (frequency/duration) was not provided. Organ weights were not assessed.	
	Metric 17: Consistency of Outcome Assessment	Medium	Outcomes appeared to be assessed consistently across study groups. A protocol for histopathology was provided, but not for clinical observations.	
	Metric 18: Sampling Adequacy	High	It is unclear whether all 6 animals/group were sampled for clinical signs. All 6 animals/group appear to have been sampled for histopathology based on Table III. Table III reports histopathology results for the lung and liver, but it is assumed that histopathology for all organs specified was carried out on these animals.	
	Metric 19: Blinding of Assessors	N/A	Blinding is not required for initial histopathology. Blinding was not specified for clinical observations.	
	Metric 20: Negative Control Response	High	Negative controls responded appropriately.	
Domain 6: Confounding / Variable Control				
	Metric 21: Confounding Variables in Test Design and Procedures	High	No confounding variables were reported or identified.	
	Metric 22: Health Outcomes Unrelated to Exposure	High	No effects unrelated to exposure were reported or identified.	
	Metric 23: Data Presentation and Analysis	N/A	Statistical analysis was not necessary given the negative findings (qualitatively described).	
	Metric 24: Reporting of Data	High	Negative data were qualitatively described.	
Additional Comments:	None			

Overall Quality Determination**High**

Study Citation:	Ress, N. B. (2002). NTP technical report on the toxicity studies of trans-1,2-dichloroethylene (CAS No. 156-60-5) administered in microcapsules in feed to F344/N rats and B6C3F1 mice. Toxicity Report Series, vol. 55 55:112 pp.			
Health Outcome(s):	Mortality			
Reported Health Effect(s):	Mortality: Survival			
Duration:	Chronic (>91 days) 14-weeks (rats)			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1739657			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1:	Test Substance Identity	High	The test substance was identified definitively by name, CASRN, structure, molecular formula, molecular weight, and several synonyms.
	Metric 2:	Test Substance Source	High	The test substance was obtained from a commercial source and the lot number was reported.
	Metric 3:	Test Substance Purity	High	The purity was confirmed to be approximately 99% via GC.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	Both an untreated and vehicle (empty microcapsules in diet) negative control groups were included in the study.
	Metric 5:	Positive Controls	N/A	Positive controls are not required for the study type.
	Metric 6:	Randomized Allocation of Animals	Medium	It was reported that animals were distributed randomly into groups of approximately equal initial mean body weights.
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and Storage of Test Substance	High	Test substance preparation in microcapsules made from corn starch and sucrose was well described and appropriate for the test substance.
	Metric 8:	Consistency of Exposure Administration	High	The test substance was administered consistently across treatment groups in diet.
	Metric 9:	Reporting of Doses/Concentrations	High	Concentrations in food and resultant doses for each treatment group were reported without ambiguity.
	Metric 10:	Exposure Frequency and Duration	High	Animals were exposed continuously in feed, which is appropriate for a dietary study.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The highest dose was chosen based on EPA guidance that substitutions of >5% in the feed interferes with nutrition; therefore, the highest concentration in pilot studies was set at 5% (50,000 ppm). Based on no overt toxicity was observed at this concentration in pilot studies, this was chosen as the highest concentration in the 14-week study. Dose spacing (2-fold) was appropriate.
	Metric 12:	Exposure Route and Method	High	Although the test substance is volatile and was administered via the diet, volatility was controlled for by administering the test substance via microcapsules mixed with the feed. Thorough analyses were conducted to assess stability over time and with exposure to open air and light to ensure animals received the intended concentrations.
Domain 4: Test Animals				
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Study Citation:	Ress, N. B. (2002). NTP technical report on the toxicity studies of trans-1,2-dichloroethylene (CAS No. 156-60-5) administered in microcapsules in feed to F344/N rats and B6C3F1 mice. Toxicity Report Series, vol. 55 55:112 pp.
Health Outcome(s):	Mortality
Reported Health Effect(s):	Mortality: Survival
Duration:	Chronic (>91 days) 14-weeks (rats)
Chemical:	trans-1,2-Dichloroethylene- Parent compound
HERO ID:	1739657

Domain	Metric	Rating	Comments
	Metric 13: Test Animal Characteristics	High	Test animal species, strains, sex, age, and starting body weights were reported and the test animals were obtained from a commercial source and appropriate for the study design.
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were reported. Male mice were housed individually rather than 5/cage, as was done for rats and female mice. It is assumed but was not specifically stated that this is due to infighting and animal wellbeing issues for a long-term study. Because the individual housing was instituted for male mice of both the control and treatment groups, this is not considered to be a deficiency for this metric and therefore a rating of High is selected.
	Metric 15: Number of Animals per Group	Medium	10/sex/species/group is considered appropriate for the study type and duration.
Domain 5: Outcome Assessment			
	Metric 16: Outcome Assessment Methodology	High	All animals were monitored for mortality throughout the study period.
	Metric 17: Consistency of Outcome Assessment	High	Outcomes were assessed consistently across study groups at the same time and using the same protocol (animals were observed twice daily).
	Metric 18: Sampling Adequacy	High	All animals/sex/species/group were assessed for mortality.
	Metric 19: Blinding of Assessors	N/A	No subjective outcomes were assessed.
	Metric 20: Negative Control Response	High	Negative control responses were appropriate.
Domain 6: Confounding / Variable Control			
	Metric 21: Confounding Variables in Test Design and Procedures	High	No confounding variables that could impact assessment were identified. Food consumption was reported for each treatment group and did not differ significantly between groups or in a dose-dependent manner.
	Metric 22: Health Outcomes Unrelated to Exposure	High	The authors specifically reported testing 5 male and 5 female rats and mice (randomly chosen) received from the supplier for parasites or signs of disease. None were found.
	Metric 23: Data Presentation and Analysis	N/A	Statistical methods were not required because no animals died.
	Metric 24: Reporting of Data	High	Mortality incidences were adequately reported for each sex, and group.

Additional Comments: None

Overall Quality Determination**High**

Study Citation:	Ress, N. B. (2002). NTP technical report on the toxicity studies of trans-1,2-dichloroethylene (CAS No. 156-60-5) administered in microcapsules in feed to F344/N rats and B6C3F1 mice. Toxicity Report Series, vol. 55 55:112 pp.			
Health Outcome(s):	Mortality			
Reported Health Effect(s):	Mortality: Survival			
Duration:	Chronic (>91 days) 14-weeks (mice)			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1739657			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1:	Test Substance Identity	High	The test substance was identified definitively by name, CASRN, structure, molecular formula, molecular weight, and several synonyms.
	Metric 2:	Test Substance Source	High	The test substance was obtained from a commercial source and the lot number was reported.
	Metric 3:	Test Substance Purity	High	The purity was confirmed to be approximately 99% via GC.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	Both an untreated and vehicle (empty microcapsules in diet) negative control groups were included in the study.
	Metric 5:	Positive Controls	N/A	Positive controls are not required for the study type.
	Metric 6:	Randomized Allocation of Animals	Medium	It was reported that animals were distributed randomly into groups of approximately equal initial mean body weights.
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and Storage of Test Substance	High	Test substance preparation in microcapsules made from corn starch and sucrose was well described and appropriate for the test substance.
	Metric 8:	Consistency of Exposure Administration	High	The test substance was administered consistently across treatment groups in diet.
	Metric 9:	Reporting of Doses/Concentrations	High	Concentrations in food and resultant doses for each treatment group were reported without ambiguity.
	Metric 10:	Exposure Frequency and Duration	High	Animals were exposed continuously in feed, which is appropriate for a dietary study.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The highest dose was chosen based on EPA guidance that substitutions of >5% in the feed interferes with nutrition; therefore, the highest concentration in pilot studies was set at 5% (50,000 ppm). Based on no overt toxicity was observed at this concentration in pilot studies, this was chosen as the highest concentration in the 14-week study. Dose spacing (2-fold) was appropriate.
	Metric 12:	Exposure Route and Method	High	Although the test substance is volatile and was administered via the diet, volatility was controlled for by administering the test substance via microcapsules mixed with the feed. Thorough analyses were conducted to assess stability over time and with exposure to open air and light to ensure animals received the intended concentrations.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	High	Test animal species, strains, sex, age, and starting body weights were reported and the test animals were obtained from a commercial source and appropriate for the study design.
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Study Citation:	Ress, N. B. (2002). NTP technical report on the toxicity studies of trans-1,2-dichloroethylene (CAS No. 156-60-5) administered in microcapsules in feed to F344/N rats and B6C3F1 mice. Toxicity Report Series, vol. 55 55:112 pp.			
Health Outcome(s):	Mortality			
Reported Health Effect(s):	Mortality: Survival			
Duration:	Chronic (>91 days) 14-weeks (mice)			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1739657			
Domain	Metric	Rating	Comments	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were reported. Male mice were housed individually rather than 5/cage, as was done for rats and female mice. It is assumed but was not specifically stated that this is due to infighting and animal wellbeing issues for a long-term study. Because the individual housing was instituted for male mice of both the control and treatment groups, this is not considered to be a deficiency for this metric and therefore a rating of High is selected.	
	Metric 15: Number of Animals per Group	Medium	10/sex/species/group is considered appropriate for the study type and duration.	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	High	All animals were monitored for mortality throughout the study period.	
	Metric 17: Consistency of Outcome Assessment	High	Outcomes were assessed consistently across study groups at the same time and using the same protocol (animals were observed twice daily).	
	Metric 18: Sampling Adequacy	High	All animals/sex/species/group were assessed for mortality.	
	Metric 19: Blinding of Assessors	N/A	No subjective outcomes were assessed.	
	Metric 20: Negative Control Response	High	Negative control responses were appropriate.	
Domain 6: Confounding / Variable Control				
	Metric 21: Confounding Variables in Test Design and Procedures	High	No confounding variables that could impact assessment were identified. Food consumption was reported for each treatment group and did not differ significantly between groups or in a dose-dependent manner.	
	Metric 22: Health Outcomes Unrelated to Exposure	Medium	Four animals from different groups died due to unspecified accidental deaths. Since the deaths did not all occur in a single group, this did not have a significant impact on the study results. The authors specifically reported testing 5 male and 5 female rats and mice (randomly chosen) received from the supplier for parasites or signs of disease. None were found.	
	Metric 23: Data Presentation and Analysis	N/A	Statistical methods were not required because the few deaths that occurred were accidental.	
	Metric 24: Reporting of Data	Medium	Mortality incidences were adequately reported for each sex and group. Although the deaths were reported to be accidental, the exact cause was not specified.	
Additional Comments: None				
Overall Quality Determination		High		

Study Citation:	Ress, N. B. (2002). NTP technical report on the toxicity studies of trans-1,2-dichloroethylene (CAS No. 156-60-5) administered in microcapsules in feed to F344/N rats and B6C3F1 mice. Toxicity Report Series, vol. 55 55:112 pp.			
Health Outcome(s):	Lung/Respiratory; Skin/Connective Tissue; Gastrointestinal; Immune/Hematological; Hepatic/Liver; Musculoskeletal; Nutritional/Metabolic; Ocular/Sensory; Cardiovascular; Thyroid;			
Reported Health Effect(s):	Lung/Respiratory: Organ weight (lung), histopathology (lung, nose); Skin/Connective Tissue: Histopathology (skin); Gastrointestinal: Histopathology (esophagus, large intestine [cecum, colon, rectum], small intestine [duodenum, jejunum, ileum], stomach [forestomach and glandular], trachea); Immune/Hematological: Hematology (automated Hct, manual Hct, Hgb, RBC count, reticulocyte count, platelet count, RBC and platelet morphology, MCV, MCH, MCHC, WBC count, WBC differentials) clinical chemistry (creatinine kinase), organ weight (thymus), histopathology (lymph nodes [mandibular and mesenteric], spleen, thymus); Hepatic/Liver: Organ weight (liver), clinical chemistry (cholesterol, ALT, ALP, 5'-nucleotidase, total bile acids, sorbitol dehydrogenase), histopathology (gallbladder [mice only], liver); Musculoskeletal: Histopathology (bone with marrow); Nutritional/Metabolic: Body weight, food consumption per cage, clinical chemistry (total protein, albumin), histopathology (adrenal gland, pancreas, parathyroid gland); Ocular/Sensory: Histopathology (Zymbal's gland (e.g., auditory sebaceous gland)); Cardiovascular: Organ weight (heart), histopathology (heart); Thyroid: Histopathology (thyroid);			
Duration:	Chronic (>91 days) 14 weeks (rats and mice)			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1739657			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	All Outcomes: The test substance was identified definitively by name, CASRN, structure, molecular formula, molecular weight, and several synonyms.	
	Metric 2: Test Substance Source	High	All Outcomes: The test substance was obtained from a commercial source and the lot number was reported.	
	Metric 3: Test Substance Purity	High	All Outcomes: The purity was confirmed to be approximately 99% via GC.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	All Outcomes: Both an untreated and vehicle (empty microcapsules in diet) negative control groups were included in the study.	
	Metric 5: Positive Controls	N/A	All Outcomes: Positive controls are not required for the study type.	
	Metric 6: Randomized Allocation of Animals	Medium	All Outcomes: It was reported that animals were distributed randomly into groups of approximately equal initial mean body weights.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	High	All Outcomes: Test substance preparation in microcapsules made from corn starch and sucrose was well described and appropriate for the test substance. Homogeneity and stability studies were conducted to confirm stability under storage conditions.	
	Metric 8: Consistency of Exposure Administration	High	All Outcomes: The test substance was administered consistently across treatment groups in diet.	
	Metric 9: Reporting of Doses/Concentrations	Medium	All Outcomes: Concentrations in food and resultant doses for each treatment group were reported with some ambiguity. Analysis of the microcapsules via GC analysis prior to the start of the study showed an overall chemical load of 47% which was considered by the study authors to be appropriate. The study text indicated that all dosing was within 10% of the target concentrations.	
	Metric 10: Exposure Frequency and Duration	High	All Outcomes: Animals were exposed continuously in feed, which is appropriate for a dietary study.	

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Study Citation:	Ress, N. B. (2002). NTP technical report on the toxicity studies of trans-1,2-dichloroethylene (CAS No. 156-60-5) administered in microcapsules in feed to F344/N rats and B6C3F1 mice. Toxicity Report Series, vol. 55 55:112 pp.			
Health Outcome(s):	Lung/Respiratory; Skin/Connective Tissue; Gastrointestinal; Immune/Hematological; Hepatic/Liver; Musculoskeletal; Nutritional/Metabolic; Ocular/Sensory; Cardiovascular; Thyroid;			
Reported Health Effect(s):	Lung/Respiratory: Organ weight (lung), histopathology (lung, nose); Skin/Connective Tissue: Histopathology (skin); Gastrointestinal: Histopathology (esophagus, large intestine [cecum, colon, rectum], small intestine [duodenum, jejunum, ileum], stomach [forestomach and glandular], trachea); Immune/Hematological: Hematology (automated Hct, manual Hct, Hgb, RBC count, reticulocyte count, platelet count, RBC and platelet morphology, MCV, MCH, MCHC, WBC count, WBC differentials) clinical chemistry (creatinine kinase), organ weight (thymus), histopathology (lymph nodes [mandibular and mesenteric], spleen, thymus); Hepatic/Liver: Organ weight (liver), clinical chemistry (cholesterol, ALT, ALP, 5'-nucleotidase, total bile acids, sorbitol dehydrogenase), histopathology (gallbladder [mice only], liver); Musculoskeletal: Histopathology (bone with marrow); Nutritional/Metabolic: Body weight, food consumption per cage, clinical chemistry (total protein, albumin), histopathology (adrenal gland, pancreas, parathyroid gland); Ocular/Sensory: Histopathology (Zymbal's gland (e.g., auditory sebaceous gland)); Cardiovascular: Organ weight (heart), histopathology (heart); Thyroid: Histopathology (thyroid);			
Duration:	Chronic (>91 days) 14 weeks (rats and mice)			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1739657			
Domain	Metric	Rating	Comments	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: The highest dose was chosen based on EPA guidance that substitutions of >5% in the feed interferes with nutrition; therefore, the highest concentration in pilot studies was set at 5% (50,000 ppm). Based on no overt toxicity was observed at this concentration in pilot studies, this was chosen as the highest concentration in the 14-week study. Dose spacing (2-fold) was appropriate.	
	Metric 12: Exposure Route and Method	High	All Outcomes: Because the test substance is volatile and insoluble in water, it was administered via the diet, volatility and low solubility were controlled for by administering the test substance via microcapsules mixed with the feed. Thorough analyses were conducted to assess stability over time and with exposure to open air and light to ensure animals received the intended concentrations.	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	High	All Outcomes: Test animal species, strains, sex, age, and starting body weights were reported and the test animals were obtained from a commercial source and appropriate for the study design.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: All husbandry conditions were reported. Male mice were housed individually rather than 5/cage, as was done for rats and female mice. It is assumed but was not specifically stated that this is due to infighting and animal wellbeing issues for a long-term study. Because the individual housing was instituted for male mice of both the control and treatment groups, this is not considered to be a deficiency for this metric and therefore a rating of High is selected.	
	Metric 15: Number of Animals per Group	Medium	All Outcomes: 10/sex/species/group is considered appropriate for the study type and duration.	
Domain 5: Outcome Assessment				
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Study Citation:	Ress, N. B. (2002). NTP technical report on the toxicity studies of trans-1,2-dichloroethylene (CAS No. 156-60-5) administered in microcapsules in feed to F344/N rats and B6C3F1 mice. Toxicity Report Series, vol. 55 55:112 pp.			
Health Outcome(s):	Lung/Respiratory; Skin/Connective Tissue; Gastrointestinal; Immune/Hematological; Hepatic/Liver; Musculoskeletal; Nutritional/Metabolic; Ocular/Sensory; Cardiovascular; Thyroid;			
Reported Health Effect(s):	Lung/Respiratory: Organ weight (lung), histopathology (lung, nose); Skin/Connective Tissue: Histopathology (skin); Gastrointestinal: Histopathology (esophagus, large intestine [cecum, colon, rectum], small intestine [duodenum, jejunum, ileum], stomach [forestomach and glandular], trachea); Immune/Hematological: Hematology (automated Hct, manual Hct, Hgb, RBC count, reticulocyte count, platelet count, RBC and platelet morphology, MCV, MCH, MCHC, WBC count, WBC differentials) clinical chemistry (creatinine kinase), organ weight (thymus), histopathology (lymph nodes [mandibular and mesenteric], spleen, thymus); Hepatic/Liver: Organ weight (liver), clinical chemistry (cholesterol, ALT, ALP, 5'-nucleotidase, total bile acids, sorbitol dehydrogenase), histopathology (gallbladder [mice only], liver); Musculoskeletal: Histopathology (bone with marrow); Nutritional/Metabolic: Body weight, food consumption per cage, clinical chemistry (total protein, albumin), histopathology (adrenal gland, pancreas, parathyroid gland); Ocular/Sensory: Histopathology (Zymbal's gland (e.g., auditory sebaceous gland)); Cardiovascular: Organ weight (heart), histopathology (heart); Thyroid: Histopathology (thyroid);			
Duration:	Chronic (>91 days) 14 weeks (rats and mice)			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1739657			
Domain	Metric	Rating	Comments	
	Metric 16: Outcome Assessment Methodology	High	Lung/Respiratory: The outcome assessment methodologies (organ weight and histopathology) were considered to be sensitive and appropriate for the intended endpoints of interest.; Skin/Connective Tissue: The outcome assessment methodology (histopathology) was considered to be sensitive and appropriate for the intended endpoints of interest.; Gastrointestinal: The outcome assessment methodology (histopathology) was considered to be sensitive and appropriate for the intended endpoints of interest.; Immune/Hematological: The outcome assessment methodologies (both automated and manual hematology and clinical chemistry evaluations, thymus organ weight, and histopathological review of lymph nodes, spleen, and thymus) were considered to be sensitive and appropriate for the intended endpoints of interest.; Hepatic/Liver: The outcome assessment methodologies (clinical chemistry evaluations, liver organ weight, and histopathological review of gallbladder [mice only] and liver) were considered to be sensitive and appropriate for the intended endpoints of interest.; Musculoskeletal: The outcome assessment methodology (histopathological review of bone with marrow) was considered to be sensitive and appropriate for the intended endpoints of interest.; Nutritional/Metabolic: The outcome assessment methodology (body weights, food consumption, clinical chemistry [total protein, albumin], histopathology [adrenal gland, pancreas, parathyroid gland]) were considered to be sensitive and appropriate for the intended endpoints of interest.; Ocular/Sensory: The outcome assessment methodology (histopathological review of Zymbal's glands) was considered to be sensitive and appropriate for the intended endpoints of interest.; Cardiovascular: The outcome assessment methodologies (heart organ weight and histopathology) were considered to be sensitive and appropriate for the intended endpoints of interest.; Thyroid: The outcome assessment methodology (histopathological review of the thyroid) was considered to be sensitive and appropriate for the intended endpoints of interest.	
	Metric 17: Consistency of Outcome Assessment	High	All Outcomes: Outcomes were assessed consistently across study groups at the same time and using the same protocol.	

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Study Citation:	Ress, N. B. (2002). NTP technical report on the toxicity studies of trans-1,2-dichloroethylene (CAS No. 156-60-5) administered in microcapsules in feed to F344/N rats and B6C3F1 mice. Toxicity Report Series, vol. 55 55:112 pp.
Health Outcome(s):	Lung/Respiratory; Skin/Connective Tissue; Gastrointestinal; Immune/Hematological; Hepatic/Liver; Musculoskeletal; Nutritional/Metabolic; Ocular/Sensory; Cardiovascular; Thyroid;
Reported Health Effect(s):	Lung/Respiratory: Organ weight (lung), histopathology (lung, nose); Skin/Connective Tissue: Histopathology (skin); Gastrointestinal: Histopathology (esophagus, large intestine [cecum, colon, rectum], small intestine [duodenum, jejunum, ileum], stomach [forestomach and glandular], trachea); Immune/Hematological: Hematology (automated Hct, manual Hct, Hgb, RBC count, reticulocyte count, platelet count, RBC and platelet morphology, MCV, MCH, MCHC, WBC count, WBC differentials) clinical chemistry (creatinine kinase), organ weight (thymus), histopathology (lymph nodes [mandibular and mesenteric], spleen, thymus); Hepatic/Liver: Organ weight (liver), clinical chemistry (cholesterol, ALT, ALP, 5'-nucleotidase, total bile acids, sorbitol dehydrogenase), histopathology (gallbladder [mice only], liver); Musculoskeletal: Histopathology (bone with marrow); Nutritional/Metabolic: Body weight, food consumption per cage, clinical chemistry (total protein, albumin), histopathology (adrenal gland, pancreas, parathyroid gland); Ocular/Sensory: Histopathology (Zymbal's gland (e.g., auditory sebaceous gland)); Cardiovascular: Organ weight (heart), histopathology (heart); Thyroid: Histopathology (thyroid);
Duration:	Chronic (>91 days) 14 weeks (rats and mice)
Chemical:	trans-1,2-Dichloroethylene- Parent compound
HERO ID:	1739657

Domain	Metric	Rating	Comments
Metric 18:	Sampling Adequacy	High	Lung/Respiratory: All animals were sampled for organ weights. Only untreated control, vehicle control, and the highest dose group (50000 ppm) were sampled for histopathology review, but this standard practice considering that no adverse lesions were observed in the highest dose group to warrant histopathology review of lower dose groups.; Skin/Connective Tissue: Only untreated control, vehicle control, and the highest dose group (50000 ppm) were sampled for histopathology review, but this standard practice considering that no adverse lesions were observed in the highest dose group to warrant histopathology review of lower dose groups.; Gastrointestinal: Only untreated control, vehicle control, and the highest dose group (50000 ppm) were sampled for histopathology review, but this standard practice considering that no adverse lesions were observed in the highest dose group to warrant histopathology review of lower dose groups.; Immune/Hematological: All animals were sampled for organ weight, hematology, and clinical chemistry endpoints. Only untreated control, vehicle control, and the highest dose group (50000 ppm) were sampled for histopathology review, but this standard practice considering that no adverse lesions were observed in the highest dose group to warrant histopathology review of lower dose groups.; Hepatic/Liver: All animals were sampled for organ weight and clinical chemistry endpoints. Only untreated control, vehicle control, and the highest dose group (50000 ppm) were sampled for histopathology review, but this standard practice considering that no adverse lesions were observed in the highest dose group to warrant histopathology review of lower dose groups.; Musculoskeletal: Only untreated control, vehicle control, and the highest dose group (50000 ppm) were sampled for histopathology review, but this standard practice considering that no adverse lesions were observed in the highest dose group to warrant histopathology review of lower dose groups.; Nutritional/Metabolic: All animals/sex/species/group and all groups were assessed for clinical chemistry, food consumption, and body weight endpoints. Only untreated control, vehicle control, and the highest dose group (50000 ppm) were sampled for histopathology review, but this standard practice considering that no adverse lesions were observed in the highest dose group to warrant histopathology review of lower dose groups.; Ocular/Sensory: Only untreated control, vehicle control, and the highest dose group (50000 ppm) were sampled for histopathology review, but this standard practice considering that no adverse lesions were observed in the highest dose group to warrant histopathology review of lower dose groups.; Cardiovascular: All animals were sampled for organ weights. Only untreated control, vehicle control, and the highest dose group (50000 ppm) were sampled for histopathology review, but this standard practice considering that no adverse lesions were observed in the highest dose group to warrant histopathology review of lower dose groups.; Thyroid: Only untreated control, vehicle control, and the highest dose group (50000 ppm) were sampled for histopathology review, but this standard practice considering that no adverse lesions were observed in the highest dose group to warrant histopathology review of lower dose groups.;

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Study Citation:	Ress, N. B. (2002). NTP technical report on the toxicity studies of trans-1,2-dichloroethylene (CAS No. 156-60-5) administered in microcapsules in feed to F344/N rats and B6C3F1 mice. Toxicity Report Series, vol. 55 55:112 pp.
Health Outcome(s):	Lung/Respiratory; Skin/Connective Tissue; Gastrointestinal; Immune/Hematological; Hepatic/Liver; Musculoskeletal; Nutritional/Metabolic; Ocular/Sensory; Cardiovascular; Thyroid;
Reported Health Effect(s):	Lung/Respiratory: Organ weight (lung), histopathology (lung, nose); Skin/Connective Tissue: Histopathology (skin); Gastrointestinal: Histopathology (esophagus, large intestine [cecum, colon, rectum], small intestine [duodenum, jejunum, ileum], stomach [forestomach and glandular], trachea); Immune/Hematological: Hematology (automated Hct, manual Hct, Hgb, RBC count, reticulocyte count, platelet count, RBC and platelet morphology, MCV, MCH, MCHC, WBC count, WBC differentials) clinical chemistry (creatinine kinase), organ weight (thymus), histopathology (lymph nodes [mandibular and mesenteric], spleen, thymus); Hepatic/Liver: Organ weight (liver), clinical chemistry (cholesterol, ALT, ALP, 5'-nucleotidase, total bile acids, sorbitol dehydrogenase), histopathology (gallbladder [mice only], liver); Musculoskeletal: Histopathology (bone with marrow); Nutritional/Metabolic: Body weight, food consumption per cage, clinical chemistry (total protein, albumin), histopathology (adrenal gland, pancreas, parathyroid gland); Ocular/Sensory: Histopathology (Zymbal's gland (e.g., auditory sebaceous gland)); Cardiovascular: Organ weight (heart), histopathology (heart); Thyroid: Histopathology (thyroid);
Duration:	Chronic (>91 days) 14 weeks (rats and mice)
Chemical:	trans-1,2-Dichloroethylene- Parent compound
HERO ID:	1739657

Domain	Metric	Rating	Comments
	Metric 19: Blinding of Assessors	N/A	All Outcomes: No subjective outcomes were assessed.
	Metric 20: Negative Control Response	High	All Outcomes: Negative control responses were appropriate.

Domain 6: Confounding / Variable Control

Metric 21:	Confounding Variables in Test Design and Procedures	High	All Outcomes: No confounding variables that could impact assessment were identified. Food consumption was reported for each treatment group and did not differ significantly between groups or in a dose-dependent manner.
Metric 22:	Health Outcomes Unrelated to Exposure	High	All Outcomes: The authors specifically reported testing 5 male and 5 female rats and mice (randomly chosen) received from the supplier for parasites or signs of disease. None were found.
Metric 23:	Data Presentation and Analysis	High	Lung/Respiratory: Statistical methods were clearly described and appropriate for continuous data.; Skin/Connective Tissue: Statistical methods were clearly described and appropriate for incidence data.; Gastrointestinal: Statistical methods were clearly described and appropriate for incidence data.; Immune/Hematological: Statistical methods were clearly described and appropriate for incidence and continuous data.; Hepatic/Liver: Statistical methods were clearly described and appropriate for incidence and continuous data.; Musculoskeletal: Statistical methods were clearly described and appropriate for incidence data.; Nutritional/Metabolic: Statistical methods were clearly described and appropriate for incidence and continuous data.; Ocular/Sensory: Statistical methods were clearly described and appropriate for incidence data.; Cardiovascular: Statistical methods were clearly described and appropriate for continuous data.; Thyroid: Statistical methods were clearly described and appropriate for incidence data.

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Study Citation:	Ress, N. B. (2002). NTP technical report on the toxicity studies of trans-1,2-dichloroethylene (CAS No. 156-60-5) administered in microcapsules in feed to F344/N rats and B6C3F1 mice. Toxicity Report Series, vol. 55 55:112 pp.
Health Outcome(s):	Lung/Respiratory; Skin/Connective Tissue; Gastrointestinal; Immune/Hematological; Hepatic/Liver; Musculoskeletal; Nutritional/Metabolic; Ocular/Sensory; Cardiovascular; Thyroid;
Reported Health Effect(s):	Lung/Respiratory: Organ weight (lung), histopathology (lung, nose); Skin/Connective Tissue: Histopathology (skin); Gastrointestinal: Histopathology (esophagus, large intestine [cecum, colon, rectum], small intestine [duodenum, jejunum, ileum], stomach [forestomach and glandular], trachea); Immune/Hematological: Hematology (automated Hct, manual Hct, Hgb, RBC count, reticulocyte count, platelet count, RBC and platelet morphology, MCV, MCH, MCHC, WBC count, WBC differentials) clinical chemistry (creatinine kinase), organ weight (thymus), histopathology (lymph nodes [mandibular and mesenteric], spleen, thymus); Hepatic/Liver: Organ weight (liver), clinical chemistry (cholesterol, ALT, ALP, 5'-nucleotidase, total bile acids, sorbitol dehydrogenase), histopathology (gallbladder [mice only], liver); Musculoskeletal: Histopathology (bone with marrow); Nutritional/Metabolic: Body weight, food consumption per cage, clinical chemistry (total protein, albumin), histopathology (adrenal gland, pancreas, parathyroid gland); Ocular/Sensory: Histopathology (Zymbal's gland (e.g., auditory sebaceous gland)); Cardiovascular: Organ weight (heart), histopathology (heart); Thyroid: Histopathology (thyroid);
Duration:	Chronic (>91 days) 14 weeks (rats and mice)
Chemical:	trans-1,2-Dichloroethylene- Parent compound
HERO ID:	1739657

Domain	Metric	Rating	Comments
Metric 24:	Reporting of Data	High	Lung/Respiratory: Negative data were reported quantitatively.; Skin/Connective Tissue: Negative data were reported qualitatively.; Gastrointestinal: Negative data were reported qualitatively.; Immune/Hematological: Grouped raw data were provided for hematology parameters, some of which showed significant differences between treatment groups. Negative data for other endpoints for this target organ/system were reported qualitatively or quantitatively.; Hepatic/Liver: Grouped raw data were provided for liver weights, some of which showed significant differences between treatment groups. Negative data for other endpoints for this target organ/system were reported qualitatively or quantitatively.; Musculoskeletal: Negative data were reported qualitatively.; Nutritional/Metabolic: Grouped raw data were provided for body weight parameters, some of which showed significant differences between treatment groups. Negative data for other endpoints for this target organ/system were reported qualitatively or quantitatively.; Ocular/Sensory: Negative data were reported qualitatively.; Cardiovascular: Negative data were reported quantitatively or qualitatively.; Thyroid: Negative data were reported qualitatively.

Additional Comments: None

Overall Quality Determination**High**

Study Citation:	Ress, N. B. (2002). NTP technical report on the toxicity studies of trans-1,2-dichloroethylene (CAS No. 156-60-5) administered in microcapsules in feed to F344/N rats and B6C3F1 mice. Toxicity Report Series, vol. 55 55:112 pp.			
Health Outcome(s):	Neurological/Behavioral			
Reported Health Effect(s):	Neurological/Behavioral: Clinical signs, functional observational battery (FOB; body position, activity level, coordination of movement, gait, general behavior, head flick, head searching, compulsive biting or licking, backward walking, self-mutilation, circling, convulsions, tremors, lacrimation or chromodacryorrhea, salivation, piloerection, pupillary dilation or constriction, unusual respiration, diarrhea, excessive or diminished urination, and vocalization), histopathology (brain)			
Duration:	Chronic (>91 days) 14 weeks (rats and mice)			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1739657			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1:	Test Substance Identity	High	The test substance was identified definitively by name, CASRN, structure, molecular formula, molecular weight, and several synonyms.
	Metric 2:	Test Substance Source	High	The test substance was obtained from a commercial source and the lot number was reported.
	Metric 3:	Test Substance Purity	High	The purity was confirmed to be approximately 99% via GC.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	Both an untreated and vehicle (empty microcapsules in diet) negative control groups were included in the study.
	Metric 5:	Positive Controls	N/A	Positive controls are not required for the study type.
	Metric 6:	Randomized Allocation of Animals	Medium	It was reported that animals were distributed randomly into groups of approximately equal initial mean body weights.
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and Storage of Test Substance	High	Test substance preparation in microcapsules made from corn starch and sucrose was well described and appropriate for the test substance. Homogeneity and stability studies were conducted to confirm stability under storage conditions.
	Metric 8:	Consistency of Exposure Administration	High	The test substance was administered consistently across treatment groups in diet.
	Metric 9:	Reporting of Doses/Concentrations	Medium	Concentrations in food and resultant doses for each treatment group were reported with some ambiguity. Analysis of the microcapsules via GC analysis prior to the start of the study showed an overall chemical load of 47% which was considered by the study authors to be appropriate. The study text indicated that all dosing was within 10% of the target concentrations.
	Metric 10:	Exposure Frequency and Duration	High	Animals were exposed continuously in feed, which is appropriate for a dietary study.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The highest dose was chosen based on EPA guidance that substitutions of >5% in the feed interferes with nutrition; therefore, the highest concentration in pilot studies was set at 5% (50,000 ppm). Based on no overt toxicity was observed at this concentration in pilot studies, this was chosen as the highest concentration in the 14-week study. Dose spacing (2-fold) was appropriate.
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Study Citation:	Ress, N. B. (2002). NTP technical report on the toxicity studies of trans-1,2-dichloroethylene (CAS No. 156-60-5) administered in microcapsules in feed to F344/N rats and B6C3F1 mice. Toxicity Report Series, vol. 55 55:112 pp.			
Health Outcome(s):	Neurological/Behavioral			
Reported Health Effect(s):	Neurological/Behavioral: Clinical signs, functional observational battery (FOB; body position, activity level, coordination of movement, gait, general behavior, head flick, head searching, compulsive biting or licking, backward walking, self-mutilation, circling, convulsions, tremors, lacrimation or chromodacryorrhea, salivation, piloerection, pupillary dilation or constriction, unusual respiration, diarrhea, excessive or diminished urination, and vocalization), histopathology (brain)			
Duration:	Chronic (>91 days) 14 weeks (rats and mice)			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1739657			
Domain	Metric	Rating	Comments	
	Metric 12:	Exposure Route and Method	High	Because the test substance is volatile and insoluble in water, it was administered via the diet, volatility and low solubility were controlled for by administering the test substance via microcapsules mixed with the feed. Thorough analyses were conducted to assess stability over time and with exposure to open air and light to ensure animals received the intended concentrations.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	High	Test animal species, strains, sex, age, and starting body weights were reported and the test animals were obtained from a commercial source and appropriate for the study design.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were reported. Male mice were housed individually rather than 5/cage, as was done for rats and female mice. It is assumed but was not specifically stated that this is due to infighting and animal wellbeing issues for a long-term study. Because the individual housing was instituted for male mice of both the control and treatment groups, this is not considered to be a deficiency for this metric and therefore a rating of High is selected.
	Metric 15:	Number of Animals per Group	Medium	10/sex/species/group is considered appropriate for the study type and duration.
Domain 5: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	High	The outcome assessment methodologies (clinical signs of toxicity, functional observational battery, and brain histopathology) were considered to be sensitive and appropriate for the intended endpoints of interest.
	Metric 17:	Consistency of Outcome Assessment	High	Outcomes were assessed consistently across study groups at the same time and using the same protocol.
	Metric 18:	Sampling Adequacy	Medium	Only the untreated control, vehicle control, and 3 highest concentration groups were assessed for the functional observational battery. This is not considered to have impacted the study substantially as control groups and sufficient dose groups (3) to observe a putative dose-response were included; furthermore, FOB examinations yielded negative outcomes. Only untreated control, vehicle control, and the highest dose group (50000 ppm) were sampled for histopathology review, but this standard practice considering that no adverse lesions were observed in the highest dose group to warrant histopathology review of lower dose groups. All 10 animals/sex/species/group and every group were sampled for the remaining endpoint for this target organ/system (clinical observations).
	Metric 19:	Blinding of Assessors	Low	No blinding was specified to have been utilized for subjective FOB observations.
	Metric 20:	Negative Control Response	High	Negative control responses were appropriate.

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Study Citation:	Ress, N. B. (2002). NTP technical report on the toxicity studies of trans-1,2-dichloroethylene (CAS No. 156-60-5) administered in microcapsules in feed to F344/N rats and B6C3F1 mice. Toxicity Report Series, vol. 55 55:112 pp.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Neurological/Behavioral: Clinical signs, functional observational battery (FOB; body position, activity level, coordination of movement, gait, general behavior, head flick, head searching, compulsive biting or licking, backward walking, self-mutilation, circling, convulsions, tremors, lacrimation or chromodacryorrhea, salivation, piloerection, pupillary dilation or constriction, unusual respiration, diarrhea, excessive or diminished urination, and vocalization), histopathology (brain)
Duration:	Chronic (>91 days) 14 weeks (rats and mice)
Chemical:	trans-1,2-Dichloroethylene- Parent compound
HERO ID:	1739657

Domain	Metric	Rating	Comments
Domain 6: Confounding / Variable Control			
Metric 21:	Confounding Variables in Test Design and Procedures	High	No confounding variables that could impact assessment were identified. Food consumption was reported for each treatment group and did not differ significantly between groups or in a dose-dependent manner.
Metric 22:	Health Outcomes Unrelated to Exposure	High	The authors specifically reported testing 5 male and 5 female rats and mice (randomly chosen) received from the supplier for parasites or signs of disease. None were found.
Metric 23:	Data Presentation and Analysis	High	Statistical methods were clearly described and appropriate for both incidence and continuous data.
Metric 24:	Reporting of Data	High	Negative data were reported qualitatively.

Additional Comments: None

Overall Quality Determination**High**

Study Citation:	Ress, N. B. (2002). NTP technical report on the toxicity studies of trans-1,2-dichloroethylene (CAS No. 156-60-5) administered in microcapsules in feed to F344/N rats and B6C3F1 mice. Toxicity Report Series, vol. 55 55:112 pp.		
Health Outcome(s):	Reproductive/Developmental		
Reported Health Effect(s):	Reproductive/Developmental: Male (spermatid heads per testis and per gram testis, spermatid counts, and epididymal spermatozoal motility and concentration), female (estrous cycle stage %, estrous cycle length), organ weight (right testis), histopathology (clitoral gland, mammary gland, ovary, pituitary gland, preputial gland, prostate gland, testis with epididymis and seminal vesicle, uterus, left cauda, left epididymis, left testis)		
Duration:	Chronic (>91 days) 14 weeks (rats and mice)		
Chemical:	trans-1,2-Dichloroethylene- Parent compound		
HERO ID:	1739657		
Domain	Metric	Rating	Comments
Domain 1: Test Substance			
	Metric 1: Test Substance Identity	High	The test substance was identified definitively by name, CASRN, structure, molecular formula, molecular weight, and several synonyms.
	Metric 2: Test Substance Source	High	The test substance was obtained from a commercial source and the lot number was reported.
	Metric 3: Test Substance Purity	High	The purity was confirmed to be approximately 99% via GC.
Domain 2: Test Design			
	Metric 4: Negative and Vehicle Controls	High	Both an untreated and vehicle (empty microcapsules in diet) negative control groups were included in the study.
	Metric 5: Positive Controls	N/A	Positive controls are not required for the study type.
	Metric 6: Randomized Allocation of Animals	Medium	It was reported that animals were distributed randomly into groups of approximately equal initial mean body weights.
Domain 3: Exposure Characterization			
	Metric 7: Preparation and Storage of Test Substance	High	Test substance preparation in microcapsules made from corn starch and sucrose was well described and appropriate for the test substance. Homogeneity and stability studies were conducted to confirm stability under storage conditions.
	Metric 8: Consistency of Exposure Administration	High	The test substance was administered consistently across treatment groups in diet.
	Metric 9: Reporting of Doses/Concentrations	Medium	Concentrations in food and resultant doses for each treatment group were reported with some ambiguity. Analysis of the microcapsules via GC analysis prior to the start of the study showed an overall chemical load of 47% which was considered by the study authors to be appropriate. The study text indicated that all dosing was within 10% of the target concentrations.
	Metric 10: Exposure Frequency and Duration	High	Animals were exposed continuously in feed, which is appropriate for a dietary study.
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	The highest dose was chosen based on EPA guidance that substitutions of >5% in the feed interferes with nutrition; therefore, the highest concentration in pilot studies was set at 5% (50,000 ppm). Based on no overt toxicity was observed at this concentration in pilot studies, this was chosen as the highest concentration in the 14-week study. Dose spacing (2-fold) was appropriate.
	Metric 12: Exposure Route and Method	High	Because the test substance is volatile and insoluble in water, it was administered via the diet, volatility and low solubility were controlled for by administering the test substance via microcapsules mixed with the feed. Thorough analyses were conducted to assess stability over time and with exposure to open air and light to ensure animals received the intended concentrations.
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Study Citation:	Ress, N. B. (2002). NTP technical report on the toxicity studies of trans-1,2-dichloroethylene (CAS No. 156-60-5) administered in microcapsules in feed to F344/N rats and B6C3F1 mice. Toxicity Report Series, vol. 55 55:112 pp.		
Health Outcome(s):	Reproductive/Developmental		
Reported Health Effect(s):	Reproductive/Developmental: Male (spermatid heads per testis and per gram testis, spermatid counts, and epididymal spermatozoal motility and concentration), female (estrous cycle stage %, estrous cycle length), organ weight (right testis), histopathology (clitoral gland, mammary gland, ovary, pituitary gland, preputial gland, prostate gland, testis with epididymis and seminal vesicle, uterus, left cauda, left epididymis, left testis)		
Duration:	Chronic (>91 days) 14 weeks (rats and mice)		
Chemical:	trans-1,2-Dichloroethylene- Parent compound		
HERO ID:	1739657		
Domain	Metric	Rating	Comments
Domain 4: Test Animals			
	Metric 13: Test Animal Characteristics	High	Test animal species, strains, sex, age, and starting body weights were reported and the test animals were obtained from a commercial source and appropriate for the study design.
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were reported. Male mice were housed individually rather than 5/cage, as was done for rats and female mice. It is assumed but was not specifically stated that this is due to infighting and animal wellbeing issues for a long-term study. Because the individual housing was instituted for male mice of both the control and treatment groups, this is not considered to be a deficiency for this metric and therefore a rating of High is selected.
	Metric 15: Number of Animals per Group	Medium	10/sex/species/group is considered appropriate for the study type and duration.
Domain 5: Outcome Assessment			
	Metric 16: Outcome Assessment Methodology	High	The outcome assessment methodologies (sperm analysis, vaginal cytology for estrous cyclicity, male reproductive organ weights, and histopathological review of several reproductive organs) were considered to be sensitive and appropriate for the intended endpoints of interest.
	Metric 17: Consistency of Outcome Assessment	High	Outcomes were assessed consistently across study groups at the same time and using the same protocol.
	Metric 18: Sampling Adequacy	Medium	Only the untreated control, vehicle control, and 3 highest concentration groups were assessed for sperm characterization and estrous cyclicity (all 10 males/species/group and all 10 females/species/group, respectively, were sampled of these groups). This is not considered to have impacted the study substantially as control groups and sufficient dose groups (3) to observe a putative dose-response were included; furthermore, these examinations yielded negative outcomes. Only untreated control, vehicle control, and the highest dose group (50000 ppm) were sampled for histopathology review, but this standard practice considering that no adverse lesions were observed in the highest dose group to warrant histopathology review of lower dose groups. All male animals were sampled for male reproductive organ weights.
	Metric 19: Blinding of Assessors	N/A	No subjective outcomes were assessed.
	Metric 20: Negative Control Response	High	Negative control responses were appropriate.
Domain 6: Confounding / Variable Control			
	Metric 21: Confounding Variables in Test Design and Procedures	High	No confounding variables that could impact assessment were identified. Food consumption was reported for each treatment group and did not differ significantly between groups or in a dose-dependent manner.

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Study Citation:	Ress, N. B. (2002). NTP technical report on the toxicity studies of trans-1,2-dichloroethylene (CAS No. 156-60-5) administered in microcapsules in feed to F344/N rats and B6C3F1 mice. Toxicity Report Series, vol. 55 55:112 pp.			
Health Outcome(s):	Reproductive/Developmental			
Reported Health Effect(s):	Reproductive/Developmental: Male (spermatid heads per testis and per gram testis, spermatid counts, and epididymal spermatozoal motility and concentration), female (estrous cycle stage %, estrous cycle length), organ weight (right testis), histopathology (clitoral gland, mammary gland, ovary, pituitary gland, preputial gland, prostate gland, testis with epididymis and seminal vesicle, uterus, left cauda, left epididymis, left testis)			
Duration:	Chronic (>91 days) 14 weeks (rats and mice)			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1739657			
Domain	Metric		Rating	Comments
	Metric 22:	Health Outcomes Unrelated to Exposure	High	The authors specifically reported testing 5 male and 5 female rats and mice (randomly chosen) received from the supplier for parasites or signs of disease. None were found.
	Metric 23:	Data Presentation and Analysis	High	Statistical methods were clearly described and appropriate for incidence and continuous data.
	Metric 24:	Reporting of Data	High	Negative data were reported qualitatively or quantitatively.
Additional Comments: None				

Overall Quality Determination**High**

Study Citation:	Ress, N. B. (2002). NTP technical report on the toxicity studies of trans-1,2-dichloroethylene (CAS No. 156-60-5) administered in microcapsules in feed to F344/N rats and B6C3F1 mice. Toxicity Report Series, vol. 55 55:112 pp.
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Renal/Kidney: Organ weight (right kidney), clinical chemistry (urea nitrogen, creatinine), histopathology (kidney, urinary bladder)
Duration:	Chronic (>91 days) 14 weeks (rats and mice)
Chemical:	trans-1,2-Dichloroethylene- Parent compound
HERO ID:	1739657

Domain	Metric	Rating	Comments
Domain 1: Test Substance			
Metric 1:	Test Substance Identity	High	The test substance was identified definitively by name, CASRN, structure, molecular formula, molecular weight, and several synonyms.
Metric 2:	Test Substance Source	High	The test substance was obtained from a commercial source and the lot number was reported.
Metric 3:	Test Substance Purity	High	The purity was confirmed to be approximately 99% via GC.
Domain 2: Test Design			
Metric 4:	Negative and Vehicle Controls	High	Both an untreated and vehicle (empty microcapsules in diet) negative control groups were included in the study.
Metric 5:	Positive Controls	N/A	Positive controls are not required for the study type.
Metric 6:	Randomized Allocation of Animals	Medium	It was reported that animals were distributed randomly into groups of approximately equal initial mean body weights.
Domain 3: Exposure Characterization			
Metric 7:	Preparation and Storage of Test Substance	High	Test substance preparation in microcapsules made from corn starch and sucrose was well described and appropriate for the test substance. Homogeneity and stability studies were conducted to confirm stability under storage conditions.
Metric 8:	Consistency of Exposure Administration	High	The test substance was administered consistently across treatment groups in diet.
Metric 9:	Reporting of Doses/Concentrations	Medium	Concentrations in food and resultant doses for each treatment group were reported with some ambiguity. Analysis of the microcapsules via GC analysis prior to the start of the study showed an overall chemical load of 47% which was considered by the study authors to be appropriate. The study text indicated that all dosing was within 10% of the target concentrations.
Metric 10:	Exposure Frequency and Duration	High	Animals were exposed continuously in feed, which is appropriate for a dietary study.
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The highest dose was chosen based on EPA guidance that substitutions of >5% in the feed interferes with nutrition; therefore, the highest concentration in pilot studies was set at 5% (50,000 ppm). Based on no overt toxicity was observed at this concentration in pilot studies, this was chosen as the highest concentration in the 14-week study. Dose spacing (2-fold) was appropriate.
Metric 12:	Exposure Route and Method	High	Because the test substance is volatile and insoluble in water, it was administered via the diet, volatility and low solubility were controlled for by administering the test substance via microcapsules mixed with the feed. Thorough analyses were conducted to assess stability over time and with exposure to open air and light to ensure animals received the intended concentrations.

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Study Citation:	Ress, N. B. (2002). NTP technical report on the toxicity studies of trans-1,2-dichloroethylene (CAS No. 156-60-5) administered in microcapsules in feed to F344/N rats and B6C3F1 mice. Toxicity Report Series, vol. 55 55:112 pp.
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Renal/Kidney: Organ weight (right kidney), clinical chemistry (urea nitrogen, creatinine), histopathology (kidney, urinary bladder)
Duration:	Chronic (>91 days) 14 weeks (rats and mice)
Chemical:	trans-1,2-Dichloroethylene- Parent compound
HERO ID:	1739657

Domain	Metric	Rating	Comments
Domain 4: Test Animals			
	Metric 13: Test Animal Characteristics	High	Test animal species, strains, sex, age, and starting body weights were reported and the test animals were obtained from a commercial source and appropriate for the study design.
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were reported. Male mice were housed individually rather than 5/cage, as was done for rats and female mice. It is assumed but was not specifically stated that this is due to infighting and animal wellbeing issues for a long-term study. Because the individual housing was instituted for male mice of both the control and treatment groups, this is not considered to be a deficiency for this metric and therefore a rating of High is selected.
	Metric 15: Number of Animals per Group	Medium	10/sex/species/group is considered appropriate for the study type and duration.
Domain 5: Outcome Assessment			
	Metric 16: Outcome Assessment Methodology	High	The outcome assessment methodologies (kidney weights, clinical chemistry [blood urea nitrogen, creatinine], and histopathological review of kidney and urinary bladder) were considered to be sensitive and appropriate for the intended endpoints of interest.
	Metric 17: Consistency of Outcome Assessment	Low	Outcomes were mostly assessed consistently across study groups at the same time and using the same protocol. However, blood urea nitrogen was only assessed at Day 5 rather than at the end of the 14-week study. It unclear why this was the only clinical chemistry parameter assessed only at Day 5 and not at Week 14; an explanation is not provided in the text. This is considered to be a deficiency that could have substantially impacted results, as the authors reported that previous studies found decreased BUN in a subchronic oral toxicity study in rats treated with the cis-isomer of 1,2-dichloroethylene. Although this was not a dose-related change in the previous study, this parameter potentially has relevance to the toxicity of trans-1,2-dichloroethylene, as BUN was significantly decreased in the present study in male rats at the highest concentration tested. Due to the lack of testing this parameter at Week 14, this metric is rated as Low.
	Metric 18: Sampling Adequacy	High	All animals were sampled for organ weights and clinical chemistry parameters. Only untreated control, vehicle control, and the highest dose group (50000 ppm) were sampled for histopathology review, but this standard practice considering that no adverse lesions were observed in the highest dose group to warrant histopathology review of lower dose groups.
	Metric 19: Blinding of Assessors	N/A	No subjective outcomes were assessed.
	Metric 20: Negative Control Response	High	Negative control responses were appropriate.
Domain 6: Confounding / Variable Control			

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Study Citation:	Ress, N. B. (2002). NTP technical report on the toxicity studies of trans-1,2-dichloroethylene (CAS No. 156-60-5) administered in microcapsules in feed to F344/N rats and B6C3F1 mice. Toxicity Report Series, vol. 55 55:112 pp.
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Renal/Kidney: Organ weight (right kidney), clinical chemistry (urea nitrogen, creatinine), histopathology (kidney, urinary bladder)
Duration:	Chronic (>91 days) 14 weeks (rats and mice)
Chemical:	trans-1,2-Dichloroethylene- Parent compound
HERO ID:	1739657

Domain	Metric	Rating	Comments
	Metric 21: Confounding Variables in Test Design and Procedures	High	No confounding variables that could impact assessment were identified. Food consumption was reported for each treatment group and did not differ significantly between groups or in a dose-dependent manner.
	Metric 22: Health Outcomes Unrelated to Exposure	High	The authors specifically reported testing 5 male and 5 female rats and mice (randomly chosen) received from the supplier for parasites or signs of disease. None were found.
	Metric 23: Data Presentation and Analysis	High	Statistical methods were clearly described and appropriate for incidence and continuous data.
	Metric 24: Reporting of Data	High	Grouped raw data were provided for clinical chemistry and organ weight data, some of which showed significant differences between treatment groups. Negative data for histopathology for this target organ/system were reported qualitatively.

Additional Comments: None

Overall Quality Determination**High**

Study Citation:	Hurtt, M. E., Valentine, R., Alvarez, L. (1993). Developmental toxicity of inhaled trans-1,2-dichloroethylene in the rat. Fundamental and Applied Toxicology 20(2):225-230.		
Health Outcome(s):	Irritation		
Reported Health Effect(s):	Irritation: Clinical observations (Eye discharge and lacrimation)		
Duration:	Reproductive/Developmental 10 days (GDs 7-16)		
Chemical:	trans-1,2-Dichloroethylene- Parent compound		
HERO ID:	1741343; Linked HERO ID(s): 1741343, 3995666		
Domain	Metric	Rating	Comments
Domain 1: Test Substance			
Metric 1:	Test Substance Identity	High	Test substance was identified as trans-1,2-dichloroethylene. CASRN and structure were not provided.
Metric 2:	Test Substance Source	Low	The source of the test substance was DuPont Chemicals (Wilmington, DE). Lot number was not reported.
Metric 3:	Test Substance Purity	High	Test substance was 99.64% pure.
Domain 2: Test Design			
Metric 4:	Negative and Vehicle Controls	High	Concurrent negative control was included.
Metric 5:	Positive Controls	N/A	Positive control was not necessary for this study.
Metric 6:	Randomized Allocation of Animals	Medium	Computerized random sampling was utilized to allocate animals.
Domain 3: Exposure Characterization			
Metric 7:	Preparation and Storage of Test Substance	High	The method and equipment used to generate the test substance vapor were appropriate and adequately described. "Test atmospheres were generated by vaporization of the test material from glass, gas-washing bottles placed in water baths regulated at 22-26C. The vaporized test material was swept into 3-neck, glass mixing flasks; filtered, conditioned dilution air was added to the mixing flasks at approximately 30 liters/min to sweep the vapors into the 150-liter square, pyramidal, stainless steel and glass exposure chambers."
Metric 8:	Consistency of Exposure Administration	High	Exposure was administered consistently across study groups.
Metric 9:	Reporting of Doses/Concentrations	Low	Nominal concentrations were reported (0, 6000, 9000, 12000ppm). Chamber concentrations were determined at ~30 minute intervals by gas chromatography. Mean daily chamber concentrations were reported to be within +/-5% of the target concentration throughout the test period. However, mean analytical chamber concentrations were not reported.
Metric 10:	Exposure Frequency and Duration	Low	Dams were exposed to test substance vapor via inhalation for 6 hours/day on GDs 7-16. Current OECD 414 guidelines recommend dosing throughout the entire period of gestation (not just organogenesis), including up to the day before caesarian section (GD 21 in the case of this study). This deficiency may impact study results.
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The concentration and number of exposure groups (i.e., 0, 6000, 9000, 12000 ppm) was acceptable and was based on the results of a pilot study.
Metric 12:	Exposure Route and Method	Medium	The number of air changes /hour was not reported.
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Study Citation:	Hurt, M. E., Valentine, R., Alvarez, L. (1993). Developmental toxicity of inhaled trans-1,2-dichloroethylene in the rat. Fundamental and Applied Toxicology 20(2):225-230.
Health Outcome(s):	Irritation
Reported Health Effect(s):	Irritation: Clinical observations (Eye discharge and lacrimation)
Duration:	Reproductive/Developmental 10 days (GDs 7-16)
Chemical:	trans-1,2-Dichloroethylene- Parent compound
HERO ID:	1741343; Linked HERO ID(s): 1741343, 3995666

Domain	Metric	Rating	Comments
Domain 4: Test Animals			
Metric 13:	Test Animal Characteristics	High	Test animal characteristics were reported.
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	Husbandry conditions were adequately reported.
Metric 15:	Number of Animals per Group	Medium	24 animals were included per treatment group.
Domain 5: Outcome Assessment			
Metric 16:	Outcome Assessment Methodology	High	Outcome assessment methodology was appropriate. Clinical observations were made daily before and after exposure and clear evidence of ocular irritation was observed in all treatment groups (lacrimation, eye discharge).
Metric 17:	Consistency of Outcome Assessment	High	Outcomes were assessed consistently across the groups.
Metric 18:	Sampling Adequacy	High	Sampling was adequate. All animals in each treatment group were observed for clinical signs of toxicity, which included lacrimation, stained periocular hair and eye discharge.
Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary for the evaluated outcomes.
Metric 20:	Negative Control Response	High	Negative control response was appropriate.
Domain 6: Confounding / Variable Control			
Metric 21:	Confounding Variables in Test Design and Procedures	Low	The test substance is a respiratory irritant and therefore respiratory rates should be reported, but were not. Water intake was not reported. Food consumption was reduced in the highest 2 treatment groups.
Metric 22:	Health Outcomes Unrelated to Exposure	Medium	No information was provided to either to support or dismiss differences in groups in health outcomes or attrition.
Metric 23:	Data Presentation and Analysis	High	Statistical methods were clearly described and were appropriate for the dataset(s).
Metric 24:	Reporting of Data	High	Data is adequately reported. Incidence of clinical observations (including lacrimation, periocular staining and eye discharge) is reported by treatment group.

Additional Comments: None

Overall Quality Determination**High**

Study Citation:	Hurtt, M. E., Valentine, R., Alvarez, L. (1993). Developmental toxicity of inhaled trans-1,2-dichloroethylene in the rat. Fundamental and Applied Toxicology 20(2):225-230.			
Health Outcome(s):	Nutritional/Metabolic			
Reported Health Effect(s):	Nutritional/Metabolic: Body weight Gain, food consumption			
Duration:	Reproductive/Developmental 10 days (GDs 7-16)			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1741343; Linked HERO ID(s): 1741343, 3995666			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	Test substance was identified as trans-1,2-dichloroethylene. CASRN and structure were not provided.	
	Metric 2: Test Substance Source	Low	The source of the test substance was DuPont Chemicals (Wilmington, DE). Lot number was not reported.	
	Metric 3: Test Substance Purity	High	Test substance was 99.64% pure.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	Concurrent negative control was included.	
	Metric 5: Positive Controls	N/A	Positive control was not necessary for this study.	
	Metric 6: Randomized Allocation of Animals	Medium	Computerized random sampling was utilized to allocate animals.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	High	The method and equipment used to generate the test substance vapor were appropriate and adequately described. "Test atmospheres were generated by vaporization of the test material from glass, gas-washing bottles placed in water baths regulated at 22-26C. The vaporized test material was swept into 3-neck, glass mixing flasks; filtered, conditioned dilution air was added to the mixing flasks at approximately 30 liters/min to sweep the vapors into the 150-liter square, pyramidal, stainless steel and glass exposure chambers."	
	Metric 8: Consistency of Exposure Administration	High	Exposure was administered consistently across study groups.	
	Metric 9: Reporting of Doses/Concentrations	Low	Nominal concentrations were reported (0, 6000, 9000, 12000ppm). Chamber concentrations were determined at ~30 minute intervals by gas chromatography. Mean daily chamber concentrations were reported to be within +/-5% of the target concentration throughout the test period. However, mean analytical chamber concentrations were not reported.	
	Metric 10: Exposure Frequency and Duration	Low	Dams were exposed to test substance vapor via inhalation for 6 hours/day on GDs 7-16. Current OECD 414 guidelines recommend dosing throughout the entire period of gestation (not just organogenesis), including up to the day before caesarian section (GD 21 in the case of this study). This deficiency may impact study results.	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	The concentration and number of exposure groups (i.e., 0, 6000, 9000, 12000 ppm) was acceptable and was based on the results of a pilot study.	
	Metric 12: Exposure Route and Method	Medium	The number of air changes /hour was not reported.	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	High	Test animal characteristics were reported.	
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Study Citation:	Hurtt, M. E., Valentine, R., Alvarez, L. (1993). Developmental toxicity of inhaled trans-1,2-dichloroethylene in the rat. Fundamental and Applied Toxicology 20(2):225-230.			
Health Outcome(s):	Nutritional/Metabolic			
Reported Health Effect(s):	Nutritional/Metabolic: Body weight Gain, food consumption			
Duration:	Reproductive/Developmental 10 days (GDs 7-16)			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1741343; Linked HERO ID(s): 1741343, 3995666			
Domain	Metric	Rating	Comments	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	High	Husbandry conditions were adequately reported.	
	Metric 15: Number of Animals per Group	Medium	24 animals were included per treatment group.	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	High	Outcome assessment methodology was appropriate. "Body weights were record on Days 1, 7-17, and 22; feed consumption was measured on alternate days from Days 1-19 and on Day 22."	
	Metric 17: Consistency of Outcome Assessment	High	Outcomes were assessed consistently across the groups.	
	Metric 18: Sampling Adequacy	High	Sampling was adequate for outcomes of interest.	
	Metric 19: Blinding of Assessors	N/A	Blinding was not necessary for the evaluated outcomes.	
	Metric 20: Negative Control Response	High	Negative control responses were reported and were adequate.	
Domain 6: Confounding / Variable Control				
	Metric 21: Confounding Variables in Test Design and Procedures	Low	The test substance is a respiratory irritant and therefore respiratory rates should be reported, but were not. Water intake was not reported.	
	Metric 22: Health Outcomes Unrelated to Exposure	Medium	No information was provided to either to support or dismiss differences in groups in health outcomes or attrition.	
	Metric 23: Data Presentation and Analysis	High	Statistical methods were clearly described and were appropriate for the dataset(s).	
	Metric 24: Reporting of Data	Low	Mean maternal feed consumption and mean maternal body weight changes were reported by treatment group. No measures of variability were provided for either outcome.	
Additional Comments: None				
Overall Quality Determination		High		

Study Citation:	Hurtt, M. E., Valentine, R., Alvarez, L. (1993). Developmental toxicity of inhaled trans-1,2-dichloroethylene in the rat. Fundamental and Applied Toxicology 20(2):225-230.			
Health Outcome(s):	Mortality			
Reported Health Effect(s):	Mortality: Death			
Duration:	Reproductive/Developmental 10 days (GDs 7-16)			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1741343; Linked HERO ID(s): 1741343, 3995666			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1:	Test Substance Identity	High	Test substance was identified as trans-1,2-dichloroethylene. CASRN and structure were not provided.
	Metric 2:	Test Substance Source	Low	The source of the test substance was DuPont Chemicals (Wilmington, DE). Lot number was not reported.
	Metric 3:	Test Substance Purity	High	Test substance was 99.64% pure.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	A concurrent negative control group was included.
	Metric 5:	Positive Controls	N/A	Positive control was not necessary for this study.
	Metric 6:	Randomized Allocation of Animals	Medium	Computerized random sampling was utilized to allocate animals.
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and Storage of Test Substance	High	The method and equipment used to generate the test substance vapor were appropriate and adequately described. "Test atmospheres were generated by vaporization of the test material from glass, gas-washing bottles placed in water baths regulated at 22-26C. The vaporized test material was swept into 3-neck, glass mixing flasks; filtered, conditioned dilution air was added to the mixing flasks at approximately 30 liters/min to sweep the vapors into the 150-liter square, pyramidal, stainless steel and glass exposure chambers."
	Metric 8:	Consistency of Exposure Administration	High	Exposure was administered consistently across study groups.
	Metric 9:	Reporting of Doses/Concentrations	Low	Nominal concentrations were reported (0, 6000, 9000, 12000ppm). Chamber concentrations were determined at ~30 minute intervals by gas chromatography. Mean daily chamber concentrations were reported to be within +/-5% of the target concentration throughout the test period. However, mean analytical chamber concentrations were not reported.
	Metric 10:	Exposure Frequency and Duration	Low	Dams were exposed to test substance vapor via inhalation for 6 hours/day on GDs 7-16. Current OECD 414 guidelines recommend dosing throughout the entire period of gestation (not just organogenesis), including up to the day before caesarian section (GD 21 in the case of this study). This deficiency may impact study results.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The concentration and number of exposure groups (i.e., 0, 6000, 9000, 12000 ppm) was acceptable and was based on the results of a pilot study.
	Metric 12:	Exposure Route and Method	Medium	A dynamic whole-body chamber was used. The number of air changes per hour was not reported.
Domain 4: Test Animals				
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Study Citation:	Hurt, M. E., Valentine, R., Alvarez, L. (1993). Developmental toxicity of inhaled trans-1,2-dichloroethylene in the rat. Fundamental and Applied Toxicology 20(2):225-230.
Health Outcome(s):	Mortality
Reported Health Effect(s):	Mortality: Death
Duration:	Reproductive/Developmental 10 days (GDs 7-16)
Chemical:	trans-1,2-Dichloroethylene- Parent compound
HERO ID:	1741343; Linked HERO ID(s): 1741343, 3995666

Domain	Metric	Rating	Comments
	Metric 13: Test Animal Characteristics	High	The test animal species, strain, sex, age, and starting body weight were reported, and the test animal was obtained from a commercial source.
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	High	Husbandry conditions were adequately reported.
	Metric 15: Number of Animals per Group	Medium	24 animals were included per treatment group.
Domain 5: Outcome Assessment			
	Metric 16: Outcome Assessment Methodology	High	Outcome assessment methodology was appropriate. Animals were examined twice daily.
	Metric 17: Consistency of Outcome Assessment	High	Outcomes were assessed consistently across the groups.
	Metric 18: Sampling Adequacy	High	Sampling was adequate for outcomes of interest.
	Metric 19: Blinding of Assessors	N/A	Blinding was not necessary for this outcome.
	Metric 20: Negative Control Response	High	Negative control response was appropriate. No mortality was reported.
Domain 6: Confounding / Variable Control			
	Metric 21: Confounding Variables in Test Design and Procedures	Low	The test substance is a respiratory irritant and therefore respiratory rates should be reported, but were not. Water intake was not reported. Food consumption was reduced in the highest 2 treatment groups.
	Metric 22: Health Outcomes Unrelated to Exposure	Medium	No information was provided to either to support or dismiss differences in groups in health outcomes or attrition.
	Metric 23: Data Presentation and Analysis	N/A	Statistical analysis was not necessary (clearly negative results for the outcome of interest; all animals survived to the scheduled necropsy)
	Metric 24: Reporting of Data	High	Negative findings were reported qualitatively. "All females survived to their scheduled sacrifices on day 22 of gestation."

Additional Comments: None

Overall Quality Determination**High**

Study Citation:	Hurtt, M. E., Valentine, R., Alvarez, L. (1993). Developmental toxicity of inhaled trans-1,2-dichloroethylene in the rat. Fundamental and Applied Toxicology 20(2):225-230.			
Health Outcome(s):	Reproductive/Developmental			
Reported Health Effect(s):	Reproductive/Developmental: Reproductive outcomes (# copulated, # pregnant, # litters, resorptions, corpora lutea) & developmental outcomes (# live/dead fetuses, fetal body weight, # stunted fetuses, fetal malformations, fetal variations)			
Duration:	Reproductive/Developmental 10 days (GDs 7-16)			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1741343; Linked HERO ID(s): 1741343, 3995666			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	Test substance was identified as trans-1,2-dichloroethylene. CASRN and structure were not provided.	
	Metric 2: Test Substance Source	Low	The source of the test substance was DuPont Chemicals (Wilmington, DE). Lot number was not reported.	
	Metric 3: Test Substance Purity	High	Test substance was 99.64% pure.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	Concurrent negative control was included.	
	Metric 5: Positive Controls	N/A	Positive control was not necessary for this study.	
	Metric 6: Randomized Allocation of Animals	Medium	Computerized random sampling was utilized to allocate animals.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	High	The method and equipment used to generate the test substance vapor were appropriate and adequately described. "Test atmospheres were generated by vaporization of the test material from glass, gas-washing bottles placed in water baths regulated at 22-26C. The vaporized test material was swept into 3-neck, glass mixing flasks; filtered, conditioned dilution air was added to the mixing flasks at approximately 30 liters/min to sweep the vapors into the 150-liter square, pyramidal, stainless steel and glass exposure chambers."	
	Metric 8: Consistency of Exposure Administration	High	Exposure was administered consistently across study groups.	
	Metric 9: Reporting of Doses/Concentrations	Low	Nominal concentrations were reported (0, 6000, 9000, 12000ppm). Chamber concentrations were determined at ~30 minute intervals by gas chromatography. Mean daily chamber concentrations were reported to be within +/-5% of the target concentration throughout the test period. However, mean analytical chamber concentrations were not reported.	
	Metric 10: Exposure Frequency and Duration	Low	Dams were exposed to test substance vapor via inhalation for 6 hours/day on GDs 7-16. Current OECD 414 guidelines recommend dosing throughout the entire period of gestation (not just organogenesis), including up to the day before caesarian section (GD 21 in the case of this study). This deficiency may impact study results.	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	The concentration and number of exposure groups (i.e., 0, 6000, 9000, 12000 ppm) was acceptable and was based on the results of a pilot study.	
	Metric 12: Exposure Route and Method	Medium	The number of air changes /hour was not reported.	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	High	Test animal characteristics were reported.	
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Study Citation:	Hurt, M. E., Valentine, R., Alvarez, L. (1993). Developmental toxicity of inhaled trans-1,2-dichloroethylene in the rat. Fundamental and Applied Toxicology 20(2):225-230.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Reproductive/Developmental: Reproductive outcomes (# copulated, # pregnant, # litters, resorptions, corpora lutea) & developmental outcomes (# live/dead fetuses, fetal body weight, # stunted fetuses, fetal malformations, fetal variations)
Duration:	Reproductive/Developmental 10 days (GDs 7-16)
Chemical:	trans-1,2-Dichloroethylene- Parent compound
HERO ID:	1741343; Linked HERO ID(s): 1741343, 3995666

Domain	Metric	Rating	Comments
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	High	Husbandry conditions were adequately reported.
	Metric 15: Number of Animals per Group	Medium	24 animals were included per treatment group.

Domain 5: Outcome Assessment

Metric 16:	Outcome Assessment Methodology	High	Outcome assessment methodology was appropriate.
Metric 17:	Consistency of Outcome Assessment	High	Outcomes were assessed consistently across the groups.
Metric 18:	Sampling Adequacy	High	Sampling was adequate for outcomes of interest.
Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary for the evaluated outcomes.
Metric 20:	Negative Control Response	Medium	The negative control responses were mostly adequate. However, the negative control group had unusually low resorption rate (0.3) compared to 0.6, 0.8, and 1.1 in the 2000, 6000, and 12000ppm groups, respectively. However, study authors state "The values observed in low, intermediate, and high concentration groups are all within the limits of historical control data from studies conducted within the past 2 years at this laboratory (i.e., 1.0, 0.8, 1.5, 0.5, and 0.9 mean resorptions per litter)."

Domain 6: Confounding / Variable Control

Metric 21:	Confounding Variables in Test Design and Procedures	Low	The test substance is a respiratory irritant and therefore respiratory rates should be reported, but were not. Water intake was not reported. Food consumption and body weight gain was reduced in the highest 2 treatment groups.
Metric 22:	Health Outcomes Unrelated to Exposure	Medium	No information was provided to either to support or dismiss differences in groups in health outcomes or attrition.
Metric 23:	Data Presentation and Analysis	High	Statistical methods were clearly described and were appropriate for the dataset(s).
Metric 24:	Reporting of Data	High	Data were adequately reported

Additional Comments: None

Overall Quality Determination**High**

Study Citation:	Hurtt, M. E., Valentine, R., Alvarez, L. (1993). Developmental toxicity of inhaled trans-1,2-dichloroethylene in the rat. Fundamental and Applied Toxicology 20(2):225-230.			
Health Outcome(s):	Neurological/Behavioral			
Reported Health Effect(s):	Neurological/Behavioral: Clinical observations (lethargy, salivation, alopecia, discharge vaginal opening), response to sound stimulus,			
Duration:	Reproductive/Developmental 10 days (GDs 7-16)			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1741343; Linked HERO ID(s): 1741343, 3995666			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	Test substance was identified as trans-1,2-dichloroethylene. CASRN and structure were not provided.	
	Metric 2: Test Substance Source	Low	The source of the test substance was DuPont Chemicals (Wilmington, DE). Lot number was not reported.	
	Metric 3: Test Substance Purity	High	Test substance was 99.64% pure.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	Concurrent negative control was included.	
	Metric 5: Positive Controls	N/A	Positive control was not necessary for this study.	
	Metric 6: Randomized Allocation of Animals	Medium	Computerized random sampling was utilized to allocate animals.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	High	The method and equipment used to generate the test substance vapor were appropriate and adequately described. "Test atmospheres were generated by vaporization of the test material from glass, gas-washing bottles placed in water baths regulated at 22-26C. The vaporized test material was swept into 3-neck, glass mixing flasks; filtered, conditioned dilution air was added to the mixing flasks at approximately 30 liters/min to sweep the vapors into the 150-liter square, pyramidal, stainless steel and glass exposure chambers."	
	Metric 8: Consistency of Exposure Administration	High	Exposure was administered consistently across study groups.	
	Metric 9: Reporting of Doses/Concentrations	Low	Nominal concentrations were reported (0, 6000, 9000, 12000ppm). Chamber concentrations were determined at ~30 minute intervals by gas chromatography. Mean daily chamber concentrations were reported to be within +/-5% of the target concentration throughout the test period. However, mean analytical chamber concentrations were not reported.	
	Metric 10: Exposure Frequency and Duration	Low	Dams were exposed to test substance vapor via inhalation for 6 hours/day on GDs 7-16. Current OECD 414 guidelines recommend dosing throughout the entire period of gestation (not just organogenesis), including up to the day before caesarian section (GD 21 in the case of this study). This deficiency may impact study results.	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	The concentration and number of exposure groups (i.e., 0, 6000, 9000, 12000 ppm) was acceptable and was based on the results of a pilot study.	
	Metric 12: Exposure Route and Method	Medium	The number of air changes /hour was not reported.	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	High	Test animal characteristics were reported.	

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Study Citation:	Hurtt, M. E., Valentine, R., Alvarez, L. (1993). Developmental toxicity of inhaled trans-1,2-dichloroethylene in the rat. Fundamental and Applied Toxicology 20(2):225-230.			
Health Outcome(s):	Neurological/Behavioral			
Reported Health Effect(s):	Neurological/Behavioral: Clinical observations (lethargy, salivation, alopecia, discharge vaginal opening), response to sound stimulus,			
Duration:	Reproductive/Developmental 10 days (GDs 7-16)			
Chemical:	trans-1,2-Dichloroethylene- Parent compound			
HERO ID:	1741343; Linked HERO ID(s): 1741343, 3995666			
Domain	Metric	Rating	Comments	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	High	Husbandry conditions were adequately reported.	
	Metric 15: Number of Animals per Group	Medium	24 animals were included per treatment group.	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	Medium	Animals were observed for clinical signs of toxicity twice daily before and after exposure. Response to sound stimulus was also observed. More sensitive indicators of neurological effect were not evaluated.	
	Metric 17: Consistency of Outcome Assessment	High	Outcomes were assessed consistently across the groups.	
	Metric 18: Sampling Adequacy	High	Sampling was adequate. All animals in each treatment group were observed for clinical signs of toxicity.	
	Metric 19: Blinding of Assessors	N/A	Blinding was not necessary for the evaluated outcomes.	
	Metric 20: Negative Control Response	High	Negative control response was appropriate.	
Domain 6: Confounding / Variable Control				
	Metric 21: Confounding Variables in Test Design and Procedures	Low	The test substance is a respiratory irritant and therefore respiratory rates should be reported, but were not. Water intake was not reported. Food consumption and body weight gain was reduced in the highest 2 treatment groups.	
	Metric 22: Health Outcomes Unrelated to Exposure	Medium	No information was provided to either to support or dismiss differences in groups in health outcomes or attrition.	
	Metric 23: Data Presentation and Analysis	High	Statistical methods were clearly described and were appropriate for the dataset(s).	
	Metric 24: Reporting of Data	High	Data is adequately reported. Incidence of clinical observations is reported by treatment group.	
Additional Comments: None				
Overall Quality Determination		High		

Study Citation:	Crebelli, R., Carere, A., Leopardi, P., Conti, L., Fassio, F., Raiteri, F., Barone, D., Ciliutti, P., Cinelli, S., Vericat, J. A. (1999). Evaluation of 10 aliphatic halogenated hydrocarbons in the mouse bone marrow micronucleus test. <i>Mutagenesis</i> 14(2):207-215.			
Health Outcome(s):	Genotoxicity (Genotoxicity)			
Reported Health Effect(s):	Genotoxicity (Genotoxicity): In vivo bone marrow micronucleus test			
Duration:	Acute (less than or equal to 24 hr) single dose			
Chemical:	trans-1,2-Dichloroethylene- Isomer: 1,2-Dichloroethylene			
HERO ID:	194679			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1:	Test Substance Identity	High	Chemical name and CAS number identified.
	Metric 2:	Test Substance Source	High	Source identified; no batch or lot number was reported.
	Metric 3:	Test Substance Purity	High	Purity reported as 98%
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	Vehicle control was used (olive oil)
	Metric 5:	Positive Controls	Medium	Colchicine and mitomycin C were tested as positive controls; a positive response was observed
	Metric 6:	Randomized Allocation of Animals	Medium	The study noted that mice were randomly allocated to treatment groups for the main in vivo bone marrow micronucleus test; it is not specified how the animals were randomized.
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and Storage of Test Substance	Medium	Limited test substance preparation details were provided; noted olive oil was used as a vehicle at 10 ml/kg bd wt. It is a single dose study; therefore, omission of details are unlikely to have an impact on the study.
	Metric 8:	Consistency of Exposure Administration	High	Single i.p. dose exposure administered consistently; the initial highest dose of 80% of LD50 was lowered to 70% of LD50 due to severity of clinical signs of toxicity.
	Metric 9:	Reporting of Doses/Concentrations	High	Administered doses were reported without ambiguity in the results section.
	Metric 10:	Exposure Frequency and Duration	High	Single dose
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The administered doses were reported in a range; dose levels were selected based on LD50 values determined in preliminary toxicity trials (EEC Guideline B.1 and OECD 401).
	Metric 12:	Exposure Route and Method	High	i.p. exposure
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Medium	Species, strain, sex, and source was reported; no starting age was reported and only the terminal weights were reported
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	Animal husbandry conditions were reported for the main in vivo bone marrow micronucleus test
	Metric 15:	Number of Animals per Group	Medium	5 animals/sex were tested for the bone marrow micronucleus assay
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Study Citation:	Crebelli, R., Carere, A., Leopardi, P., Conti, L., Fassio, F., Raiteri, F., Barone, D., Ciliutti, P., Cinelli, S., Vericat, J. A. (1999). Evaluation of 10 aliphatic halogenated hydrocarbons in the mouse bone marrow micronucleus test. <i>Mutagenesis</i> 14(2):207-215.			
Health Outcome(s):	Genotoxicity (Genotoxicity)			
Reported Health Effect(s):	Genotoxicity (Genotoxicity): In vivo bone marrow micronucleus test			
Duration:	Acute (less than or equal to 24 hr) single dose			
Chemical:	trans-1,2-Dichloroethylene- Isomer: 1,2-Dichloroethylene			
HERO ID:	194679			
Domain	Metric	Rating	Comments	
Domain 5: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	High	The outcome assessment methodology was reported and scoring method described.
	Metric 17:	Consistency of Outcome Assessment	High	Details of the assessment protocol were reported including harvest/scoring times
	Metric 18:	Sampling Adequacy	High	5 animals/sex
	Metric 19:	Blinding of Assessors	N/A	Not applicable
	Metric 20:	Negative Control Response	High	The biological response of the control was appropriate and adequate; "the incidence of micronucleated PCEs in vehicle-treated mice was within the accepted spontaneous range for this strain of mouse with no significant sex differences"
Domain 6: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	The study did not report all information to determine confounding factors; however, reported information did not identify differences among study groups
	Metric 22:	Health Outcomes Unrelated to Exposure	High	There was no attrition in animals in any treated animal or controls
	Metric 23:	Data Presentation and Analysis	High	Statistical methods were described; incidence were compared by X-square test, controlling for within group heterogeneity with analysis of variance. PCE/NCE ration were compared by t-test.
	Metric 24:	Reporting of Data	High	Data for exposure-related findings were presented for all outcomes by exposure group and sex
Additional Comments:	The study included results from a preliminary toxicity test used to determine dose levels for the main in vivo bone marrow micronucleus assay. The purpose of the study was the mouse bone marrow micronucleus assay, which is categorized as mechanistic/genotoxicity data.			

Overall Quality Determination**High**

Study Citation:	Crebelli, R., Carere, A., Leopardi, P., Conti, L., Fassio, F., Raiteri, F., Barone, D., Ciliutti, P., Cinelli, S., Vericat, J. A. (1999). Evaluation of 10 aliphatic halogenated hydrocarbons in the mouse bone marrow micronucleus test. <i>Mutagenesis</i> 14(2):207-215.			
Health Outcome(s):	Clinical signs (Clinical signs of toxicity)			
Reported Health Effect(s):	Clinical signs (Clinical signs of toxicity): Acute clinical signs of toxicity: piloerection, hypoactivity, hunched posture, sedation, shallow breathing			
Duration:	Acute (less than or equal to 24 hr) single dose			
Chemical:	trans-1,2-Dichloroethylene- Isomer: 1,2-Dichloroethylene			
HERO ID:	194679			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1:	Test Substance Identity	High	Chemical name and CAS number identified. Chemical name and CAS number identified.1,2-Dichloroethylene - 540-59-0; isomer of trans-1,2-dichloroethylene; reported as mixture of cis and trans isomers
	Metric 2:	Test Substance Source	High	Source identified; no batch or lot number was reported.
	Metric 3:	Test Substance Purity	High	Purity reported
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	N/A	It is not clear if negative controls were used for the preliminary acute toxicity test, though no control is required for acute lethality tests.
	Metric 5:	Positive Controls	N/A	not required for this study design
	Metric 6:	Randomized Allocation of Animals	Low	The study noted that mice were randomly allocated to treatment groups for the main in vivo bone marrow micronucleus test; however, did not specify if this was done in the preliminary toxicity trials. The preliminary toxicity trials were noted to have followed the EEC guideline B.1 and OECD 401, which required that animals are randomly selected
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and Storage of Test Substance	Medium	Limited test substance preparation details were provided; noted olive oil was used as a vehicle at 10 ml/kg bd wt.; it is a single dose study; therefore, omission of details are unlikely to have an impact on the study.
	Metric 8:	Consistency of Exposure Administration	Low	Details of exposure administration are incompletely reported for the acute lethality toxicity test
	Metric 9:	Reporting of Doses/Concentrations	Low	Administered doses were reported as a range
	Metric 10:	Exposure Frequency and Duration	High	Single dose
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Uninformative	The administered doses were reported in a range; it is unclear how many doses were tested. dose levels were selected on the basis of published LD50 values.
	Metric 12:	Exposure Route and Method	High	i.p. exposure
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Medium	Species, strain, sex, and source was reported; no starting age was reported and only the terminal weights were reported
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Animal husbandry conditions were reported for the main in vivo bone marrow micronucleus test; however, husbandry conditions for the preliminary toxicity test were not; it is unclear if they were similar.

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Study Citation:	Crebelli, R., Carere, A., Leopardi, P., Conti, L., Fassio, F., Raiteri, F., Barone, D., Ciliutti, P., Cinelli, S., Vericat, J. A. (1999). Evaluation of 10 aliphatic halogenated hydrocarbons in the mouse bone marrow micronucleus test. Mutagenesis 14(2):207-215.			
Health Outcome(s):	Clinical signs (Clinical signs of toxicity)			
Reported Health Effect(s):	Clinical signs (Clinical signs of toxicity): Acute clinical signs of toxicity: piloerection, hypoactivity, hunched posture, sedation, shallow breathing			
Duration:	Acute (less than or equal to 24 hr) single dose			
Chemical:	trans-1,2-Dichloroethylene- Isomer: 1,2-Dichloroethylene			
HERO ID:	194679			
Domain		Metric	Rating	Comments
	Metric 15:	Number of Animals per Group	Low	5 animals/sex were tested for the preliminary toxicity test; number of animals were not reported in the methods section but were reported in the results table. It is unclear how many dose groups there were and it is unclear if 5 animals per dose group were tested
Domain 5: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	Medium	The outcome assessment methodology was partially addressed; observations of clinical signs of toxicity
	Metric 17:	Consistency of Outcome Assessment	Low	There was incomplete reporting of details of outcome assessment protocol execution
	Metric 18:	Sampling Adequacy	Medium	5 animals/sex for a preliminary toxicity test; unclear if 5 animals per sex per dose
	Metric 19:	Blinding of Assessors	N/A	Not applicable
	Metric 20:	Negative Control Response	N/A	A negative control was not required
Domain 6: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	The preliminary toxicity study did not report information to determine confounding variable, but no information was reported that identified differences among the group
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	For the preliminary toxicity test, there was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure
	Metric 23:	Data Presentation and Analysis	N/A	Statistical analysis not necessary; observations of an acute toxicity test; incidence not reported.
	Metric 24:	Reporting of Data	Low	Clinical signs of toxicity were not reported by sex; incidence data were not reported
Additional Comments:	The study included results from a preliminary toxicity test used to determine dose levels for the main in vivo bone marrow micronucleus assay. The methodology and reporting are limited for the toxicity test. The purpose of the study was the mouse bone marrow micronucleus assay, which is categorized as mechanistic data. Only the apical endpoints (mortality [LD50] and signs of clinical toxicity) are included in this evaluation for this study.			

Overall Quality Determination**Uninformative**

Study Citation:	Crebelli, R., Carere, A., Leopardi, P., Conti, L., Fassio, F., Raiteri, F., Barone, D., Ciliutti, P., Cinelli, S., Vericat, J. A. (1999). Evaluation of 10 aliphatic halogenated hydrocarbons in the mouse bone marrow micronucleus test. <i>Mutagenesis</i> 14(2):207-215.
Health Outcome(s):	Mortality
Reported Health Effect(s):	Mortality: LD50
Duration:	Acute (less than or equal to 24 hr) single dose
Chemical:	trans-1,2-Dichloroethylene- Isomer: 1,2-Dichloroethylene
HERO ID:	194679

Domain	Metric	Rating	Comments
Domain 1: Test Substance			
	Metric 1: Test Substance Identity	High	Chemical name and CAS number identified. 1,2-Dichloroethylene - 540-59-0; isomer of trans-1,2-dichloroethylene; reported as mixture of cis and trans isomers
	Metric 2: Test Substance Source	High	Source identified; no batch or lot number was reported.
	Metric 3: Test Substance Purity	High	Purity reported as 98%
Domain 2: Test Design			
	Metric 4: Negative and Vehicle Controls	N/A	It is not clear if negative controls were used for the preliminary acute toxicity test, though no control is required for acute lethality tests.
	Metric 5: Positive Controls	N/A	Not required for this study design
	Metric 6: Randomized Allocation of Animals	Low	The study noted that mice were randomly allocated to treatment groups for the main in vivo bone marrow micronucleus test; however, did not specify if this was done in the preliminary toxicity trials. The preliminary toxicity trials were noted to have followed the EEC guideline B.1 and OECD 401, which required that animals are randomly selected
Domain 3: Exposure Characterization			
	Metric 7: Preparation and Storage of Test Substance	Medium	Limited test substance preparation details were provided; noted olive oil was used as a vehicle at 10 ml/kg bd wt.; it is a single dose study; therefore, omission of details are unlikely to have an impact on the study.
	Metric 8: Consistency of Exposure Administration	Low	Details of exposure administration are incompletely reported for the acute lethality toxicity test
	Metric 9: Reporting of Doses/Concentrations	Low	Administered doses were reported as a range
	Metric 10: Exposure Frequency and Duration	High	Single dose
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	Uninformative	The administered doses were reported in a range; it is unclear how many doses were tested. dose levels were selected on the basis of published LD50 values. The LD50 was higher than the upper range of administered doses
	Metric 12: Exposure Route and Method	High	i.p. exposure
Domain 4: Test Animals			
	Metric 13: Test Animal Characteristics	Medium	Species, strain, sex, and source was reported; no starting age was reported and only the terminal weights were reported
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Low	Animal husbandry conditions were reported for the main in vivo bone marrow micronucleus test; however, husbandry conditions for the preliminary toxicity test were not; it is unclear if they were similar.

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Study Citation:	Crebelli, R., Carere, A., Leopardi, P., Conti, L., Fassio, F., Raiteri, F., Barone, D., Ciliutti, P., Cinelli, S., Vericat, J. A. (1999). Evaluation of 10 aliphatic halogenated hydrocarbons in the mouse bone marrow micronucleus test. <i>Mutagenesis</i> 14(2):207-215.			
Health Outcome(s):	Mortality			
Reported Health Effect(s):	Mortality: LD50			
Duration:	Acute (less than or equal to 24 hr) single dose			
Chemical:	trans-1,2-Dichloroethylene- Isomer: 1,2-Dichloroethylene			
HERO ID:	194679			
Domain		Metric	Rating	Comments
	Metric 15:	Number of Animals per Group	Low	5 animals/sex were tested for the preliminary toxicity test; number of animals were not reported in the methods section but were reported in the results table. It is unclear how many dose groups there were and it is unclear if 5 animals per dose group were tested
Domain 5: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	Medium	The outcome assessment methodology was partially addressed; observations of deaths and 24- and 48-hour LD50 are appropriate outcomes for this endpoint.
	Metric 17:	Consistency of Outcome Assessment	Medium	There was incomplete reporting of details of outcome assessment protocol execution, but unlikely to have substantial impact on results.
	Metric 18:	Sampling Adequacy	Medium	5 animals/sex for a preliminary toxicity test; unclear if 5/sex/dose group
	Metric 19:	Blinding of Assessors	N/A	Not applicable
	Metric 20:	Negative Control Response	N/A	A negative control was not required
Domain 6: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	The preliminary toxicity study did not report information to determine confounding variable, but no information was reported that identified differences among the group
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	For the preliminary toxicity test, there was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure
	Metric 23:	Data Presentation and Analysis	Low	Methods used to derive LD50s were not reported.
	Metric 24:	Reporting of Data	Low	LD50 was not reported by sex; no confidence intervals were reported with the LD50; mortality incidence data were not reported
Additional Comments:	The study included results from a preliminary toxicity test used to determine dose levels for the main in vivo bone marrow micronucleus assay. The methodology and reporting are limited for the toxicity test. The purpose of the study was the mouse bone marrow micronucleus assay, which is categorized as mechanistic data. Only the apical endpoints (mortality [LD50] and signs of clinical toxicity) are included in this evaluation for this study.			

Overall Quality Determination**Low**

Study Citation:	[Redacted] (1999). [Redacted] Trans-1,2-dichloroethylene and cis-1,2-dichloroethylene: Inhalation median lethal concentration (LC50) study in rats.			
Health Outcome(s):	Clinical signs (Clinical signs, gross necropsy)			
Reported Health Effect(s):	Clinical signs (Clinical signs, gross necropsy): Clinical signs of toxicity, gross necropsy			
Duration:	Acute (less than or equal to 24 hr) 4 hours			
Chemical:	trans-1,2-Dichloroethylene- Isomer: cis-1,2-Dichloroethylene			
HERO ID:	8875453			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1:	Test Substance Identity	High	The test substance was identified definitively (name, synonyms, CAS No.)
	Metric 2:	Test Substance Source	Low	The test substance was supplied by the sponsor, but no other information was provided. This appears to be a confidential study in which some of the identifying information has been redacted.
	Metric 3:	Test Substance Purity	High	The purity (>99%) and known impurities were provided.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	The appropriate negative control was included (a set of male and female rats exposed to air only).
	Metric 5:	Positive Controls	N/A	A positive control is not needed for this type of study.
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups, only that rats exhibiting a normal pattern of weight gain and no overt signs of disease were selected.
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and Storage of Test Substance	High	The vapor generation system was adequately described, and storage was not necessary as it was a single exposure.
	Metric 8:	Consistency of Exposure Administration	Medium	Details of exposure administration were not completely reported, but the missing information is unlikely to have a substantial impact on results.
	Metric 9:	Reporting of Doses/Concentrations	High	The test concentration mean, S.D., range, and number of samples taken were reported.
	Metric 10:	Exposure Frequency and Duration	High	The exposure duration and frequency were appropriate for the purpose of the study (acute lethality).
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The number of exposure groups and dose space were appropriate for the purpose of the study (acute lethality).
	Metric 12:	Exposure Route and Method	High	The route and method of exposure were reported and appropriate for the test substance.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	High	The test animal species, strain, sex, age, and starting body weights were reported. The source of the animals was redacted. The test species was appropriate for the outcome of interest (acute toxicity).
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were reported (temperature, humidity, light/dark cycle, diet, and water availability). The water source was redacted. There is no indication that any of these conditions differed between groups.
	Metric 15:	Number of Animals per Group	Medium	The number of animals per group was reported and acceptable for this type of study.

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Study Citation:	[Redacted] (1999). [Redacted] Trans-1,2-dichloroethylene and cis-1,2-dichloroethylene: Inhalation median lethal concentration (LC50) study in rats.		
Health Outcome(s):	Clinical signs (Clinical signs, gross necropsy)		
Reported Health Effect(s):	Clinical signs (Clinical signs, gross necropsy): Clinical signs of toxicity, gross necropsy		
Duration:	Acute (less than or equal to 24 hr) 4 hours		
Chemical:	trans-1,2-Dichloroethylene- Isomer: cis-1,2-Dichloroethylene		
HERO ID:	8875453		
Domain	Metric	Rating	Comments
Domain 5: Outcome Assessment			
Metric 16:	Outcome Assessment Methodology	High	The outcome methodology was adequate and addressed the intended outcome (clinical signs/gross necropsy).
Metric 17:	Consistency of Outcome Assessment	Medium	No information was provided on the timing of the outcome assessment, but it is unlikely to impact results.
Metric 18:	Sampling Adequacy	High	The sampling was adequate for the intended outcome.
Metric 19:	Blinding of Assessors	Medium	Blinding was not reported, although the concern for bias was mitigated due to the simple nature of the outcome (basic clinical signs/gross necropsy).
Metric 20:	Negative Control Response	High	No effects were noted in the negative control group.
Domain 6: Confounding / Variable Control			
Metric 21:	Confounding Variables in Test Design and Procedures	Medium	There is no information to suggest or dismiss that confounders were present. All animals were accounted for, but some measures were not reported (breathing rates, food and water intake).
Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
Metric 23:	Data Presentation and Analysis	N/A	Statistical analysis was not conducted but is not required for the measured outcome (clinical signs/gross necropsy).
Metric 24:	Reporting of Data	High	Clinical signs and gross necropsy data were presented for individual animals.
Additional Comments:	This form is associated with the cis-1,2-Dichloroethylene study.		

Overall Quality Determination**High**

Study Citation:	[Redacted] (1999). [Redacted] Trans-1,2-dichloroethylene and cis-1,2-dichloroethylene: Inhalation median lethal concentration (LC50) study in rats.			
Health Outcome(s):	Nutritional/Metabolic			
Reported Health Effect(s):	Nutritional/Metabolic: Body weight			
Duration:	Acute (less than or equal to 24 hr) 4 hours			
Chemical:	trans-1,2-Dichloroethylene- Isomer: cis-1,2-Dichloroethylene			
HERO ID:	8875453			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	The test substance was identified definitively (name, synonyms, CAS No.)	
	Metric 2: Test Substance Source	Low	The test substance was supplied by the sponsor, but no other information was provided. This appears to be a confidential study in which some of the identifying information has been redacted.	
	Metric 3: Test Substance Purity	High	The purity (>99%) and known impurities were provided.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	The appropriate negative control was included (a set of male and female rats exposed to air only).	
	Metric 5: Positive Controls	N/A	A positive control is not needed for this type of study.	
	Metric 6: Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups, only that rats exhibiting a normal pattern of weight gain and no overt signs of disease were selected.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	High	The vapor generation system was adequately described, and storage was not necessary as it was a single exposure.	
	Metric 8: Consistency of Exposure Administration	Medium	Details of exposure administration were not completely reported, but the missing information is unlikely to have a substantial impact on results.	
	Metric 9: Reporting of Doses/Concentrations	High	The test concentration mean, S.D., range, and number of samples taken were reported.	
	Metric 10: Exposure Frequency and Duration	High	The exposure duration and frequency were appropriate for the purpose of the study (acute lethality).	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	The number of exposure groups and dose space were appropriate for the purpose of the study (acute lethality).	
	Metric 12: Exposure Route and Method	High	The route and method of exposure were reported and appropriate for the test substance.	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	High	The test animal species, strain, sex, age, and starting body weights were reported. The source of the animals was redacted. The test species was appropriate for the outcome of interest (acute toxicity).	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were reported (temperature, humidity, light/dark cycle, diet, and water availability). The water source was redacted. There is no indication that any of these conditions differed between groups.	
	Metric 15: Number of Animals per Group	Medium	The number of animals per group was reported and acceptable for this type of study.	
Domain 5: Outcome Assessment				
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Study Citation:	[Redacted] (1999). [Redacted] Trans-1,2-dichloroethylene and cis-1,2-dichloroethylene: Inhalation median lethal concentration (LC50) study in rats.			
Health Outcome(s):	Nutritional/Metabolic			
Reported Health Effect(s):	Nutritional/Metabolic: Body weight			
Duration:	Acute (less than or equal to 24 hr) 4 hours			
Chemical:	trans-1,2-Dichloroethylene- Isomer: cis-1,2-Dichloroethylene			
HERO ID:	8875453			
Domain	Metric	Rating	Comments	
	Metric 16: Outcome Assessment Methodology	High	The outcome methodology was adequate and addressed the intended outcome (body weight effects).	
	Metric 17: Consistency of Outcome Assessment	Medium	No information was provided on the timing of the outcome assessment, but it is unlikely to impact results.	
	Metric 18: Sampling Adequacy	High	The sampling was adequate for the intended outcome.	
	Metric 19: Blinding of Assessors	N/A	Blinding was not reported, although it was a simple and objective measure (body weight).	
	Metric 20: Negative Control Response	High	No effects were noted in the negative control group.	
Domain 6: Confounding / Variable Control				
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	There is no information to suggest or dismiss that confounders were present. All animals were accounted for, but some measures were not reported (breathing rates, food and water intake).	
	Metric 22: Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.	
	Metric 23: Data Presentation and Analysis	High	Statistical analysis was not conducted, but individual body weight data were reported and sufficient to conduct an independent analysis.	
	Metric 24: Reporting of Data	High	Body weight data were presented for individual animals.	
Additional Comments:	This form is associated with the cis-1,2-Dichloroethylene study.			

Overall Quality Determination**High**

Study Citation:	[Redacted] (1999). [Redacted] Trans-1,2-dichloroethylene and cis-1,2-dichloroethylene: Inhalation median lethal concentration (LC50) study in rats.			
Health Outcome(s):	Mortality			
Reported Health Effect(s):	Mortality: LC50			
Duration:	Acute (less than or equal to 24 hr) 4 hours			
Chemical:	trans-1,2-Dichloroethylene- Isomer: cis-1,2-Dichloroethylene			
HERO ID:	8875453			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	The test substance was identified definitively (name, synonyms, CAS No.)	
	Metric 2: Test Substance Source	Low	The test substance was supplied by the sponsor, but no other information was provided. This appears to be a confidential study in which some of the identifying information has been redacted.	
	Metric 3: Test Substance Purity	High	The purity (>99%) and known impurities were provided.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	The appropriate negative control was included (a set of male and female rats exposed to air only).	
	Metric 5: Positive Controls	N/A	A positive control is not needed for this type of study.	
	Metric 6: Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups, only that rats exhibiting a normal pattern of weight gain and no overt signs of disease were selected.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	High	The vapor generation system was adequately described, and storage was not necessary as it was a single exposure.	
	Metric 8: Consistency of Exposure Administration	Medium	Details of exposure administration were not completely reported, but the missing information is unlikely to have a substantial impact on results.	
	Metric 9: Reporting of Doses/Concentrations	High	The test concentration mean, S.D., range, and number of samples taken were reported.	
	Metric 10: Exposure Frequency and Duration	High	The exposure duration and frequency were appropriate for the purpose of the study (acute lethality).	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	The number of exposure groups and dose space were appropriate for the purpose of the study (acute lethality).	
	Metric 12: Exposure Route and Method	High	The route and method of exposure were reported and appropriate for the test substance.	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	High	The test animal species, strain, sex, age, and starting body weights were reported. The source of the animals was redacted. The test species was appropriate for the outcome of interest (acute toxicity).	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were reported (temperature, humidity, light/dark cycle, diet, and water availability). The water source was redacted. There is no indication that any of these conditions differed between groups.	
	Metric 15: Number of Animals per Group	Medium	The number of animals per group was reported and acceptable for this type of study.	
Domain 5: Outcome Assessment				
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Study Citation:	[Redacted] (1999). [Redacted] Trans-1,2-dichloroethylene and cis-1,2-dichloroethylene: Inhalation median lethal concentration (LC50) study in rats.			
Health Outcome(s):	Mortality			
Reported Health Effect(s):	Mortality: LC50			
Duration:	Acute (less than or equal to 24 hr) 4 hours			
Chemical:	trans-1,2-Dichloroethylene- Isomer: cis-1,2-Dichloroethylene			
HERO ID:	8875453			
Domain	Metric	Rating	Comments	
	Metric 16: Outcome Assessment Methodology	High	The outcome methodology was adequate and addressed the intended outcome (lethality).	
	Metric 17: Consistency of Outcome Assessment	Medium	No information was provided on the timing of the outcome assessment, but it is unlikely to impact results.	
	Metric 18: Sampling Adequacy	High	The sampling was adequate for the intended outcome.	
	Metric 19: Blinding of Assessors	N/A	Blinding was not reported or required.	
	Metric 20: Negative Control Response	High	No effects were noted in the negative control group.	
Domain 6: Confounding / Variable Control				
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	There is no information to suggest or dismiss that confounders were present. All animals were accounted for, but some measures were not reported (breathing rates, food and water intake).	
	Metric 22: Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.	
	Metric 23: Data Presentation and Analysis	N/A	Statistical analysis was not conducted but is not required for mortality data.	
	Metric 24: Reporting of Data	High	Mortality data were presented across exposure groups and for individual animals.	
Additional Comments:	This form is associated with the cis-1,2-Dichloroethylene study.			
Overall Quality Determination		High		

Study Citation:	[Redacted] (1999). [Redacted] Trans-1,2-dichloroethylene and cis-1,2-dichloroethylene: Inhalation median lethal concentration (LC50) study in rats.			
Health Outcome(s):	Renal/Kidney; Cardiovascular; Lung/Respiratory; Hepatic/Liver;			
Reported Health Effect(s):	Renal/Kidney: Kidney histopathology; Cardiovascular: Heart histopathology; Lung/Respiratory: Lung histopathology; Hepatic/Liver: Liver histopathology;			
Duration:	Acute (less than or equal to 24 hr) 4 hours			
Chemical:	trans-1,2-Dichloroethylene- Isomer: cis-1,2-Dichloroethylene			
HERO ID:	8875453			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
Metric 1:	Test Substance Identity	High	All Outcomes: The test substance was identified definitively (name, synonyms, CAS No.)	
Metric 2:	Test Substance Source	Low	All Outcomes: The test substance was supplied by the sponsor, but no other information was provided. This appears to be a confidential study in which some of the identifying information has been redacted.	
Metric 3:	Test Substance Purity	High	All Outcomes: The purity (>99%) and known impurities were provided.	
Domain 2: Test Design				
Metric 4:	Negative and Vehicle Controls	High	All Outcomes: The appropriate negative control was included (a set of male and female rats exposed to air only).	
Metric 5:	Positive Controls	N/A	All Outcomes: A positive control is not needed for this type of study.	
Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: The study did not report how animals were allocated to study groups, only that rats exhibiting a normal pattern of weight gain and no overt signs of disease were selected.	
Domain 3: Exposure Characterization				
Metric 7:	Preparation and Storage of Test Substance	High	All Outcomes: The vapor generation system was adequately described, and storage was not necessary as it was a single exposure.	
Metric 8:	Consistency of Exposure Administration	Medium	All Outcomes: Details of exposure administration were not completely reported, but the missing information is unlikely to have a substantial impact on results.	
Metric 9:	Reporting of Doses/Concentrations	High	All Outcomes: The test concentration mean, S.D., range, and number of samples taken were reported.	
Metric 10:	Exposure Frequency and Duration	High	All Outcomes: The exposure duration and frequency were appropriate for the purpose of the study (acute lethality).	
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: The number of exposure groups and dose space were appropriate for the purpose of the study (acute lethality).	
Metric 12:	Exposure Route and Method	High	All Outcomes: The route and method of exposure were reported and appropriate for the test substance.	
Domain 4: Test Animals				
Metric 13:	Test Animal Characteristics	High	All Outcomes: The test animal species, strain, sex, age, and starting body weights were reported. The source of the animals was redacted. The test species was appropriate for the outcome of interest (acute toxicity).	
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: All husbandry conditions were reported (temperature, humidity, light/dark cycle, diet, and water availability). The water source was redacted. There is no indication that any of these conditions differed between groups.	
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Study Citation:	[Redacted] (1999). [Redacted] Trans-1,2-dichloroethylene and cis-1,2-dichloroethylene: Inhalation median lethal concentration (LC50) study in rats.			
Health Outcome(s):	Renal/Kidney; Cardiovascular; Lung/Respiratory; Hepatic/Liver;			
Reported Health Effect(s):	Renal/Kidney: Kidney histopathology; Cardiovascular: Heart histopathology; Lung/Respiratory: Lung histopathology; Hepatic/Liver: Liver histopathology;			
Duration:	Acute (less than or equal to 24 hr) 4 hours			
Chemical:	trans-1,2-Dichloroethylene- Isomer: cis-1,2-Dichloroethylene			
HERO ID:	8875453			
Domain	Metric	Rating	Comments	
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: The number of animals per group was reported and acceptable for this type of study.
Domain 5: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	Medium	Renal/Kidney: The outcome methodology partially addressed the intended outcome (kidney effects) as histology was conducted without examining kidney weight or function.; Cardiovascular: The outcome methodology partially addressed the intended outcome (heart effects) as histology was conducted without examining heart weight or function.; Lung/Respiratory: The outcome methodology partially addressed the intended outcome (lung effects) as histology was conducted without examining lung weight or function.; Hepatic/Liver: The outcome methodology partially addressed the intended outcome (liver effects) as histology was conducted without examining liver weight or function.
	Metric 17:	Consistency of Outcome Assessment	Medium	All Outcomes: No information was provided on the timing of the outcome assessment, but it is unlikely to impact results.
	Metric 18:	Sampling Adequacy	High	All Outcomes: The sampling was adequate for the intended outcome.
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding was not reported, although it is not recommended for screening level histopathology.
	Metric 20:	Negative Control Response	High	All Outcomes: No effects were noted in the negative control group.
Domain 6: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: There is no information to suggest or dismiss that confounders were present. All animals were accounted for, but some measures were not reported (breathing rates, food and water intake).
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.
	Metric 23:	Data Presentation and Analysis	N/A	Renal/Kidney: Statistical analysis was not conducted but is not required for the measured outcome (kidney histopathology).; Cardiovascular: Statistical analysis was not conducted but is not required for the measured outcome (heart histopathology).; Lung/Respiratory: Statistical analysis was not conducted but is not required for the measured outcome (lung histopathology).; Hepatic/Liver: Statistical analysis was not conducted but is not required for the measured outcome (liver histopathology).
	Metric 24:	Reporting of Data	High	Renal/Kidney: Kidney histopathology data were presented for individual animals.; Cardiovascular: Heart histopathology data were presented for individual animals.; Lung/Respiratory: Lung histopathology data were presented for individual animals.; Hepatic/Liver: Liver histopathology data were presented for individual animals.
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Study Citation:	[Redacted] (1999). [Redacted] Trans-1,2-dichloroethylene and cis-1,2-dichloroethylene: Inhalation median lethal concentration (LC50) study in rats.
Health Outcome(s):	Renal/Kidney; Cardiovascular; Lung/Respiratory; Hepatic/Liver;
Reported Health Effect(s):	Renal/Kidney: Kidney histopathology; Cardiovascular: Heart histopathology; Lung/Respiratory: Lung histopathology; Hepatic/Liver: Liver histopathology;
Duration:	Acute (less than or equal to 24 hr) 4 hours
Chemical:	trans-1,2-Dichloroethylene- Isomer: cis-1,2-Dichloroethylene
HERO ID:	8875453

Domain	Metric	Rating	Comments
Additional Comments:	This form is associated with the cis-1,2-Dichloroethylene study.		

Overall Quality Determination**High**

Study Citation:	Eger, E. I., Halsey, M. J., Koblin, D. D., Laster, M. J., Ionescu, P., Königsberger, K., Fan, R., Nguyen, B. V., Hudlicky, T. (2001). The convulsant and anesthetic properties of cis-trans isomers of 1,2-dichlorohexafluorocyclobutane and 1,2-dichloroethylene. <i>Anesthesia and Analgesia</i> 93(4):922-927.			
Health Outcome(s):	Neurological/Behavioral			
Reported Health Effect(s):	Neurological/Behavioral: Convulsant and anesthetic properties			
Duration:	Acute (less than or equal to 24 hr) Acute; cis-1,2-DCE			
Chemical:	trans-1,2-Dichloroethylene- Isomer: cis-1,2-Dichloroethylene			
HERO ID:	2310561			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
Metric 1:	Test Substance Identity	High	Test substance was clearly identified by standard nomenclature; structure also provided.	
Metric 2:	Test Substance Source	Low	A commercial source was identified; batch and lot numbers were not provided	
Metric 3:	Test Substance Purity	Medium	The purity of the purchased isomer was 97%. Enrichment of the 2N mixture for the cis isomer yielded enriched mixtures containing 93.6% cis and 6.4% trans-1,2-DCE for one batch, and 91.0% and 9% cis and trans isomers, respectively, for the second batch. The overall purity was reported to be 99.8%, but it was noted that the mixture also contained 3.2% of the 1,3 isomers.	
Domain 2: Test Design				
Metric 4:	Negative and Vehicle Controls	N/A	Not relevant to the study type	
Metric 5:	Positive Controls	N/A	Not relevant for the study type	
Metric 6:	Randomized Allocation of Animals	Low	Allocation method not described.	
Domain 3: Exposure Characterization				
Metric 7:	Preparation and Storage of Test Substance	Low	Generation of test substance atmospheres was partially described	
Metric 8:	Consistency of Exposure Administration	Low	Details of exposure administration were insufficiently reported to determine whether there was consistency of exposure between the two groups of 4 animals	
Metric 9:	Reporting of Doses/Concentrations	Uninformative	No administered exposure concentrations were explicitly reported. The test system was injected with amounts estimated to achieve approximately 60% of the predicted MAC	
Metric 10:	Exposure Frequency and Duration	Low	This information is not clearly reported. At least 20 min to reach equilibrium was indicated; another description in the text indicated it took 100 min to determine MAC	
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Uninformative	Concentrations were not provided, increasing concentrations (not specified) were added until an MAC was reached. There was a single group.	
Metric 12:	Exposure Route and Method	Low	Details of exposure administration were not clearly described.	
Domain 4: Test Animals				
Metric 13:	Test Animal Characteristics	Medium	Species, strain, sex, source, and body weight ranges were reported. Animal age was not provided.	
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Some animal husbandry conditions were reported: light/dark cycle, #/cage, and access to food and water.	
Metric 15:	Number of Animals per Group	Medium	There were 8 animal/group for some experiments, and 4/group for others. The numbers seemed to be appropriate for evaluating the outcome of interest.	

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Study Citation:	Eger, E. I., Halsey, M. J., Koblin, D. D., Laster, M. J., Ionescu, P., Königsberger, K., Fan, R., Nguyen, B. V., Hudlicky, T. (2001). The convulsant and anesthetic properties of cis-trans isomers of 1,2-dichlorohexafluorocyclobutane and 1,2-dichloroethylene. Anesthesia and Analgesia 93(4):922-927.			
Health Outcome(s):	Neurological/Behavioral			
Reported Health Effect(s):	Neurological/Behavioral: Convulsant and anesthetic properties			
Duration:	Acute (less than or equal to 24 hr) Acute; cis-1,2-DCE			
Chemical:	trans-1,2-Dichloroethylene- Isomer: cis-1,2-Dichloroethylene			
HERO ID:	2310561			
Domain	Metric	Rating	Comments	
Domain 5: Outcome Assessment				
Metric 16:	Outcome Assessment Methodology	Medium	Some outcome methods (e.g., determination olive oil/gas; octanol/gas; and saline/gas partition coefficients) were cited to another reference (Full-text/FT not available)	
Metric 17:	Consistency of Outcome Assessment	Low	Consistency of outcome assessment was limited or not reported.	
Metric 18:	Sampling Adequacy	Low	Details regarding sampling of outcomes were not reported	
Metric 19:	Blinding of Assessors	N/A	Not necessary for this study type	
Metric 20:	Negative Control Response	N/A	No control groups were included	
Domain 6: Confounding / Variable Control				
Metric 21:	Confounding Variables in Test Design	Medium	The study did not report confounding variables	
Metric 22:	and Procedures Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure (e.g., infection) that could influence the outcome assessment.	
Metric 23:	Data Presentation and Analysis	N/A	No comparisons were made	
Metric 24:	Reporting of Data	Medium	Means and measures of variance were reported for the outcomes of interest.	
Additional Comments:	The purpose of the study was to investigate the correlation of convulsant and anesthetic properties with lipophilicity. The primary endpoint of interest was to determine the MAC (minimum alveolar concentration of anesthetic required to produce an absence of motor response to electrical stimulation of the tail in 50% of test rats) or immobility. Several metrics on this form were not applicable to the design of this study. This study does not provide usable data for evaluating the toxicity of the compound(s) of interest and is more informative for ADME.Additional experiments were performed to determine blood/gas partition coefficients as well as olive-oil/gas, octanol/gas, and saline/gas partition coefficients for each isomer, these were not considered in the evaluation.			

Overall Quality Determination**Uninformative**

Study Citation:	Jenkins, L. J., Trabulus, M. J., Murphy, S. D. (1972). Biochemical effects of 1,1-dichloroethylene in rats - Comparison with carbon-tetrachloride and 1,2-dichloroethylene. Toxicology and Applied Pharmacology 23(3):501-510.			
Health Outcome(s):	Hepatic/Liver			
Reported Health Effect(s):	Hepatic/Liver: Plasma ALT, ALP and liver enzymes (glucose-6-phosphatase, tyrosine transaminase, alkaline phosphatase)			
Duration:	Acute (less than or equal to 24 hr) Single dose			
Chemical:	trans-1,2-Dichloroethylene- Isomer: cis-1,2-Dichloroethylene			
HERO ID:	1748282			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1:	Test Substance Identity	High	Test substance was identified as cis 1,2-dichloroethylene.
	Metric 2:	Test Substance Source	High	The source of the test substance was K & K Laboratories, Inc., Plainview, NY.
	Metric 3:	Test Substance Purity	Low	The test substance purity not reported.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	Negative controls received the vehicle corn oil.
	Metric 5:	Positive Controls	N/A	Positive control was not required in this study.
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated.
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and Storage of Test Substance	Medium	Storage is not reported however the assay is a single dose study so this is unlikely to have a substantial impact.
	Metric 8:	Consistency of Exposure Administration	High	Exposure was administered consistently across study groups. Gavage volume was appropriate (2ml/kg).
	Metric 9:	Reporting of Doses/Concentrations	Medium	Only the nominal level was reported but this is unlikely to have a substantial impact on results.
	Metric 10:	Exposure Frequency and Duration	High	Exposure to test substance was appropriate (single exposure).
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	There were minor limitations on concentrations (full range of responses not seen); justification for choosing doses was not provided.
	Metric 12:	Exposure Route and Method	High	The route of exposure was appropriate.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Medium	Age of rats were not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Temperature, humidity, and light-dark cycle were not reported.
	Metric 15:	Number of Animals per Group	Low	The number of animals evaluated/group was reported to be 3-4, which is lower than is typically used for this type of study.
Domain 5: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	Medium	Liver and serum enzymes were measured, however, liver histology or weights were not evaluated.
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Study Citation:	Jenkins, L. J., Trabulus, M. J., Murphy, S. D. (1972). Biochemical effects of 1,1-dichloroethylene in rats - Comparison with carbon-tetrachloride and 1,2-dichloroethylene. Toxicology and Applied Pharmacology 23(3):501-510.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	Hepatic/Liver: Plasma ALT, ALP and liver enzymes (glucose-6-phosphatase, tyrosine transaminase, alkaline phosphatase)
Duration:	Acute (less than or equal to 24 hr) Single dose
Chemical:	trans-1,2-Dichloroethylene- Isomer: cis-1,2-Dichloroethylene
HERO ID:	1748282

Domain	Metric	Rating	Comments
	Metric 17: Consistency of Outcome Assessment	Medium	Details of protocols were minimal and cited in other papers. Authors state all animals were sacrificed between 10am and noon.
	Metric 18: Sampling Adequacy	Low	The number of animals evaluated/group was adequate n= 3-4. The small number of animals per group could have impacted the number of results that could have been found to be statistically significant.
	Metric 19: Blinding of Assessors	N/A	Blinding was not necessary for this study because outcomes were not subjective.
	Metric 20: Negative Control Response	High	The negative control responses were appropriate.
Domain 6: Confounding / Variable Control			
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	Although the study did not report all information to determine confounding, reported information did not identify differences among study groups.
	Metric 22: Health Outcomes Unrelated to Exposure	Medium	No information was provided to either to support or dismiss differences in groups in health outcomes or attrition.
	Metric 23: Data Presentation and Analysis	Low	Statistical analysis was performed but not described adequately.
	Metric 24: Reporting of Data	High	Outcome data were reported sufficiently.

Additional Comments: None

Overall Quality Determination**Medium**

Study Citation:	Nakahama, T., Sarutani, S., Inouye, Y. (2000). Effects of chlorinated ethylenes on expression of rat CYP forms: Comparative study on correlation between biological activities and chemical structures. Journal of Health Science 46(4):251-258.			
Health Outcome(s):	Nutritional/Metabolic			
Reported Health Effect(s):	Nutritional/Metabolic: Change in body weight			
Duration:	Acute (less than or equal to 24 hr) Single injection- cis-1,2-dichloroethylene			
Chemical:	trans-1,2-Dichloroethylene- Isomer: cis-1,2-Dichloroethylene			
HERO ID:	1747837			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	Test substance was identified as cis-1,2-dichloroethylene.	
	Metric 2: Test Substance Source	High	The source of the test substance was Aldrich Chemical Co. (USA).	
	Metric 3: Test Substance Purity	Low	The purity of test substance was not reported.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	Appropriate negative controls were included (corn-oil dosing).	
	Metric 5: Positive Controls	N/A	A positive control was not needed.	
	Metric 6: Randomized Allocation of Animals	Low	The study does not report how animals were allocated.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Low	The preparation and storage of test substance were not reported. Given the volatility of the test substance this information is needed.	
	Metric 8: Consistency of Exposure Administration	Low	The volume of test substance or corn oil per body weight administered was not reported.	
	Metric 9: Reporting of Doses/Concentrations	High	Dose was reported without ambiguity.	
	Metric 10: Exposure Frequency and Duration	High	Exposure frequency was appropriate (single injection).	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	Low	Only one dose was studied, and justification was not provided.	
	Metric 12: Exposure Route and Method	High	The route and method of exposure was appropriate for a volatile compound.	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	Medium	Starting body weights were reported as approximately 200 g (exact body weight was not provided). The sex of the animals was only reported in the abstract.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were not reported.	
	Metric 15: Number of Animals per Group	Medium	The numbers of animals/group were appropriate (n=4-6).	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	High	The outcome assessment methodology addresses the outcome of interest.	
	Metric 17: Consistency of Outcome Assessment	Medium	The timing of body weight measurements was reported and it is assumed the methodology was applied consistently. However, the method of how the animals were sacrificed was not reported.	

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Study Citation:	Nakahama, T., Sarutani, S., Inouye, Y. (2000). Effects of chlorinated ethylenes on expression of rat CYP forms: Comparative study on correlation between biological activities and chemical structures. Journal of Health Science 46(4):251-258.
Health Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Nutritional/Metabolic: Change in body weight
Duration:	Acute (less than or equal to 24 hr) Single injection- cis-1,2-dichloroethylene
Chemical:	trans-1,2-Dichloroethylene- Isomer: cis-1,2-Dichloroethylene
HERO ID:	1747837

Domain	Metric	Rating	Comments
	Metric 18: Sampling Adequacy	High	The number of animals evaluated was adequate for outcomes of interest.
	Metric 19: Blinding of Assessors	N/A	Blinding was not needed to assess outcomes.
	Metric 20: Negative Control Response	High	The negative control response was appropriate.
Domain 6: Confounding / Variable Control			
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	Body weight changes were identified, but not food/water intake differences.
	Metric 22: Health Outcomes Unrelated to Exposure	Medium	There was no information to support or dismiss the suggestion of health outcomes differences unrelated to exposure.
	Metric 23: Data Presentation and Analysis	High	Statistical analysis was performed and appropriate.
	Metric 24: Reporting of Data	Medium	Data were reported for changes to body weight as the mean of the percent change in body weight +/- S.E (n=4-6). The actual body weights of the mice during the course of the study were not reported.

Additional Comments: The main goal of the study is to characterize changes to cytochrome P450 activity and protein content. Therefore, the only endpoints used to evaluate organ toxicity was changes to liver and lung weights. As this was an acute, single dose study, there may not have been a significant dosing window to show a change in organ weights, and the route of administration may not be the best choice to study acute pulmonary toxicity.

Overall Quality Determination

Medium

Study Citation:	Nakahama, T., Sarutani, S., Inouye, Y. (2000). Effects of chlorinated ethylenes on expression of rat CYP forms: Comparative study on correlation between biological activities and chemical structures. Journal of Health Science 46(4):251-258.			
Health Outcome(s):	Hepatic/Liver			
Reported Health Effect(s):	Hepatic/Liver: Change in liver weight			
Duration:	Acute (less than or equal to 24 hr) Single injection- cis-1,2-dichloroethylene			
Chemical:	trans-1,2-Dichloroethylene- Isomer: cis-1,2-Dichloroethylene			
HERO ID:	1747837			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1:	Test Substance Identity	High	Test substance was identified as cis-1,2-dichloroethylene.
	Metric 2:	Test Substance Source	High	The source of the test substance was Aldrich Chemical Co. (USA).
	Metric 3:	Test Substance Purity	Low	The purity of test substance was not reported.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	Appropriate negative controls were included (corn-oil dosing).
	Metric 5:	Positive Controls	N/A	A positive control was not needed.
	Metric 6:	Randomized Allocation of Animals	Low	The study does not report how animals were allocated.
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and Storage of Test Substance	Low	The preparation and storage of test substance were not reported. Given the volatility of the test substance this information is needed.
	Metric 8:	Consistency of Exposure Administration	Low	The volume of test substance or corn oil per body weight administered was not reported.
	Metric 9:	Reporting of Doses/Concentrations	High	Dose was reported without ambiguity.
	Metric 10:	Exposure Frequency and Duration	High	Exposure frequency was appropriate (single injection).
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	Only one dose was studied, and justification was not provided.
	Metric 12:	Exposure Route and Method	High	The route and method of exposure was appropriate for a volatile compound.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Medium	Starting body weights were reported as approximately 200 g (exact body weight was not provided). The sex of the animals was only reported in the abstract.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were not reported.
	Metric 15:	Number of Animals per Group	Medium	The numbers of animals/group were appropriate (n=4-6).
Domain 5: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	Medium	The only measure of hepatic toxicity was changes to liver weight. No serum chemistry or histopathology was performed.
	Metric 17:	Consistency of Outcome Assessment	Medium	There was incomplete reporting of minor detail of outcome assessment protocol execution, but these are unlikely to substantially impact results.
	Metric 18:	Sampling Adequacy	High	The number of animals evaluated was adequate for outcomes of interest.
	Metric 19:	Blinding of Assessors	N/A	Blinding was not needed to assess outcomes.

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Study Citation:	Nakahama, T., Sarutani, S., Inouye, Y. (2000). Effects of chlorinated ethylenes on expression of rat CYP forms: Comparative study on correlation between biological activities and chemical structures. Journal of Health Science 46(4):251-258.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	Hepatic/Liver: Change in liver weight
Duration:	Acute (less than or equal to 24 hr) Single injection- cis-1,2-dichloroethylene
Chemical:	trans-1,2-Dichloroethylene- Isomer: cis-1,2-Dichloroethylene
HERO ID:	1747837

Domain	Metric	Rating	Comments
	Metric 20: Negative Control Response	High	The negative control response was appropriate.
Domain 6: Confounding / Variable Control			
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	Body weight changes were identified, but not food/water intake differences.
	Metric 22: Health Outcomes Unrelated to Exposure	Medium	There was no information to support or dismiss the suggestion of health outcomes differences unrelated to exposure.
	Metric 23: Data Presentation and Analysis	High	Statistical analysis was performed and appropriate.
	Metric 24: Reporting of Data	Medium	Data were reported for changes to liver weights as the mean +/- S.E (n=4-6). Liver weights were reported g/100 g body weight. The absolute weights were not reported.

Additional Comments: The main goal of the study is to characterize changes to cytochrome P450 activity and protein content. Therefore, the only endpoints used to evaluate organ toxicity was changes to liver and lung weights. As this was an acute, single dose study, there may not have been a significant dosing window to show a change in organ weights, and the route of administration may not be the best choice to study acute pulmonary toxicity.

Overall Quality Determination

Medium

Study Citation:	Nakahama, T., Sarutani, S., Inouye, Y. (2000). Effects of chlorinated ethylenes on expression of rat CYP forms: Comparative study on correlation between biological activities and chemical structures. Journal of Health Science 46(4):251-258.			
Health Outcome(s):	Lung/Respiratory			
Reported Health Effect(s):	Lung/Respiratory: Change in lung weight			
Duration:	Acute (less than or equal to 24 hr) Single injection- cis-1,2-dichloroethylene			
Chemical:	trans-1,2-Dichloroethylene- Isomer: cis-1,2-Dichloroethylene			
HERO ID:	1747837			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	Test substance was identified as cis-1,2-dichloroethylene.	
	Metric 2: Test Substance Source	High	The source of the test substance was Aldrich Chemical Co. (USA).	
	Metric 3: Test Substance Purity	Low	The purity of test substance was not reported.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	Appropriate negative controls were included (corn-oil dosing).	
	Metric 5: Positive Controls	N/A	A positive control was not needed.	
	Metric 6: Randomized Allocation of Animals	Low	The study does not report how animals were allocated.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Low	The preparation and storage of test substance were not reported. Given the volatility of the test substance this information is needed.	
	Metric 8: Consistency of Exposure Administration	Low	The volume of test substance or corn oil per body weight administered was not reported.	
	Metric 9: Reporting of Doses/Concentrations	High	Dose was reported without ambiguity.	
	Metric 10: Exposure Frequency and Duration	High	Exposure frequency was appropriate (single injection).	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	Low	Only one dose was studied, and justification was not provided.	
	Metric 12: Exposure Route and Method	Medium	Route of exposure was appropriate for a volatile compound. However, as this looked to assess toxicity to the lung the route of administration was not the most appropriate. Inhalation would have been the best choice for this type of assay.	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	Medium	Starting body weights were reported as approximately 200 g (exact body weight was not provided). The sex of the animals was only reported in the abstract.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were not reported.	
	Metric 15: Number of Animals per Group	Medium	The numbers of animals/group were appropriate (n=4-6).	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	Medium	The only measure of pulmonary toxicity was changes to weight of the lungs. No histopathology or assessment of pulmonary function was performed.	
	Metric 17: Consistency of Outcome Assessment	Medium	There was incomplete reporting of minor detail of outcome assessment protocol execution, but these are unlikely to substantially impact results.	

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Study Citation:	Nakahama, T., Sarutani, S., Inouye, Y. (2000). Effects of chlorinated ethylenes on expression of rat CYP forms: Comparative study on correlation between biological activities and chemical structures. Journal of Health Science 46(4):251-258.
Health Outcome(s):	Lung/Respiratory
Reported Health Effect(s):	Lung/Respiratory: Change in lung weight
Duration:	Acute (less than or equal to 24 hr) Single injection- cis-1,2-dichloroethylene
Chemical:	trans-1,2-Dichloroethylene- Isomer: cis-1,2-Dichloroethylene
HERO ID:	1747837

Domain	Metric	Rating	Comments
	Metric 18: Sampling Adequacy	High	The number of animals evaluated was adequate for outcomes of interest.
	Metric 19: Blinding of Assessors	N/A	Blinding was not needed to assess outcomes.
	Metric 20: Negative Control Response	High	The negative control response was appropriate.
Domain 6: Confounding / Variable Control			
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	Body weight changes were identified, but not food/water intake differences.
	Metric 22: Health Outcomes Unrelated to Exposure	Medium	There was no information to support or dismiss the suggestion of health outcomes differences unrelated to exposure.
	Metric 23: Data Presentation and Analysis	High	Statistical analysis was preformed and appropriate.
	Metric 24: Reporting of Data	Medium	Data were reported for changes to lung weights as the mean +/- S.E (n=4-6). Lung weights were reported g/100 g body weight. The absolute weights were not reported.
Additional Comments:	The main goal of the study is to characterize changes to cytochrome P450 activity and protein content. Therefore, the only endpoints used to evaluate organ toxicity was changes to liver and lung weights. As this was an acute, single dose study, there may not have been a significant dosing window to show a change in organ weights, and the route of administration may not be the best choice to study acute pulmonary toxicity.		

Overall Quality Determination**Medium**

Study Citation:	Plaa, G. L., Larson, R. E. (1965). Relative nephrotoxic properties of chlorinated methane, ethane, and ethylene derivatives in mice. Toxicology and Applied Pharmacology 7(1):37-44.			
Health Outcome(s):	Renal/Kidney			
Reported Health Effect(s):	Renal/Kidney: Urinary glucose and protein; renal histopathology			
Duration:	Acute (less than or equal to 24 hr) Acute- single dose			
Chemical:	trans-1,2-Dichloroethylene- Isomer: cis-1,2-Dichloroethylene			
HERO ID:	64411			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
Metric 1:	Test Substance Identity	High	Test substance was identified as cis-1,2-dichloroethylene.	
Metric 2:	Test Substance Source	Low	The source of the test substance was not reported.	
Metric 3:	Test Substance Purity	Low	The purity of the test substance was not reported.	
Domain 2: Test Design				
Metric 4:	Negative and Vehicle Controls	Uninformative	Details of negative control are not reported. It appears the data on the negative controls come from historic data. The strain, age, sex of the animals are not provided nor is information on if the animals were sham or untreated.	
Metric 5:	Positive Controls	N/A	Not applicable for this study.	
Metric 6:	Randomized Allocation of Animals	Low	Authors do not report if how study groups were formed.	
Domain 3: Exposure Characterization				
Metric 7:	Preparation and Storage of Test Substance	Low	Preparation and storage conditions were not properly reported given the volatility of the test substance.	
Metric 8:	Consistency of Exposure Administration	Medium	Details of exposure administration are incomplete.	
Metric 9:	Reporting of Doses/Concentrations	High	Exposure doses were reported without ambiguity.	
Metric 10:	Exposure Frequency and Duration	High	Exposure and frequency were appropriate for outcome studied.	
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	There were minor limitation in dose spacing.	
Metric 12:	Exposure Route and Method	High	Route of exposure was i.p. injection.	
Domain 4: Test Animals				
Metric 13:	Test Animal Characteristics	Low	The source and age of the mice was not reported.	
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were not reported.	
Metric 15:	Number of Animals per Group	Medium	The number of animals exposed/group was not reported as 10 in each group (Table 4 legend).	
Domain 5: Outcome Assessment				
Metric 16:	Outcome Assessment Methodology	Medium	Some details regarding the outcome assessment methodology were lacking (e.g how long urine was collected for).	

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Study Citation:	Plaa, G. L., Larson, R. E. (1965). Relative nephrotoxic properties of chlorinated methane, ethane, and ethylene derivatives in mice. Toxicology and Applied Pharmacology 7(1):37-44.			
Health Outcome(s):	Renal/Kidney			
Reported Health Effect(s):	Renal/Kidney: Urinary glucose and protein; renal histopathology			
Duration:	Acute (less than or equal to 24 hr) Acute- single dose			
Chemical:	trans-1,2-Dichloroethylene- Isomer: cis-1,2-Dichloroethylene			
HERO ID:	64411			
Domain	Metric	Rating	Comments	
	Metric 17: Consistency of Outcome Assessment	High	Outcomes were assessed consistently across study groups.	
	Metric 18: Sampling Adequacy	Medium	The sampling was adequate (all surviving mice)	
	Metric 19: Blinding of Assessors	N/A	Blinding was not necessary for outcomes studied.	
	Metric 20: Negative Control Response	High	Negative control responses for urinary parameters were reported in text and were appropriate for some outcomes.	
Domain 6: Confounding / Variable Control				
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	Study did not report all information to determine confounding, reported information did not identify differences among study groups.	
	Metric 22: Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure.	
	Metric 23: Data Presentation and Analysis	Low	Statistics analysis were not performed. Significance of increased urinary glucose or protein was determined by a cutoff number set by the authors.	
	Metric 24: Reporting of Data	Medium	Incidence data is provided for presence of urinary glucose or protein above cutoff level. The measured level of glucose and protein would be more useful.	

Additional Comments: Study is rated as unacceptable based on lack of information regarding the negative control.

Overall Quality Determination

Uninformative

Study Citation:	Plaa, G. L., Larson, R. E. (1965). Relative nephrotoxic properties of chlorinated methane, ethane, and ethylene derivatives in mice. Toxicology and Applied Pharmacology 7(1):37-44.			
Health Outcome(s):	Mortality			
Reported Health Effect(s):	Mortality: Mortality			
Duration:	Acute (less than or equal to 24 hr) Acute- single dose			
Chemical:	trans-1,2-Dichloroethylene- Isomer: cis-1,2-Dichloroethylene			
HERO ID:	64411			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1:	Test Substance Identity	High	Test substance was identified as cis-1,1-dichloroethylene.
	Metric 2:	Test Substance Source	Low	The source of the test substance was not reported.
	Metric 3:	Test Substance Purity	Low	The purity of the test substance was not reported.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	Uninformative	Details of negative control are not reported. It appears the data on the negative controls come from historic data. The strain, age, sex of the animals are not provided nor is information on if the animals were sham or untreated.
	Metric 5:	Positive Controls	N/A	Not applicable for this study.
	Metric 6:	Randomized Allocation of Animals	Low	Authors do not report if how study groups were formed.
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and Storage of Test Substance	Low	Preparation and storage conditions were not properly reported given the volatility of the test substance.
	Metric 8:	Consistency of Exposure Administration	Medium	Details of exposure administration are incomplete.
	Metric 9:	Reporting of Doses/Concentrations	High	Exposure doses were reported without ambiguity.
	Metric 10:	Exposure Frequency and Duration	High	Exposure and frequency were appropriate for outcome studied.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	There were minor limitation in dose spacing.
	Metric 12:	Exposure Route and Method	High	Route of exposure was i.p. injection.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Low	The source and age of the mice was not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were not reported.
	Metric 15:	Number of Animals per Group	Medium	The number of animals exposed/group was not reported as 10 in each group (Table 4 legend).
Domain 5: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	Medium	Details regarding the outcome assessment methodology were lacking.
	Metric 17:	Consistency of Outcome Assessment	High	Outcomes were assessed consistently across study groups.
	Metric 18:	Sampling Adequacy	Medium	The sampling was adequate.
	Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary for outcomes studied.

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Study Citation:	Plaa, G. L., Larson, R. E. (1965). Relative nephrotoxic properties of chlorinated methane, ethane, and ethylene derivatives in mice. Toxicology and Applied Pharmacology 7(1):37-44.			
Health Outcome(s):	Mortality			
Reported Health Effect(s):	Mortality: Mortality			
Duration:	Acute (less than or equal to 24 hr) Acute- single dose			
Chemical:	trans-1,2-Dichloroethylene- Isomer: cis-1,2-Dichloroethylene			
HERO ID:	64411			
Domain	Metric		Rating	Comments
	Metric 20:	Negative Control Response	Low	Negative control responses was not reported.
Domain 6: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Study did not report all information to determine confounding, reported information did not identify differences among study groups.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure.
	Metric 23:	Data Presentation and Analysis	High	Statistics analysis were not performed but data is presented so that independent analysis can be done.
	Metric 24:	Reporting of Data	High	Mortality data is adequately presented.
Additional Comments: Study is rated as unacceptable based on lack of information regarding the negative control.				

Overall Quality Determination**Uninformative**

Study Citation:	McCauley, P. T., Robinson, M., Daniel, F. B., Olson, G. R. (1995). The effects of subacute and subchronic oral exposure to cis-1,2-dichloroethylene in Sprague-Dawley rats. Drug and Chemical Toxicology 18(2-3):171-184.			
Health Outcome(s):	Hepatic/Liver; Renal/Kidney;			
Reported Health Effect(s):	Hepatic/Liver: Organ weights, related clinical chemistry (ALT, LDH, AST, cholesterol), and histopathology; (note: glucose may also be relevant); Renal/Kidney: Kidney weights, associated clinical chemistry (BUN, creatinine), histopathology (kidney, bladder); note (glucose may also be relevant);			
Duration:	Short-term (>1-30 days) 14 days			
Chemical:	trans-1,2-Dichloroethylene- Isomer: cis-1,2-Dichloroethylene			
HERO ID:	5237			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
Metric 1:	Test Substance Identity	High	All Outcomes: Identified by name and CASRN: cis-1,2-dichloroethylene (CASRN: 156-59-2)	
Metric 2:	Test Substance Source	High	All Outcomes: Commercial source and lot numbers were provided.	
Metric 3:	Test Substance Purity	High	All Outcomes: Reported as 97% pure; impurities were not reported, but 97% purity is considered acceptably high.	
Domain 2: Test Design				
Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Concurrent Vehicle (corn oil) control	
Metric 5:	Positive Controls	N/A	All Outcomes: Not necessary for the study type	
Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: Animals were ear tagged and randomly assigned to vehicle and control groups using a computer generated set of random numbers	
Domain 3: Exposure Characterization				
Metric 7:	Preparation and Storage of Test Substance	Low	All Outcomes: Information on preparation and storage were not provided and the test substance is a volatile chemical	
Metric 8:	Consistency of Exposure Administration	High	All Outcomes: A low, but appropriate gavage volume (3mL/kg) was consistently applied daily across all groups.	
Metric 9:	Reporting of Doses/Concentrations	High	All Outcomes: Doses were clearly reported both as mmol/kg/day and as mg/kg/day	
Metric 10:	Exposure Frequency and Duration	High	All Outcomes: Daily gavage	
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: The study included 5 exposure groups (including control)	
Metric 12:	Exposure Route and Method	High	All Outcomes: Oral gavage	
Domain 4: Test Animals				
Metric 13:	Test Animal Characteristics	Medium	All Outcomes: Animal species, strain, age, sex, and commercial source were reported. Starting body weights were not provided, but since animals were randomly assigned, this is unlikely to have an impact on results.	
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: Animal husbandry conditions (temp, humidity, light/dark cycle, food and water availability) were reported and appropriate. The study noted all aspects of the study were conducted under guidelines of the American Association of Accreditation of Laboratory Animal Care.	
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Study Citation:	McCauley, P. T., Robinson, M., Daniel, F. B., Olson, G. R. (1995). The effects of subacute and subchronic oral exposure to cis-1,2-dichloroethylene in Sprague-Dawley rats. Drug and Chemical Toxicology 18(2-3):171-184.			
Health Outcome(s):	Hepatic/Liver; Renal/Kidney;			
Reported Health Effect(s):	Hepatic/Liver: Organ weights, related clinical chemistry (ALT, LDH, AST, cholesterol), and histopathology; (note: glucose may also be relevant); Renal/Kidney: Kidney weights, associated clinical chemistry (BUN, creatinine), histopathology (kidney, bladder); note (glucose may also be relevant);			
Duration:	Short-term (>1-30 days) 14 days			
Chemical:	trans-1,2-Dichloroethylene- Isomer: cis-1,2-Dichloroethylene			
HERO ID:	5237			
Domain	Metric	Rating	Comments	
	Metric 15: Number of Animals per Group	Low	All Outcomes: The number of animals per group was not reported; however, appropriate statistical tests were performed indicating enough animals were included for statistical analysis.	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	High	All Outcomes: Relative but not absolute organ weights were measured.	
	Metric 17: Consistency of Outcome Assessment	High	All Outcomes: Consistent assessment across groups for some endpoints.	
	Metric 18: Sampling Adequacy	Medium	All Outcomes: Some endpoints (histology) performed on control and high-dose groups only. The number of animals evaluated/group was not provided.	
	Metric 19: Blinding of Assessors	N/A	All Outcomes: Blinding of assessors is not necessary for the outcome evaluated.	
	Metric 20: Negative Control Response	High	All Outcomes: The study did not indicate any concerns over control responses for this organ/system.	
Domain 6: Confounding / Variable Control				
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	All Outcomes: The study did not report all information to determine confounding. High-dose animals (both sexes) were reported to have a significant increase in water consumption (20% increase for females and 35% increase for males) compared with controls. It is unclear what impact this could have had on the outcomes of interest.	
	Metric 22: Health Outcomes Unrelated to Exposure	Low	All Outcomes: The study summary indicates there were "gavage-related deaths" in the high dose group in the 14-day study, and that there were "gavage-related deaths in both controls and high dose groups in the 90-day study. Although not explicitly stated, it is assumed these are procedural mortalities (due to gavage) and not related to the test substance. It is unclear what confounding effects these deaths may have had on accurately assessing the actual outcome of interest (e.g., it is unclear how many animals in each group died).	
	Metric 23: Data Presentation and Analysis	High	All Outcomes: Statistical analysis was described and appropriate for the outcomes of interest.	
	Metric 24: Reporting of Data	Medium	All Outcomes: Histology results were reported in the text-only indicating no significant compound-related changes were observed. Bodyweight measurements were not provided in conjunction with relative organ weights.	
Additional Comments:	This study had several reporting deficiencies including the number of animals treated/group and details of the number and sex of animals that died at the high-dose, which makes interpretation of results from that dose-group difficult. For example, it is unclear how many high-dose animals remained for organ weight measurements and histopathology (n = not reported). Histopathology was performed on control and high-dose animals only; due to the reported deaths at the high-dose, it would have been appropriate to perform histopathological examinations on tissues from other dose groups.			

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Study Citation:	McCauley, P. T., Robinson, M., Daniel, F. B., Olson, G. R. (1995). The effects of subacute and subchronic oral exposure to cis-1,2-dichloroethylene in Sprague-Dawley rats. Drug and Chemical Toxicology 18(2-3):171-184.
Health Outcome(s):	Hepatic/Liver; Renal/Kidney;
Reported Health Effect(s):	Hepatic/Liver: Organ weights, related clinical chemistry (ALT, LDH, AST, cholesterol), and histopathology; (note: glucose may also be relevant); Renal/Kidney: Kidney weights, associated clinical chemistry (BUN, creatinine), histopathology (kidney, bladder); note (glucose may also be relevant);
Duration:	Short-term (>1-30 days) 14 days
Chemical:	trans-1,2-Dichloroethylene- Isomer: cis-1,2-Dichloroethylene
HERO ID:	5237

Domain	Metric	Rating	Comments
Overall Quality Determination		High	

Study Citation:	McCauley, P. T., Robinson, M., Daniel, F. B., Olson, G. R. (1995). The effects of subacute and subchronic oral exposure to cis-1,2-dichloroethylene in Sprague-Dawley rats. Drug and Chemical Toxicology 18(2-3):171-184.			
Health Outcome(s):	Mortality			
Reported Health Effect(s):	Mortality: Mortality			
Duration:	Short-term (>1-30 days) 14 days			
Chemical:	trans-1,2-Dichloroethylene- Isomer: cis-1,2-Dichloroethylene			
HERO ID:	5237			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
Metric 1:	Test Substance Identity	High	Identified by name and CASRN: cis-1,2-dichloroethylene (CASRN: 156-59-2)	
Metric 2:	Test Substance Source	High	Commercial source and lot numbers were provided.	
Metric 3:	Test Substance Purity	High	Reported as 97% pure; impurities were not reported, but 97% purity is considered acceptably high.	
Domain 2: Test Design				
Metric 4:	Negative and Vehicle Controls	High	Concurrent Vehicle (corn oil) control	
Metric 5:	Positive Controls	N/A	Not necessary for the study type	
Metric 6:	Randomized Allocation of Animals	Medium	Animals were ear tagged and randomly assigned to vehicle and control groups using a computer generated set of random numbers	
Domain 3: Exposure Characterization				
Metric 7:	Preparation and Storage of Test Substance	Low	Information on preparation and storage were not provided and the test substance is a volatile chemical	
Metric 8:	Consistency of Exposure Administration	High	A low, but appropriate gavage volume (3mL/kg) was consistently applied daily across all groups.	
Metric 9:	Reporting of Doses/Concentrations	High	Doses were clearly reported both as mmol/kg/day and as mg/kg/day	
Metric 10:	Exposure Frequency and Duration	High	Daily gavage	
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The study included 5 exposure groups (including control)	
Metric 12:	Exposure Route and Method	High	Oral gavage	
Domain 4: Test Animals				
Metric 13:	Test Animal Characteristics	Medium	Animal species, strain, age, sex, and commercial source were reported. Starting body weights were not provided, but since animals were randomly assigned, this is unlikely to have an impact on results.	
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	Animal husbandry conditions (temp, humidity, light/dark cycle, food and water availability) were reported and appropriate. The study noted all aspects of the study were conducted under guidelines of the American Association of Accreditation of Laboratory Animal Care.	
Metric 15:	Number of Animals per Group	Low	The number of animals per group was not reported; however, appropriate statistical tests were performed indicating enough animals were included for statistical analysis.	
Domain 5: Outcome Assessment				
Metric 16:	Outcome Assessment Methodology	High	Out come assessment methodology was appropriate	
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Study Citation:	McCauley, P. T., Robinson, M., Daniel, F. B., Olson, G. R. (1995). The effects of subacute and subchronic oral exposure to cis-1,2-dichloroethylene in Sprague-Dawley rats. Drug and Chemical Toxicology 18(2-3):171-184.			
Health Outcome(s):	Mortality			
Reported Health Effect(s):	Mortality: Mortality			
Duration:	Short-term (>1-30 days) 14 days			
Chemical:	trans-1,2-Dichloroethylene- Isomer: cis-1,2-Dichloroethylene			
HERO ID:	5237			
Domain	Metric		Rating	Comments
	Metric 17:	Consistency of Outcome Assessment	Medium	Limited details of outcome assessment were reported (frequency of monitoring for mortality); this is unlikely to have have an impact on the results.
	Metric 18:	Sampling Adequacy	High	It is assumed that all animals in all treatment groups were monitored for mortality.
	Metric 19:	Blinding of Assessors	N/A	Blinding of assessors is not necessary for the outcome evaluated.
	Metric 20:	Negative Control Response	Low	Specific results from the control group were not reported.
Domain 6: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	The study did not report all information to determine confounding. High-dose animals (both sexes) were reported to have a significant increase in water consumption (20% increase for females and 35% increase for males) compared with controls. It is unclear what impact this could have had on the outcomes of interest. No changes in final body weights were noted despite increased water consumption
	Metric 22:	Health Outcomes Unrelated to Exposure	Low	The study summary indicates there were "gavage-related deaths" in the high dose group in the 14-day study, and that there were "gavage-related deaths in both controls and high dose groups in the 90-day study. Although not explicitly stated, it is assumed these are procedural mortalities (due to gavage) and not related to the test substance. It is unclear what confounding effects these deaths may have had on accurately assessing the actual outcome of interest.
	Metric 23:	Data Presentation and Analysis	High	statistical analysis was described and appropriate for the outcomes of interest.
	Metric 24:	Reporting of Data	Low	Results for the endpoint of interest were ambiguously reported in the text only. The text does not specifically report if mortalities were or were not observed in specific dose groups. Only that "gavage related deaths were present at the high dose," without further explanation.
Additional Comments:	Mortality results were ambiguously reported in a 14-day RD study in which male and female rats (number per group unknown) were administered the test substance orally, via gavage.			

Overall Quality Determination**Medium**

Study Citation:	McCauley, P. T., Robinson, M., Daniel, F. B., Olson, G. R. (1995). The effects of subacute and subchronic oral exposure to cis-1,2-dichloroethylene in Sprague-Dawley rats. Drug and Chemical Toxicology 18(2-3):171-184.			
Health Outcome(s):	Clinical chemistry (Clinical chemistry): Remaining clinical chemistry parameters that may be relevant to multiple organ systems (calcium and phosphorus, glucose)			
Reported Health Effect(s):	Clinical chemistry (Clinical chemistry): Remaining clinical chemistry parameters that may be relevant to multiple organ systems (calcium and phosphorus, glucose)			
Duration:	Short-term (>1-30 days) 14 days			
Chemical:	trans-1,2-Dichloroethylene- Isomer: cis-1,2-Dichloroethylene			
HERO ID:	5237			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	Identified by name and CASRN: cis-1,2-dichloroethylene (CASRN: 156-59-2)	
	Metric 2: Test Substance Source	High	Commercial source and lot numbers were provided.	
	Metric 3: Test Substance Purity	High	Reported as 97% pure; impurities were not reported, but 97% purity is considered acceptably high.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	Concurrent Vehicle (corn oil) control	
	Metric 5: Positive Controls	N/A	Not necessary for the study type	
	Metric 6: Randomized Allocation of Animals	Medium	Animals were ear tagged and randomly assigned to vehicle and control groups using a computer generated set of random numbers	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Low	Information on preparation and storage were not provided and the test substance is a volatile chemical	
	Metric 8: Consistency of Exposure Administration	High	A low, but appropriate gavage volume (3mL/kg) was consistently applied daily across all groups.	
	Metric 9: Reporting of Doses/Concentrations	High	Doses were clearly reported both as mmol/kg/day and as mg/kg/day	
	Metric 10: Exposure Frequency and Duration	High	Daily gavage	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	The study included 5 exposure groups (including control)	
	Metric 12: Exposure Route and Method	High	Oral gavage	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	Medium	Animal species, strain, age, sex, and commercial source were reported. Starting body weights were not provided, but since animals were randomly assigned, this is unlikely to have an impact on results.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	High	Animal husbandry conditions (temp, humidity, light/dark cycle, food and water availability) were reported and appropriate. The study noted all aspects of the study were conducted under guidelines of the American Association of Accreditation of Laboratory Animal Care.	
	Metric 15: Number of Animals per Group	Low	The number of animals per group was not reported; however, appropriate statistical tests were performed indicating enough animals were included for statistical analysis.	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	Medium	Limited evaluation of organ/system-related endpoints (histology on limited tissues only)	
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Study Citation:	McCauley, P. T., Robinson, M., Daniel, F. B., Olson, G. R. (1995). The effects of subacute and subchronic oral exposure to cis-1,2-dichloroethylene in Sprague-Dawley rats. Drug and Chemical Toxicology 18(2-3):171-184.			
Health Outcome(s):	Clinical chemistry (Clinical chemistry): Remaining clinical chemistry parameters that may be relevant to multiple organ systems (calcium and phosphorus, glucose)			
Reported Health Effect(s):	Clinical chemistry (Clinical chemistry): Remaining clinical chemistry parameters that may be relevant to multiple organ systems (calcium and phosphorus, glucose)			
Duration:	Short-term (>1-30 days) 14 days			
Chemical:	trans-1,2-Dichloroethylene- Isomer: cis-1,2-Dichloroethylene			
HERO ID:	5237			
Domain	Metric	Rating	Comments	
	Metric 17: Consistency of Outcome Assessment	High	Consistent assessment across groups for some endpoints.	
	Metric 18: Sampling Adequacy	Medium	Some endpoints (histology) performed on control and high-dose groups only. The number of animals evaluated/group was not provided.	
	Metric 19: Blinding of Assessors	N/A	Blinding of assessors is not necessary for the outcome evaluated.	
	Metric 20: Negative Control Response	High	The study did not indicate any concerns over control responses for this organ/system.	
Domain 6: Confounding / Variable Control				
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	The study did not report all information to determine confounding. High-dose animals (both sexes) were reported to have a significant increase in water consumption (20% increase for females and 35% increase for males) compared with controls. It is unclear what impact this could have had on the outcomes of interest.	
	Metric 22: Health Outcomes Unrelated to Exposure	Low	The study summary indicates there were "gavage-related deaths" in the high dose group in the 14-day study, and that there were "gavage-related deaths in both controls and high dose groups in the 90-day study. Although not explicitly stated, it is assumed these are procedural mortalities (due to gavage) and not related to the test substance. It is unclear what confounding effects these deaths may have had on accurately assessing the actual outcome of interest (e.g., it is unclear how many animals in each group died).	
	Metric 23: Data Presentation and Analysis	High	Statistical analysis was described and appropriate for the outcomes of interest. The text indicated that due to extreme values and high variability, a nonparametric analysis of variance was used.	
	Metric 24: Reporting of Data	High	Data for all dose groups was reported	
Additional Comments:	This study had several reporting deficiencies including the number of animals treated/group and details of the number and sex of animals that died at the high-dose, making interpretation of results from that dose-group difficult. For example, it is unclear how many high-dose animals remained at the end of the study (n = not reported).			

Overall Quality Determination**High**

Study Citation:	McCauley, P. T., Robinson, M., Daniel, F. B., Olson, G. R. (1995). The effects of subacute and subchronic oral exposure to cis-1,2-dichloroethylene in Sprague-Dawley rats. Drug and Chemical Toxicology 18(2-3):171-184.			
Health Outcome(s):	Neurological/Behavioral; Nutritional/Metabolic;			
Reported Health Effect(s):	Neurological/Behavioral: Clinical signs (agitation, lethargy, ataxia); brain organ weight; histology (brain, sciatic nerve); Nutritional/Metabolic: Body weight; food and water consumption;			
Duration:	Short-term (>1-30 days) 14 days			
Chemical:	trans-1,2-Dichloroethylene- Isomer: cis-1,2-Dichloroethylene			
HERO ID:	5237			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1:	Test Substance Identity	High	All Outcomes: Identified by name and CASRN: cis-1,2-dichloroethylene (CASRN: 156-59-2)
	Metric 2:	Test Substance Source	High	All Outcomes: Commercial source and lot numbers were provided.
	Metric 3:	Test Substance Purity	High	All Outcomes: Reported as 97% pure; impurities were not reported, but 97% purity is considered acceptably high.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Concurrent Vehicle (corn oil) control
	Metric 5:	Positive Controls	N/A	All Outcomes: Not necessary for the study type
	Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: Animals were ear tagged and randomly assigned to vehicle and control groups using a computer generated set of random numbers
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and Storage of Test Substance	Low	All Outcomes: Information on preparation and storage were not provided and the test substance is a volatile chemical
	Metric 8:	Consistency of Exposure Administration	High	All Outcomes: A low, but appropriate gavage volume (3mL/kg) was consistently applied daily across all groups.
	Metric 9:	Reporting of Doses/Concentrations	High	All Outcomes: Doses were clearly reported both as mmol/kg/day and as mg/kg/day
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: Daily gavage
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: The study included 5 exposure groups (including control)
	Metric 12:	Exposure Route and Method	High	All Outcomes: Oral gavage
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Medium	All Outcomes: Animal species, strain, age, sex, and commercial source were reported. Starting body weights were not provided, but since animals were randomly assigned, this is unlikely to have an impact on results.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: Animal husbandry conditions (temp, humidity, light/dark cycle, food and water availability) were reported and appropriate. The study noted all aspects of the study were conducted under guidelines of the American Association of Accreditation of Laboratory Animal Care.
	Metric 15:	Number of Animals per Group	Low	All Outcomes: The number of animals per group was not reported; however, appropriate statistical tests were performed indicating enough animals were included for statistical analysis.

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Study Citation:	McCauley, P. T., Robinson, M., Daniel, F. B., Olson, G. R. (1995). The effects of subacute and subchronic oral exposure to cis-1,2-dichloroethylene in Sprague-Dawley rats. Drug and Chemical Toxicology 18(2-3):171-184.
Health Outcome(s):	Neurological/Behavioral; Nutritional/Metabolic;
Reported Health Effect(s):	Neurological/Behavioral: Clinical signs (agitation, lethargy, ataxia); brain organ weight; histology (brain, sciatic nerve); Nutritional/Metabolic: Body weight; food and water consumption;
Duration:	Short-term (>1-30 days) 14 days
Chemical:	trans-1,2-Dichloroethylene- Isomer: cis-1,2-Dichloroethylene
HERO ID:	5237

Domain	Metric	Rating	Comments
Domain 5: Outcome Assessment			
	Metric 16: Outcome Assessment Methodology	Medium	Neurological/Behavioral: Limited evaluation of neurological endpoints. Relative but not absolute organ weights were measured.; Nutritional/Metabolic: Limited evaluation of organ/system-related endpoints.
	Metric 17: Consistency of Outcome Assessment	High	All Outcomes: Consistent assessment across groups for some endpoints.
	Metric 18: Sampling Adequacy	Medium	All Outcomes: Some endpoints (histology) performed on control and high-dose groups only. The number of animals evaluated/group was not provided.
	Metric 19: Blinding of Assessors	N/A	All Outcomes: Blinding of assessors is not necessary for the outcome evaluated.
	Metric 20: Negative Control Response	High	All Outcomes: The study did not indicate any concerns over control responses for this organ/system.
Domain 6: Confounding / Variable Control			
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	All Outcomes: The study did not report all information to determine confounding. High-dose animals (both sexes) were reported to have a significant increase in water consumption (20% increase for females and 35% increase for males) compared with controls. It is unclear what impact this could have had on the outcomes of interest.
	Metric 22: Health Outcomes Unrelated to Exposure	Low	All Outcomes: The study summary indicates there were "gavage-related deaths" in the high dose group in the 14-day study, and that there were "gavage-related deaths in both controls and high dose groups in the 90-day study. Although not explicitly stated, it is assumed these are procedural mortalities (due to gavage) and not related to the test substance. It is unclear what confounding effects these deaths may have had on accurately assessing the actual outcome of interest (e.g., it is unclear how many animals in each group died).
	Metric 23: Data Presentation and Analysis	High	All Outcomes: Statistical analysis was described and appropriate for the outcomes of interest.
	Metric 24: Reporting of Data	Low	Neurological/Behavioral: Histology results were reported in the text-only indicating no significant compound-related changes were observed. Bodyweight measurements were not provided in conjunction with relative organ weights, although the text indicated no differences were observed. Incidence data for clinical observations were not provided.; Nutritional/Metabolic: Weekly body weight data were collected, but not reported. Empirical body weight measurements were not provided. The text reported no changes.
Additional Comments:	This study had several reporting deficiencies including the number of animals treated/group and details of the number and sex of animals that died at the high-dose, which makes interpretation of results from that dose-group difficult. For example, it is unclear how many high-dose animals remained at the end of the study for tissue collection (n = not reported). Histopathology was performed on control and high-dose animals only; due to the reported deaths at the high-dose, it would have been appropriate to perform histopathological examinations on tissues from other dose groups.		

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Study Citation:	McCauley, P. T., Robinson, M., Daniel, F. B., Olson, G. R. (1995). The effects of subacute and subchronic oral exposure to cis-1,2-dichloroethylene in Sprague-Dawley rats. Drug and Chemical Toxicology 18(2-3):171-184.
Health Outcome(s):	Neurological/Behavioral; Nutritional/Metabolic;
Reported Health Effect(s):	Neurological/Behavioral: Clinical signs (agitation, lethargy, ataxia); brain organ weight; histology (brain, sciatic nerve); Nutritional/Metabolic: Body weight; food and water consumption;
Duration:	Short-term (>1-30 days) 14 days
Chemical:	trans-1,2-Dichloroethylene- Isomer: cis-1,2-Dichloroethylene
HERO ID:	5237

Domain	Metric	Rating	Comments
Overall Quality Determination		High	

Study Citation:	McCauley, P. T., Robinson, M., Daniel, F. B., Olson, G. R. (1995). The effects of subacute and subchronic oral exposure to cis-1,2-dichloroethylene in Sprague-Dawley rats. Drug and Chemical Toxicology 18(2-3):171-184.			
Health Outcome(s):	Lung/Respiratory; Reproductive/Developmental; Cardiovascular; Gastrointestinal; Endocrine (Endocrine); Skin/Connective Tissue; Musculoskeletal; Ocular/Sensory; Immune/Hematological;			
Reported Health Effect(s):	Lung/Respiratory: Histology (lung, brochi, nasal cavity, nasal turbinates); Reproductive/Developmental: Ovary Wt.; Histology (seminal vesicles, prostate, testes, epididymides, uterus, mammary glands, preputial or clitoral glands); Cardiovascular: Histology (heart, aorta); Gastrointestinal: Histology (ileum, duodenum, colon, jejunum, stomach, esophagus, tongue, salivary gland, cecum); Endocrine (Endocrine): Adrenal Organ Wt.; Histology (pituitary, adrenals, thyroid, pancreas, parathyroid); Skin/Connective Tissue: Histology (skin); Musculoskeletal: Histology (thigh muscle, femur or vertebrae, sternum); Ocular/Sensory: Histology (Zymbal gland); Immune/Hematological: Hematology (RBC, WBC, hemoglobin, hematocrit etc.); Spleen and thymus organ weights; histology (spleen, madibular and mesenteric lymph nodes, bone marrow, thymus);			
Duration:	Short-term (>1-30 days) 14 days			
Chemical:	trans-1,2-Dichloroethylene- Isomer: cis-1,2-Dichloroethylene			
HERO ID:	5237			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	All Outcomes: Identified by name and CASRN: cis-1,2-dichloroethylene (CASRN: 156-59-2)	
	Metric 2: Test Substance Source	High	All Outcomes: Commercial source and lot numbers were provided.	
	Metric 3: Test Substance Purity	High	All Outcomes: Reported as 97% pure; impurities were not reported, but 97% purity is considered acceptably high.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	All Outcomes: Concurrent Vehicle (corn oil) control	
	Metric 5: Positive Controls	N/A	All Outcomes: Not necessary for the study type	
	Metric 6: Randomized Allocation of Animals	Medium	All Outcomes: Animals were ear tagged and randomly assigned to vehicle and control groups using a computer generated set of random numbers	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Low	All Outcomes: Information on preparation and storage were not provided and the test substance is a volatile chemical	
	Metric 8: Consistency of Exposure Administration	High	All Outcomes: A low, but appropriate gavage volume (3mL/kg) was consistently applied daily across all groups.	
	Metric 9: Reporting of Doses/Concentrations	High	All Outcomes: Doses were clearly reported both as mmol/kg/day and as mg/kg/day	
	Metric 10: Exposure Frequency and Duration	High	All Outcomes: Daily gavage	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: The study included 5 exposure groups (including control)	
	Metric 12: Exposure Route and Method	High	All Outcomes: Oral gavage	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	Medium	All Outcomes: Animal species, strain, age, sex, and commercial source were reported. Starting body weights were not provided, but since animals were randomly assigned, this is unlikely to have an impact on results.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: Animal husbandry conditions (temp, humidity, light/dark cycle, food and water availability) were reported and appropriate. The study noted all aspects of the study were conducted under guidelines of the American Association of Accreditation of Laboratory Animal Care.	
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Study Citation:	McCauley, P. T., Robinson, M., Daniel, F. B., Olson, G. R. (1995). The effects of subacute and subchronic oral exposure to cis-1,2-dichloroethylene in Sprague-Dawley rats. Drug and Chemical Toxicology 18(2-3):171-184.
Health Outcome(s):	Lung/Respiratory; Reproductive/Developmental; Cardiovascular; Gastrointestinal; Endocrine (Endocrine); Skin/Connective Tissue; Musculoskeletal; Ocular/Sensory; Immune/Hematological;
Reported Health Effect(s):	Lung/Respiratory: Histology (lung, brochi, nasal cavity, nasal turbinates); Reproductive/Developmental: Ovary Wt.; Histology (seminal vesicles, prostate, testes, epididymides, uterus, mammary glands, preputial or clitoral glands); Cardiovascular: Histology (heart, aorta); Gastrointestinal: Histology (ileum, duodenum, colon, jejunum, stomach, esophagus, tongue, salivary gland, cecum); Endocrine (Endocrine): Adrenal Organ Wt.; Histology (pituitary, adrenals, thyroid, pancreas, parathyroid); Skin/Connective Tissue: Histology (skin); Musculoskeletal: Histology (thigh muscle, femur or vertebrae, sternum); Ocular/Sensory: Histology (Zymbal gland); Immune/Hematological: Hematology (RBC, WBC, hemoglobin, hematocrit etc.); Spleen and thymus organ weights; histology (spleen, madibular and mesenteric lymph nodes, bone marrow, thymus);
Duration:	Short-term (>1-30 days) 14 days
Chemical:	trans-1,2-Dichloroethylene- Isomer: cis-1,2-Dichloroethylene
HERO ID:	5237

Domain	Metric	Rating	Comments
	Metric 15: Number of Animals per Group	Low	All Outcomes: The number of animals per group was not reported; however, appropriate statistical tests were performed indicating enough animals were included for statistical analysis.
Domain 5: Outcome Assessment			
	Metric 16: Outcome Assessment Methodology	Medium	Lung/Respiratory: Limited evaluation of organ/system-related endpoints (histology on limited tissues only); Reproductive/Developmental: Limited evaluation of organ/system-related endpoints. Relative but not absolute organ weights were measured.; Cardiovascular: Limited evaluation of organ/system-related endpoints (histology on limited tissues only); Gastrointestinal: Limited evaluation of organ/system-related endpoints (histology on limited tissues only); Endocrine (Endocrine): Limited evaluation of organ/system-related endpoints. Relative but not absolute organ weights were measured.; Skin/Connective Tissue: Limited evaluation of organ/system-related endpoints (histology on limited tissues only); Musculoskeletal: Limited evaluation of organ/system-related endpoints (histology on limited tissues only); Ocular/Sensory: Limited evaluation of organ/system-related endpoints (histology on limited tissues only); Immune/Hematological: Limited evaluation of immunological endpoints. Relative but not absolute organ weights were measured.
	Metric 17: Consistency of Outcome Assessment	High	All Outcomes: Consistent assessment across groups for some endpoints.
	Metric 18: Sampling Adequacy	Medium	All Outcomes: Some endpoints (histology) performed on control and high-dose groups only. The number of animals evaluated/group was not provided.
	Metric 19: Blinding of Assessors	N/A	All Outcomes: Blinding of assessors is not necessary for the outcome evaluated.
	Metric 20: Negative Control Response	High	All Outcomes: The study did not indicate any concerns over control responses for this organ/system.
Domain 6: Confounding / Variable Control			
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Study Citation:	McCauley, P. T., Robinson, M., Daniel, F. B., Olson, G. R. (1995). The effects of subacute and subchronic oral exposure to cis-1,2-dichloroethylene in Sprague-Dawley rats. Drug and Chemical Toxicology 18(2-3):171-184.
Health Outcome(s):	Lung/Respiratory; Reproductive/Developmental; Cardiovascular; Gastrointestinal; Endocrine (Endocrine); Skin/Connective Tissue; Musculoskeletal; Ocular/Sensory; Immune/Hematological;
Reported Health Effect(s):	Lung/Respiratory: Histology (lung, brochi, nasal cavity, nasal turbinates); Reproductive/Developmental: Ovary Wt.; Histology (seminal vesicles, prostate, testes, epididymides, uterus, mammary glands, preputial or clitoral glands); Cardiovascular: Histology (heart, aorta); Gastrointestinal: Histology (ileum, duodenum, colon, jejunum, stomach, esophagus, tongue, salivary gland, cecum); Endocrine (Endocrine): Adrenal Organ Wt.; Histology (pituitary, adrenals, thyroid, pancreas, parathyroid); Skin/Connective Tissue: Histology (skin); Musculoskeletal: Histology (thigh muscle, femur or vertebrae, sternum); Ocular/Sensory: Histology (Zymbal gland); Immune/Hematological: Hematology (RBC, WBC, hemoglobin, hematocrit etc.); Spleen and thymus organ weights; histology (spleen, madibular and mesenteric lymph nodes, bone marrow, thymus);
Duration:	Short-term (>1-30 days) 14 days
Chemical:	trans-1,2-Dichloroethylene- Isomer: cis-1,2-Dichloroethylene
HERO ID:	5237

Domain	Metric	Rating	Comments
Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Lung/Respiratory: The study did not report all information to determine confounding. High-dose animals (both sexes) were reported to have a significant increase in water consumption (20% increase for females and 35% increase for males) compared with controls. It is unclear what impact this could have had on the outcomes of interest.; Reproductive/Developmental: The study did not report all information to determine confounding. High-dose animals (both sexes) were reported to have a significant increase in water consumption (20% increase for females and 35% increase for males) compared with controls. It is unclear what impact this could have had on the outcomes of interest.; Cardiovascular: The study did not report all information to determine confounding. High-dose animals (both sexes) were reported to have a significant increase in water consumption (20% increase for females and 35% increase for males) compared with controls. It is unclear what impact this could have had on the outcomes of interest.; Gastrointestinal: The study did not report all information to determine confounding. High-dose animals (both sexes) were reported to have a significant increase in water consumption (20% increase for females and 35% increase for males) compared with controls. It is unclear what impact this could have had on the outcomes of interest.; Endocrine (Endocrine): The study did not report all information to determine confounding. High-dose animals (both sexes) were reported to have a significant increase in water consumption (20% increase for females and 35% increase for males) compared with controls. It is unclear what impact this could have had on the outcomes of interest.; Skin/Connective Tissue: The study did not report all information to determine confounding. High-dose animals (both sexes) were reported to have a significant increase in water consumption (20% increase for females and 35% increase for males) compared with controls. It is unclear what impact this could have had on the outcomes of interest.; Musculoskeletal: The study did not report all information to determine confounding. High-dose animals (both sexes) were reported to have a significant increase in water consumption (20% increase for females and 35% increase for males) compared with controls. It is unclear what impact this could have had on the outcomes of interest. No changes in final body weights were noted despite increased water consumption.; Ocular/Sensory: The study did not report all information to determine confounding. High-dose animals (both sexes) were reported to have a significant increase in water consumption (20% increase for females and 35% increase for males) compared with controls. It is unclear what impact this could have had on the outcomes of interest.; Immune/Hematological: The study did not report all information to determine confounding. High-dose animals (both sexes) were reported to have a significant increase in water consumption (20% increase for females and 35% increase for males) compared with controls. It is unclear what impact this could have had on the outcomes of interest.

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Study Citation:	McCauley, P. T., Robinson, M., Daniel, F. B., Olson, G. R. (1995). The effects of subacute and subchronic oral exposure to cis-1,2-dichloroethylene in Sprague-Dawley rats. Drug and Chemical Toxicology 18(2-3):171-184.			
Health Outcome(s):	Lung/Respiratory; Reproductive/Developmental; Cardiovascular; Gastrointestinal; Endocrine (Endocrine); Skin/Connective Tissue; Musculoskeletal; Ocular/Sensory; Immune/Hematological;			
Reported Health Effect(s):	Lung/Respiratory: Histology (lung, brochi, nasal cavity, nasal turbinates); Reproductive/Developmental: Ovary Wt.; Histology (seminal vesicles, prostate, testes, epididymides, uterus, mammary glands, preputial or clitoral glands); Cardiovascular: Histology (heart, aorta); Gastrointestinal: Histology (ileum, duodenum, colon, jejunum, stomach, esophagus, tongue, salivary gland, cecum); Endocrine (Endocrine): Adrenal Organ Wt.; Histology (pituitary, adrenals, thyroid, pancreas, parathyroid); Skin/Connective Tissue: Histology (skin); Musculoskeletal: Histology (thigh muscle, femur or vertebrae, sternum); Ocular/Sensory: Histology (Zymbal gland); Immune/Hematological: Hematology (RBC, WBC, hemoglobin, hematocrit etc.); Spleen and thymus organ weights; histology (spleen, madibular and mesenteric lymph nodes, bone marrow, thymus);			
Duration:	Short-term (>1-30 days) 14 days			
Chemical:	trans-1,2-Dichloroethylene- Isomer: cis-1,2-Dichloroethylene			
HERO ID:	5237			
Domain	Metric	Rating	Comments	
	Metric 22: Health Outcomes Unrelated to Exposure	Low	All Outcomes: The study summary indicates there were "gavage-related deaths" in the high dose group in the 14-day study, and that there were "gavage-related deaths in both controls and high dose groups in the 90-day study. Although not explicitly stated, it is assumed these are procedural mortalities (due to gavage) and not related to the test substance. It is unclear what confounding effects these deaths may have had on accurately assessing the actual outcome of interest (e.g., it is unclear how many animals in each group died).	
	Metric 23: Data Presentation and Analysis	High	All Outcomes: Statistical analysis was described and appropriate for the outcomes of interest.	
	Metric 24: Reporting of Data	Medium	Lung/Respiratory: Histology results were reported in the text-only indicating no significant compound-related changes were observed.; Reproductive/Developmental: Histology results were reported in the text-only indicating no significant compound-related changes were observed. Bodyweight measurements were not provided in conjunction with relative organ weights, although the text indicated no differences were observed.; Cardiovascular: Histology results were reported in the text-only indicating no significant compound-related changes were observed.; Gastrointestinal: Histology results were reported in the text-only indicating no significant compound-related changes were observed.; Endocrine (Endocrine): Histology results were reported in the text-only indicating no significant compound-related changes were observed. Bodyweight measurements were not provided in conjunction with relative organ weights, although the text indicated no differences were observed.; Skin/Connective Tissue: Histology results were reported in the text-only indicating no significant compound-related changes were observed.; Musculoskeletal: Histology results were reported in the text-only indicating no significant compound-related changes were observed.; Ocular/Sensory: Histology results were reported in the text-only indicating no significant compound-related changes were observed.; Immune/Hematological: Histology results were reported in the text-only indicating no significant compound-related changes were observed. Bodyweight measurements were not provided in conjunction with relative organ weights, although the text indicated no differences were observed.	
Additional Comments:	This study had several reporting deficiencies including the number of animals treated/group and details of the number and sex of animals that died at the high-dose, making interpretation of results from that dose-group difficult. For example, it is unclear how many high-dose animals remained at the end of the study (n = not reported). Histopathology was performed on control and high-dose animals only; due to the reported deaths at the high-dose, it would have been appropriate to perform histopathological examinations on tissues from other dose groups.			

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Study Citation:	McCauley, P. T., Robinson, M., Daniel, F. B., Olson, G. R. (1995). The effects of subacute and subchronic oral exposure to cis-1,2-dichloroethylene in Sprague-Dawley rats. Drug and Chemical Toxicology 18(2-3):171-184.
Health Outcome(s):	Lung/Respiratory; Reproductive/Developmental; Cardiovascular; Gastrointestinal; Endocrine (Endocrine); Skin/Connective Tissue; Musculoskeletal; Ocular/Sensory; Immune/Hematological;
Reported Health Effect(s):	Lung/Respiratory: Histology (lung, brochi, nasal cavity, nasal turbinates); Reproductive/Developmental: Ovary Wt.; Histology (seminal vesicles, prostate, testes, epididymides, uterus, mammary glands, preputial or clitoral glands); Cardiovascular: Histology (heart, aorta); Gastrointestinal: Histology (ileum, duodenum, colon, jejunum, stomach, esophagus, tongue, salivary gland, cecum); Endocrine (Endocrine): Adrenal Organ Wt.; Histology (pituitary, adrenals, thyroid, pancreas, parathyroid); Skin/Connective Tissue: Histology (skin); Musculoskeletal: Histology (thigh muscle, femur or vertebrae, sternum); Ocular/Sensory: Histology (Zymbal gland); Immune/Hematological: Hematology (RBC, WBC, hemoglobin, hematocrit etc.); Spleen and thymus organ weights; histology (spleen, madibular and mesenteric lymph nodes, bone marrow, thymus);
Duration:	Short-term (>1-30 days) 14 days
Chemical:	trans-1,2-Dichloroethylene- Isomer: cis-1,2-Dichloroethylene
HERO ID:	5237

Domain	Metric	Rating	Comments
Overall Quality Determination		High	

Study Citation:	Plaa, G. L., Larson, R. E. (1965). Relative nephrotoxic properties of chlorinated methane, ethane, and ethylene derivatives in mice. Toxicology and Applied Pharmacology 7(1):37-44.			
Health Outcome(s):	Renal/Kidney			
Reported Health Effect(s):	Renal/Kidney: Urinary glucose and protein; renal histopathology			
Duration:	Short-term (>1-30 days) Short-term- 3 days			
Chemical:	trans-1,2-Dichloroethylene- Isomer: cis-1,2-Dichloroethylene			
HERO ID:	64411			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1:	Test Substance Identity	High	Test substance was identified as cis-1,2-dichloroethylene.
	Metric 2:	Test Substance Source	Low	The source of the test substance was not reported.
	Metric 3:	Test Substance Purity	Low	The purity of the test substance was not reported.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	Uninformative	Details of negative control are not reported. It appears the data on the negative controls come from historic data. The strain, age, sex of the animals are not provided nor is information on if the animals were sham or untreated.
	Metric 5:	Positive Controls	N/A	Not applicable for this study.
	Metric 6:	Randomized Allocation of Animals	Low	Authors do not report if how study groups were formed.
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and Storage of Test Substance	Low	Preparation and storage conditions were not properly reported given the volatility of the test substance.
	Metric 8:	Consistency of Exposure Administration	Medium	Details of exposure administration are incomplete.
	Metric 9:	Reporting of Doses/Concentrations	High	Exposure doses were reported without ambiguity.
	Metric 10:	Exposure Frequency and Duration	High	Exposure and frequency were appropriate for outcome studied.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	The one dose studied was the highest one that did not cause lethality.
	Metric 12:	Exposure Route and Method	High	Route of exposure was i.p. injection.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Low	The source and age of mice were not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were not reported.
	Metric 15:	Number of Animals per Group	Low	The number of animals/group were not reported.
Domain 5: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	Low	Some details regarding the outcome assessment methodology were lacking (e.g how long urine was collected for, histological evaluations)
	Metric 17:	Consistency of Outcome Assessment	High	Outcomes were assessed consistently across study groups.

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Study Citation:	Plaa, G. L., Larson, R. E. (1965). Relative nephrotoxic properties of chlorinated methane, ethane, and ethylene derivatives in mice. Toxicology and Applied Pharmacology 7(1):37-44.			
Health Outcome(s):	Renal/Kidney			
Reported Health Effect(s):	Renal/Kidney: Urinary glucose and protein; renal histopathology			
Duration:	Short-term (> 1-30 days) Short-term- 3 days			
Chemical:	trans-1,2-Dichloroethylene- Isomer: cis-1,2-Dichloroethylene			
HERO ID:	64411			
Domain	Metric	Rating	Comments	
	Metric 18: Sampling Adequacy	Uninformative	Histology was not performed on controls.	
	Metric 19: Blinding of Assessors	N/A	Blinding was not necessary for outcomes studied.	
	Metric 20: Negative Control Response	Low	Negative control histology was not reported.	
Domain 6: Confounding / Variable Control				
	Metric 21: Confounding Variables in Test Design and Procedures	Low	Potential confounding variables were not reported.	
	Metric 22: Health Outcomes Unrelated to Exposure	Medium	There was no information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure.	
	Metric 23: Data Presentation and Analysis	High	Statistical analysis was not performed; independent statistics could be done.	
	Metric 24: Reporting of Data	Low	Combistix analysis data were not presented.	
Additional Comments:	Lack of information on the negative control group makes the study unacceptable.			

Overall Quality Determination**Uninformative**

Study Citation:	McCauley, P. T., Robinson, M., Daniel, F. B., Olson, G. R. (1995). The effects of subacute and subchronic oral exposure to cis-1,2-dichloroethylene in Sprague-Dawley rats. Drug and Chemical Toxicology 18(2-3):171-184.			
Health Outcome(s):	Endocrine (Endocrine); Cardiovascular; Skin/Connective Tissue; Musculoskeletal; Ocular/Sensory; Clinical chemistry (Non-organ specific clinical chemistry); Clinical chemistry (Non-organ specific clinical chemistry); Nutritional/Metabolic; Reproductive/Developmental; Renal/Kidney; Hepatic/Liver; Lung/Respiratory; Gastrointestinal;			
Reported Health Effect(s):	Endocrine (Endocrine): Adrenal Organ Wt.; Histology (pituitary, adrenals, thyroid, pancreas, parathyroid); Cardiovascular: Histology (heart, aorta); Skin/Connective Tissue: Histology (skin); Musculoskeletal: Histology (thigh muscle, femur or vertebrae, sternum); Ocular/Sensory: Histology (Zym bal gland); Clinical chemistry (Non-organ specific clinical chemistry): Remaining clinical chemistry parameters that may be relevant to multiple organ systems (calcium and phosphorus, glucose); Clinical chemistry (Non-organ specific clinical chemistry): Remaining clinical chemistry parameters that may be relevant to multiple organ systems (calcium and phosphorus, glucose); Nutritional/Metabolic: Body weight; food and water consumption; Reproductive/Developmental: Ovary Wt.; Histology (seminal vesicles, prostate, testes, epididymides, uterus, mammary glands, preputial or clitoral glands); Renal/Kidney: Kidney weights, associated clinical chemistry (BUN, creatinine), histopathology (kidney, bladder); note (glucose may also be relevant); Hepatic/Liver: Organ weights, related clinical chemistry (ALT, LDH, AST, cholesterol), and histopathology; (note: glucose may also be relevant); Lung/Respiratory: Histology (lung, brochi, nasal cavity, nasal turbinates); Gastrointestinal: Histology (ileum, duodenum, colon, jejunum, stomach, esophagus, tongue, salivary gland, cecum);			
Duration:	Subchronic (>30-91 days) 90-days			
Chemical:	trans-1,2-Dichloroethylene- Isomer: cis-1,2-Dichloroethylene			
HERO ID:	5237			
Domain		Metric	Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test Substance Identity	High	All Outcomes: Identified by name and CASRN: cis-1,2-dichloroethylene (CASRN: 156-59-2)
	Metric 2:	Test Substance Source	High	All Outcomes: Commercial source and lot numbers were provided.
	Metric 3:	Test Substance Purity	High	All Outcomes: Reported as 97% pure; impurities were not reported, but 97% purity is considered acceptably high.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Concurrent Vehicle (corn oil) control
	Metric 5:	Positive Controls	N/A	All Outcomes: Not necessary for the study type
	Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: Animals were ear tagged and randomly assigned to vehicle and control groups using a computer generated set of random numbers
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and Storage of Test Substance	Low	All Outcomes: Information on preparation and storage were not provided and the test substance is a volatile chemical
	Metric 8:	Consistency of Exposure Administration	High	All Outcomes: A low, but appropriate gavage volume (3mL/kg) was consistently applied daily across all groups.
	Metric 9:	Reporting of Doses/Concentrations	High	All Outcomes: Doses were clearly reported both as mmol/kg/day and as mg/kg/day
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: Daily gavage
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: The study included 5 exposure groups (including control)
	Metric 12:	Exposure Route and Method	High	All Outcomes: Oral gavage

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Study Citation:	McCauley, P. T., Robinson, M., Daniel, F. B., Olson, G. R. (1995). The effects of subacute and subchronic oral exposure to cis-1,2-dichloroethylene in Sprague-Dawley rats. Drug and Chemical Toxicology 18(2-3):171-184.
Health Outcome(s):	Endocrine (Endocrine); Cardiovascular; Skin/Connective Tissue; Musculoskeletal; Ocular/Sensory; Clinical chemistry (Non-organ specific clinical chemistry); Clinical chemistry (Non-organ specific clinical chemistry); Nutritional/Metabolic; Reproductive/Developmental; Renal/Kidney; Hepatic/Liver; Lung/Respiratory; Gastrointestinal;
Reported Health Effect(s):	Endocrine (Endocrine): Adrenal Organ Wt.; Histology (pituitary, adrenals, thyroid, pancreas, parathyroid); Cardiovascular: Histology (heart, aorta); Skin/Connective Tissue: Histology (skin); Musculoskeletal: Histology (thigh muscle, femur or vertebrae, sternum); Ocular/Sensory: Histology (Zym-bal gland); Clinical chemistry (Non-organ specific clinical chemistry): Remaining clinical chemistry parameters that may be relevant to multiple or-gan systems (calcium and phosphorus, glucose); Clinical chemistry (Non-organ specific clinical chemistry): Remaining clinical chemistry parameters that may be relevant to multiple organ systems (calcium and phosphorus, glucose); Nutritional/Metabolic: Body weight; food and water consumption; Reproductive/Developmental: Ovary Wt.; Histology (seminal vesicles, prostate, testes, epididymides, uterus, mammary glands, preputial or clitoral glands); Renal/Kidney: Kidney weights, associated clinical chemistry (BUN, creatinine), histopathology (kidney, bladder); note (glucose may also be relevant); Hepatic/Liver: Organ weights, related clinical chemistry (ALT, LDH, AST, cholesterol), and histopathology; (note: glucose may also be rele-vant); Lung/Respiratory: Histology (lung, brochi, nasal cavity, nasal turbinates); Gastrointestinal: Histology (ileum, duodenum, colon, jejunum, stomach, esophagus, tongue, salivary gland, cecum);
Duration:	Subchronic (>30-91 days) 90-days
Chemical:	trans-1,2-Dichloroethylene- Isomer: cis-1,2-Dichloroethylene
HERO ID:	5237

Domain	Metric	Rating	Comments
Domain 4: Test Animals			
Metric 13:	Test Animal Characteristics	Medium	All Outcomes: Animal species, strain, age, sex, and commercial source were reported. Starting body weights were not provided, but since animals were randomly assigned, this is unlikely to have an impact on results.
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: Animal husbandry conditions (temp, humidity, light/dark cycle, food and water availability) were reported and appropriate. The study noted all aspects of the study were conducted under guidelines of the American Association of Accreditation of Laboratory Animal Care.
Metric 15:	Number of Animals per Group	Low	All Outcomes: The number of animals per group was not reported; however, appropriate statistical tests were performed indicating enough animals were included for statistical analysis.
Domain 5: Outcome Assessment			
Metric 16:	Outcome Assessment Methodology	High	Endocrine (Endocrine): limited endpoints evaluated for this organ/system; Cardio-vascular: limited endpoints evaluated for this organ/system; Skin/Connective Tissue: limited endpoints evaluated for this organ/system; Musculoskeletal: limited endpoints evaluated for this organ/system; Ocular/Sensory: limited endpoints evaluated for this organ/system; Clinical chemistry (Non-organ specific clinical chemistry): limited end-points evaluated for this organ/system; Clinical chemistry (Non-organ specific clinical chemistry): limited endpoints evaluated for this organ/system; Nutritional/Metabolic: Out come assessment methodology was appropriate; Reproductive/Developmental: Relative but not absolute organ weights were measured.; Renal/Kidney: Relative but not absolute organ weights were measured.; Hepatic/Liver: Relative but not absolute organ weights were measured.; Lung/Respiratory: limited endpoints evaluated for this organ/system; Gastrointestinal: limited endpoints evaluated for this organ/system
Metric 17:	Consistency of Outcome Assessment	High	All Outcomes: Consistent assessment across groups for some endpoints.

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Study Citation:	McCauley, P. T., Robinson, M., Daniel, F. B., Olson, G. R. (1995). The effects of subacute and subchronic oral exposure to cis-1,2-dichloroethylene in Sprague-Dawley rats. Drug and Chemical Toxicology 18(2-3):171-184.
Health Outcome(s):	Endocrine (Endocrine); Cardiovascular; Skin/Connective Tissue; Musculoskeletal; Ocular/Sensory; Clinical chemistry (Non-organ specific clinical chemistry); Clinical chemistry (Non-organ specific clinical chemistry); Nutritional/Metabolic; Reproductive/Developmental; Renal/Kidney; Hepatic/Liver; Lung/Respiratory; Gastrointestinal;
Reported Health Effect(s):	Endocrine (Endocrine): Adrenal Organ Wt.; Histology (pituitary, adrenals, thyroid, pancreas, parathyroid); Cardiovascular: Histology (heart, aorta); Skin/Connective Tissue: Histology (skin); Musculoskeletal: Histology (thigh muscle, femur or vertebrae, sternum); Ocular/Sensory: Histology (Zym-bal gland); Clinical chemistry (Non-organ specific clinical chemistry): Remaining clinical chemistry parameters that may be relevant to multiple or-gan systems (calcium and phosphorus, glucose); Clinical chemistry (Non-organ specific clinical chemistry): Remaining clinical chemistry parameters that may be relevant to multiple organ systems (calcium and phosphorus, glucose); Nutritional/Metabolic: Body weight; food and water consumption; Reproductive/Developmental: Ovary Wt.; Histology (seminal vesicles, prostate, testes, epididymides, uterus, mammary glands, preputial or clitoral glands); Renal/Kidney: Kidney weights, associated clinical chemistry (BUN, creatinine), histopathology (kidney, bladder); note (glucose may also be relevant); Hepatic/Liver: Organ weights, related clinical chemistry (ALT, LDH, AST, cholesterol), and histopathology; (note: glucose may also be rele-vant); Lung/Respiratory: Histology (lung, brochi, nasal cavity, nasal turbinates); Gastrointestinal: Histology (ileum, duodenum, colon, jejunum, stomach, esophagus, tongue, salivary gland, cecum);
Duration:	Subchronic (>30-91 days) 90-days
Chemical:	trans-1,2-Dichloroethylene- Isomer: cis-1,2-Dichloroethylene
HERO ID:	5237

Domain	Metric	Rating	Comments
Metric 18:	Sampling Adequacy	Medium	Endocrine (Endocrine): Some endpoints (histology) performed on control and high-dose groups only. Deaths were reported in these groups, and the number of animals evaluated/group was not provided.; Cardiovascular: Some endpoints (histology) per-formed on control and high-dose groups only. Deaths were reported in these groups, and the number of animals evaluated/group was not provided.; Skin/Connective Tissue: Some endpoints (histology) performed on control and high-dose groups only. Deaths were reported in these groups, and the number of animals evaluated/group was not provided.; Musculoskeletal: Some endpoints (histology) performed on control and high-dose groups only. Deaths were reported in these groups, and the number of animals evaluated/group was not provided.; Ocular/Sensory: Some endpoints (histology) per-formed on control and high-dose groups only. Deaths were reported in these groups, and the number of animals evaluated/group was not provided.; Clinical chemistry (Non-organ specific clinical chemistry): Some endpoints (histology) performed on control and high-dose groups only. Deaths were reported in these groups, and the number of animals evaluated/group was not provided.; Clinical chemistry (Non-organ specific clinical chemistry): Some endpoints (histology) performed on control and high-dose groups only. Deaths were reported in these groups, and the number of animals evaluated/group was not provided.; Nutritional/Metabolic: Some endpoints (histology) performed on control and high-dose groups only. The number of animals evaluated/group was not pro-vided.; Reproductive/Developmental: Some endpoints (histology) performed on control and high-dose groups only. Deaths were reported in these groups, and the number of animals evaluated/group was not provided.; Renal/Kidney: Some endpoints (histology) performed on control and high-dose groups only. Deaths were reported in these groups, and the number of animals evaluated/group was not provided.; Hepatic/Liver: Some endpoints (histology) performed on control and high-dose groups only. Deaths were re-ported in these groups, and the number of animals evaluated/group was not provided.; Lung/Respiratory: Some endpoints (histology) performed on control and high-dose groups only. Deaths were reported in these groups, and the number of animals evalu-ated/group was not provided.; Gastrointestinal: Some endpoints (histology) performed on control and high-dose groups only. Deaths were reported in these groups, and the number of animals evaluated/group was not provided.

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Health Outcome(s):	Endocrine (Endocrine); Cardiovascular; Skin/Connective Tissue; Musculoskeletal; Ocular/Sensory; Clinical chemistry (Non-organ specific clinical chemistry); Clinical chemistry (Non-organ specific clinical chemistry); Nutritional/Metabolic; Reproductive/Developmental; Renal/Kidney; Hepatic/Liver; Lung/Respiratory; Gastrointestinal;
Reported Health Effect(s):	Endocrine (Endocrine): Adrenal Organ Wt.; Histology (pituitary, adrenals, thyroid, pancreas, parathyroid); Cardiovascular: Histology (heart, aorta); Skin/Connective Tissue: Histology (skin); Musculoskeletal: Histology (thigh muscle, femur or vertebrae, sternum); Ocular/Sensory: Histology (Zym-bal gland); Clinical chemistry (Non-organ specific clinical chemistry): Remaining clinical chemistry parameters that may be relevant to multiple or-gan systems (calcium and phosphorus, glucose); Clinical chemistry (Non-organ specific clinical chemistry): Remaining clinical chemistry parameters that may be relevant to multiple organ systems (calcium and phosphorus, glucose); Nutritional/Metabolic: Body weight; food and water consumption; Reproductive/Developmental: Ovary Wt.; Histology (seminal vesicles, prostate, testes, epididymides, uterus, mammary glands, preputial or clitoral glands); Renal/Kidney: Kidney weights, associated clinical chemistry (BUN, creatinine), histopathology (kidney, bladder); note (glucose may also be relevant); Hepatic/Liver: Organ weights, related clinical chemistry (ALT, LDH, AST, cholesterol), and histopathology; (note: glucose may also be rele-vant); Lung/Respiratory: Histology (lung, brochi, nasal cavity, nasal turbinates); Gastrointestinal: Histology (ileum, duodenum, colon, jejunum, stomach, esophagus, tongue, salivary gland, cecum);
Duration:	Subchronic (>30-91 days) 90-days
Chemical:	trans-1,2-Dichloroethylene- Isomer: cis-1,2-Dichloroethylene
HERO ID:	5237

Domain	Metric	Rating	Comments
	Metric 19: Blinding of Assessors	N/A	Endocrine (Endocrine): Blinding of assessors is not necessary for the outcomes eval-uated.; Cardiovascular: Blinding of assessors is not necessary for the outcomes evalu-ated.; Skin/Connective Tissue: Blinding of assessors is not necessary for the outcomes evaluated.; Musculoskeletal: Blinding of assessors is not necessary for the outcomes evaluated.; Ocular/Sensory: Blinding of assessors is not necessary for the outcomes evaluated.; Clinical chemistry (Non-organ specific clinical chemistry): Blinding of as-sessors is not necessary for the outcomes evaluated.; Clinical chemistry (Non-organ specific clinical chemistry): Blinding of assessors is not necessary for the outcomes evaluated.; Nutritional/Metabolic: Blinding of assessors is not necessary for the outcome evaluated.; Reproductive/Developmental: Blinding of assessors is not necessary for the outcomes evaluated.; Renal/Kidney: Blinding of assessors is not necessary for the out-comes evaluated.; Hepatic/Liver: Blinding of assessors is not necessary for the outcomes evaluated.; Lung/Respiratory: Blinding of assessors is not necessary for the outcomes evaluated.; Gastrointestinal: Blinding of assessors is not necessary for the outcomes evaluated.
	Metric 20: Negative Control Response	High	All Outcomes: The study did not indicate any concerns over control responses for this organ/system.
Domain 6: Confounding / Variable Control			
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	All Outcomes: The study did not report all information to determine confounding. No differences were identified

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Health Outcome(s):	Endocrine (Endocrine); Cardiovascular; Skin/Connective Tissue; Musculoskeletal; Ocular/Sensory; Clinical chemistry (Non-organ specific clinical chemistry); Clinical chemistry (Non-organ specific clinical chemistry); Nutritional/Metabolic; Reproductive/Developmental; Renal/Kidney; Hepatic/Liver; Lung/Respiratory; Gastrointestinal;
Reported Health Effect(s):	Endocrine (Endocrine): Adrenal Organ Wt.; Histology (pituitary, adrenals, thyroid, pancreas, parathyroid); Cardiovascular: Histology (heart, aorta); Skin/Connective Tissue: Histology (skin); Musculoskeletal: Histology (thigh muscle, femur or vertebrae, sternum); Ocular/Sensory: Histology (Zym-bal gland); Clinical chemistry (Non-organ specific clinical chemistry): Remaining clinical chemistry parameters that may be relevant to multiple or-gan systems (calcium and phosphorus, glucose); Clinical chemistry (Non-organ specific clinical chemistry): Remaining clinical chemistry parameters that may be relevant to multiple organ systems (calcium and phosphorus, glucose); Nutritional/Metabolic: Body weight; food and water consumption; Reproductive/Developmental: Ovary Wt.; Histology (seminal vesicles, prostate, testes, epididymides, uterus, mammary glands, preputial or clitoral glands); Renal/Kidney: Kidney weights, associated clinical chemistry (BUN, creatinine), histopathology (kidney, bladder); note (glucose may also be relevant); Hepatic/Liver: Organ weights, related clinical chemistry (ALT, LDH, AST, cholesterol), and histopathology; (note: glucose may also be rele-vant); Lung/Respiratory: Histology (lung, brochi, nasal cavity, nasal turbinates); Gastrointestinal: Histology (ileum, duodenum, colon, jejunum, stomach, esophagus, tongue, salivary gland, cecum);
Duration:	Subchronic (>30-91 days) 90-days
Chemical:	trans-1,2-Dichloroethylene- Isomer: cis-1,2-Dichloroethylene
HERO ID:	5237

Domain	Metric	Rating	Comments
Metric 22:	Health Outcomes Unrelated to Exposure	Low	Endocrine (Endocrine): The study summary indicates there were "gavage-related deaths" in both controls and high dose groups in the 90-day study. Although not explicitly stated, it is assumed these are procedural mortalities (due to gavage) and not related to the test substance. It is unclear what confounding effects these deaths may have had on accurately assessing the actual outcome of interest (e.g., it is unclear how many animals in each group died).; Cardiovascular: The study summary indicates there were "gavage-related deaths" in both controls and high dose groups in the 90-day study. Although not explicitly stated, it is assumed these are procedural mortalities (due to gavage) and not related to the test substance. It is unclear what confounding effects these deaths may have had on accurately assessing the actual outcome of interest (e.g., it is unclear how many animals in each group died).; Skin/Connective Tissue: The study summary indicates there were "gavage-related deaths" in both controls and high dose groups in the 90-day study. Although not explicitly stated, it is assumed these are procedural mortalities (due to gavage) and not related to the test substance. It is unclear what confounding effects these deaths may have had on accurately assessing the actual outcome of interest (e.g., it is unclear how many animals in each group died).; Mus-culoskeletal: The study summary indicates there were "gavage-related deaths" in both controls and high dose groups in the 90-day study. Although not explicitly stated, it is assumed these are procedural mortalities (due to gavage) and not related to the test substance. It is unclear what confounding effects these deaths may have had on accurately assessing the actual outcome of interest (e.g., it is unclear how many animals in each group died).; Ocular/Sensory: The study summary indicates there were "gavage-related deaths" in both controls and high dose groups in the 90-day study. Although not explicitly stated, it is assumed these are procedural mortalities (due to gavage) and not related to the test substance. It is unclear what confounding effects these deaths may have had on accurately assessing the actual outcome of interest (e.g., it is unclear how many animals in each group died).; Clinical chemistry (Non-organ specific clinical chemistry): The study summary indicates there were "gavage-related deaths" in both controls and high dose groups in the 90-day study. Although not explicitly stated, it is assumed these are procedural mortalities (due to gavage) and not related to the test substance. It is unclear what confounding effects these deaths may have had on accurately assessing the actual outcome of interest (e.g., it is unclear how many animals in each group died).; Clinical chemistry (Non-organ specific clinical chemistry): The study summary indi-cates there were "gavage-related deaths" in both controls and high dose groups in the 90-day study. Although not explicitly stated, it is assumed these are procedural mortali-

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Health Outcome(s):	Endocrine (Endocrine); Cardiovascular; Skin/Connective Tissue; Musculoskeletal; Ocular/Sensory; Clinical chemistry (Non-organ specific clinical chemistry); Clinical chemistry (Non-organ specific clinical chemistry); Nutritional/Metabolic; Reproductive/Developmental; Renal/Kidney; Hepatic/Liver; Lung/Respiratory; Gastrointestinal;
Reported Health Effect(s):	Endocrine (Endocrine): Adrenal Organ Wt.; Histology (pituitary, adrenals, thyroid, pancreas, parathyroid); Cardiovascular: Histology (heart, aorta); Skin/Connective Tissue: Histology (skin); Musculoskeletal: Histology (thigh muscle, femur or vertebrae, sternum); Ocular/Sensory: Histology (Zym-bal gland); Clinical chemistry (Non-organ specific clinical chemistry): Remaining clinical chemistry parameters that may be relevant to multiple or-gan systems (calcium and phosphorus, glucose); Clinical chemistry (Non-organ specific clinical chemistry): Remaining clinical chemistry parameters that may be relevant to multiple organ systems (calcium and phosphorus, glucose); Nutritional/Metabolic: Body weight; food and water consumption; Reproductive/Developmental: Ovary Wt.; Histology (seminal vesicles, prostate, testes, epididymides, uterus, mammary glands, preputial or clitoral glands); Renal/Kidney: Kidney weights, associated clinical chemistry (BUN, creatinine), histopathology (kidney, bladder); note (glucose may also be relevant); Hepatic/Liver: Organ weights, related clinical chemistry (ALT, LDH, AST, cholesterol), and histopathology; (note: glucose may also be rele-vant); Lung/Respiratory: Histology (lung, brochi, nasal cavity, nasal turbinates); Gastrointestinal: Histology (ileum, duodenum, colon, jejunum, stomach, esophagus, tongue, salivary gland, cecum);
Duration:	Subchronic (>30-91 days) 90-days
Chemical:	trans-1,2-Dichloroethylene- Isomer: cis-1,2-Dichloroethylene
HERO ID:	5237

Domain	Metric	Rating	Comments
Metric 23:	Data Presentation and Analysis	High	Endocrine (Endocrine): Statistical analysis was described and appropriate for the out-comes of interest.; Cardiovascular: Statistical analysis was described and appropriate for the outcomes of interest.; Skin/Connective Tissue: Statistical analysis was described and appropriate for the outcomes of interest.; Musculoskeletal: Statistical analysis was described and appropriate for the outcomes of interest.; Ocular/Sensory: Statistical anal-ysis was described and appropriate for the outcomes of interest.; Clinical chemistry (Non-organ specific clinical chemistry): Statistical analysis was described and appropri-ate for the outcomes of interest.; Clinical chemistry (Non-organ specific clinical chem-istry): Statistical analysis was described and appropriate for the outcomes of interest.; Nutritional/Metabolic: Statistical analysis methods described were appropriate for the outcomes of interest.; Reproductive/Developmental: Statistical analysis was described and appropriate for the outcomes of interest.; Renal/Kidney: Statistical analysis was de-scribed and appropriate for the outcomes of interest.; Hepatic/Liver: Statistical analysis was described and appropriate for the outcomes of interest.; Lung/Respiratory: Statisti-cal analysis was described and appropriate for the outcomes of interest.; Gastrointesti-nal: Statistical analysis was described and appropriate for the outcomes of interest.

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Study Citation:	McCauley, P. T., Robinson, M., Daniel, F. B., Olson, G. R. (1995). The effects of subacute and subchronic oral exposure to cis-1,2-dichloroethylene in Sprague-Dawley rats. Drug and Chemical Toxicology 18(2-3):171-184.
Health Outcome(s):	Endocrine (Endocrine); Cardiovascular; Skin/Connective Tissue; Musculoskeletal; Ocular/Sensory; Clinical chemistry (Non-organ specific clinical chemistry); Clinical chemistry (Non-organ specific clinical chemistry); Nutritional/Metabolic; Reproductive/Developmental; Renal/Kidney; Hepatic/Liver; Lung/Respiratory; Gastrointestinal;
Reported Health Effect(s):	Endocrine (Endocrine): Adrenal Organ Wt.; Histology (pituitary, adrenals, thyroid, pancreas, parathyroid); Cardiovascular: Histology (heart, aorta); Skin/Connective Tissue: Histology (skin); Musculoskeletal: Histology (thigh muscle, femur or vertebrae, sternum); Ocular/Sensory: Histology (Zym-bal gland); Clinical chemistry (Non-organ specific clinical chemistry): Remaining clinical chemistry parameters that may be relevant to multiple or-gan systems (calcium and phosphorus, glucose); Clinical chemistry (Non-organ specific clinical chemistry): Remaining clinical chemistry parameters that may be relevant to multiple organ systems (calcium and phosphorus, glucose); Nutritional/Metabolic: Body weight; food and water consumption; Reproductive/Developmental: Ovary Wt.; Histology (seminal vesicles, prostate, testes, epididymides, uterus, mammary glands, preputial or clitoral glands); Renal/Kidney: Kidney weights, associated clinical chemistry (BUN, creatinine), histopathology (kidney, bladder); note (glucose may also be relevant); Hepatic/Liver: Organ weights, related clinical chemistry (ALT, LDH, AST, cholesterol), and histopathology; (note: glucose may also be rele-vant); Lung/Respiratory: Histology (lung, brochi, nasal cavity, nasal turbinates); Gastrointestinal: Histology (ileum, duodenum, colon, jejunum, stomach, esophagus, tongue, salivary gland, cecum);
Duration:	Subchronic (>30-91 days) 90-days
Chemical:	trans-1,2-Dichloroethylene- Isomer: cis-1,2-Dichloroethylene
HERO ID:	5237

Domain	Metric	Rating	Comments
Metric 24:	Reporting of Data	Medium	Endocrine (Endocrine): Histology results were reported in the text-only indicating no significant compound-related changes were observed. Bodyweight measurements were not provided in conjunction with relative organ weights, although the text indicated no differences were observed.; Cardiovascular: Histology results were reported in the text-only indicating no significant compound-related changes were observed. Body-weight measurements were not provided in conjunction with relative organ weights, although the text indicated no differences were observed.; Skin/Connective Tissue: His-tology results were reported in the text-only indicating no significant compound-related changes were observed. Bodyweight measurements were not provided in conjunction with relative organ weights, although the text indicated no differences were observed.; Musculoskeletal: Histology results were reported in the text-only indicating no sig-nificant compound-related changes were observed. Bodyweight measurements were not provided in conjunction with relative organ weights, although the text indicated no differences were observed.; Ocular/Sensory: Histology results were reported in the text-only indicating no significant compound-related changes were observed. Bodyweight measurements were not provided in conjunction with relative organ weights, although the text indicated no differences were observed.; Clinical chemistry (Non-organ spe-cific clinical chemistry): Histology results were reported in the text-only indicating no significant compound-related changes were observed. Bodyweight measurements were not provided in conjunction with relative organ weights, although the text indicated no differences were observed.; Clinical chemistry (Non-organ specific clinical chemistry): Histology results were reported in the text-only indicating no significant compound-related changes were observed. Bodyweight measurements were not provided in con-junction with relative organ weights, although the text indicated no differences were observed.; Nutritional/Metabolic: Weekly body weight data were collected, but not re-ported. Empirical body weight measurements were not provided. The text reported no changes.; Reproductive/Developmental: Histology results were reported in the text-only indicating no significant compound-related changes were observed. Bodyweight measurements were not provided in conjunction with relative organ weights, although the text indicated no differences were observed.; Renal/Kidney: Histology results were reported in the text-only indicating no significant compound-related changes were ob-served. Bodyweight measurements were not provided in conjunction with relative organ weights, although the text indicated no differences were observed.; Hepatic/Liver: His-tology results were reported in the text-only indicating no significant compound-related changes were observed. Bodyweight measurements were not provided in conjunction

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Study Citation:	McCauley, P. T., Robinson, M., Daniel, F. B., Olson, G. R. (1995). The effects of subacute and subchronic oral exposure to cis-1,2-dichloroethylene in Sprague-Dawley rats. Drug and Chemical Toxicology 18(2-3):171-184.
Health Outcome(s):	Endocrine (Endocrine); Cardiovascular; Skin/Connective Tissue; Musculoskeletal; Ocular/Sensory; Clinical chemistry (Non-organ specific clinical chemistry); Clinical chemistry (Non-organ specific clinical chemistry); Nutritional/Metabolic; Reproductive/Developmental; Renal/Kidney; Hepatic/Liver; Lung/Respiratory; Gastrointestinal;
Reported Health Effect(s):	Endocrine (Endocrine): Adrenal Organ Wt.; Histology (pituitary, adrenals, thyroid, pancreas, parathyroid); Cardiovascular: Histology (heart, aorta); Skin/Connective Tissue: Histology (skin); Musculoskeletal: Histology (thigh muscle, femur or vertebrae, sternum); Ocular/Sensory: Histology (Zym-bal gland); Clinical chemistry (Non-organ specific clinical chemistry): Remaining clinical chemistry parameters that may be relevant to multiple or-gan systems (calcium and phosphorus, glucose); Clinical chemistry (Non-organ specific clinical chemistry): Remaining clinical chemistry parameters that may be relevant to multiple organ systems (calcium and phosphorus, glucose); Nutritional/Metabolic: Body weight; food and water consumption; Reproductive/Developmental: Ovary Wt.; Histology (seminal vesicles, prostate, testes, epididymides, uterus, mammary glands, preputial or clitoral glands); Renal/Kidney: Kidney weights, associated clinical chemistry (BUN, creatinine), histopathology (kidney, bladder); note (glucose may also be relevant); Hepatic/Liver: Organ weights, related clinical chemistry (ALT, LDH, AST, cholesterol), and histopathology; (note: glucose may also be rele-vant); Lung/Respiratory: Histology (lung, brochi, nasal cavity, nasal turbinates); Gastrointestinal: Histology (ileum, duodenum, colon, jejunum, stomach, esophagus, tongue, salivary gland, cecum);
Duration:	Subchronic (>30-91 days) 90-days
Chemical:	trans-1,2-Dichloroethylene- Isomer: cis-1,2-Dichloroethylene
HERO ID:	5237

Domain	Metric	Rating	Comments
Additional Comments:	This study had several reporting deficiencies including the number of animals treated/group and details of the number and sex of animals that died in the control and at the high-dose, which makes interpretation of results difficult. For example, it is unclear how many animals remained in those groups at the end of the study (n = not reported). A discussion as to whether deaths in the control group influenced outcome assessment was not included. Histopathology was performed on control and high-dose animals only; the two groups that reported deaths.		

Overall Quality Determination**High**

Study Citation:	McCauley, P. T., Robinson, M., Daniel, F. B., Olson, G. R. (1995). The effects of subacute and subchronic oral exposure to cis-1,2-dichloroethylene in Sprague-Dawley rats. Drug and Chemical Toxicology 18(2-3):171-184.			
Health Outcome(s):	Mortality			
Reported Health Effect(s):	Mortality: Mortality			
Duration:	Subchronic (>30-91 days) 90-days			
Chemical:	trans-1,2-Dichloroethylene- Isomer: cis-1,2-Dichloroethylene			
HERO ID:	5237			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1:	Test Substance Identity	High	Identified by name and CASRN: cis-1,2-dichloroethylene (CASRN: 156-59-2)
	Metric 2:	Test Substance Source	High	Commercial source and lot numbers were provided.
	Metric 3:	Test Substance Purity	High	Reported as 97% pure; impurities were not reported, but 97% purity is considered acceptably high.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	Concurrent Vehicle (corn oil) control
	Metric 5:	Positive Controls	N/A	Not necessary for the study type
	Metric 6:	Randomized Allocation of Animals	Medium	Animals were ear tagged and randomly assigned to vehicle and control groups using a computer generated set of random numbers
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and Storage of Test Substance	Low	Information on preparation and storage were not provided and the test substance is a volatile chemical
	Metric 8:	Consistency of Exposure Administration	High	A low, but appropriate gavage volume (3mL/kg) was consistently applied daily across all groups.
	Metric 9:	Reporting of Doses/Concentrations	High	Doses were clearly reported both as mmol/kg/day and as mg/kg/day
	Metric 10:	Exposure Frequency and Duration	High	Daily gavage
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The study included 5 exposure groups (including control)
	Metric 12:	Exposure Route and Method	High	Oral gavage
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Medium	Animal species, strain, age, sex, and commercial source were reported. Starting body weights were not provided, but since animals were randomly assigned, this is unlikely to have an impact on results.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	Animal husbandry conditions (temp, humidity, light/dark cycle, food and water availability) were reported and appropriate. The study noted all aspects of the study were conducted under guidelines of the American Association of Accreditation of Laboratory Animal Care.
	Metric 15:	Number of Animals per Group	Low	The number of animals per group was not reported; however, appropriate statistical tests were performed indicating enough animals were included for statistical analysis.
Domain 5: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	High	Out come assessment methodology was appropriate
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Health Outcome(s):	Mortality			
Reported Health Effect(s):	Mortality: Mortality			
Duration:	Subchronic (>30-91 days) 90-days			
Chemical:	trans-1,2-Dichloroethylene- Isomer: cis-1,2-Dichloroethylene			
HERO ID:	5237			
Domain	Metric	Rating	Comments	
	Metric 17:	Consistency of Outcome Assessment	Medium	Limited details of outcome assessment were reported (frequency of monitoring for mortality); this is unlikely to have have an impact on the results.
	Metric 18:	Sampling Adequacy	High	It is assumed that all animals in all treatment groups were monitored for mortality.
	Metric 19:	Blinding of Assessors	N/A	Blinding of assessors is not necessary for the outcome evaluated.
	Metric 20:	Negative Control Response	Uninformative	Gavage-related deaths were reported in the control group making it difficult to evaluate the effect of treatment.
Domain 6: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	The study did not report all information to determine confounding; reported information did not identify any differences
	Metric 22:	Health Outcomes Unrelated to Exposure	Low	The study summary indicates there were "gavage-related deaths" in the high dose group in the 14-day study, and that there were "gavage-related deaths in both controls and high dose groups in the 90-day study. Although not explicitly stated, it is assumed these are procedural mortalities (due to gavage) and not related to the test substance. It is unclear what confounding effects these deaths may have had on accurately assessing the actual outcome of interest.
	Metric 23:	Data Presentation and Analysis	High	statistical analysis was described and appropriate for the outcomes of interest.
	Metric 24:	Reporting of Data	Low	Results for the endpoint of interest were ambiguously reported in the text only. The text does not specifically report if mortalities were or were not observed in specific dose groups. Only that "gavage related deaths were present at the high dose," without further explanation.
Additional Comments:	Due to gavage-related deaths in the control group (number of deaths not reported), the effect of treatment on mortality could not be accurately evaluated.			

Overall Quality Determination**Uninformative**

Study Citation:	McCauley, P. T., Robinson, M., Daniel, F. B., Olson, G. R. (1995). The effects of subacute and subchronic oral exposure to cis-1,2-dichloroethylene in Sprague-Dawley rats. Drug and Chemical Toxicology 18(2-3):171-184.			
Health Outcome(s):	Neurological/Behavioral; Immune/Hematological;			
Reported Health Effect(s):	Neurological/Behavioral: Clinical signs (agitation, lethargy, ataxia); brain organ weight; histology (brain, sciatic nerve); Immune/Hematological: Hematology (RBC, WBC, hemoglobin, hematocrit etc.); Spleen and thymus organ weights; histology (spleen, madibular and mesenteric lymph nodes, bone marrow, thymus);			
Duration:	Subchronic (>30-91 days) 90-days			
Chemical:	trans-1,2-Dichloroethylene- Isomer: cis-1,2-Dichloroethylene			
HERO ID:	5237			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1:	Test Substance Identity	High	All Outcomes: Identified by name and CASRN: cis-1,2-dichloroethylene (CASRN: 156-59-2)
	Metric 2:	Test Substance Source	High	All Outcomes: Commercial source and lot numbers were provided.
	Metric 3:	Test Substance Purity	High	All Outcomes: Reported as 97% pure; impurities were not reported, but 97% purity is considered acceptably high.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Concurrent Vehicle (corn oil) control
	Metric 5:	Positive Controls	N/A	All Outcomes: Not necessary for the study type
	Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: Animals were ear tagged and randomly assigned to vehicle and control groups using a computer generated set of random numbers
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and Storage of Test Substance	Low	All Outcomes: Information on preparation and storage were not provided and the test substance is a volatile chemical
	Metric 8:	Consistency of Exposure Administration	High	All Outcomes: A low, but appropriate gavage volume (3mL/kg) was consistently applied daily across all groups.
	Metric 9:	Reporting of Doses/Concentrations	High	All Outcomes: Doses were clearly reported both as mmol/kg/day and as mg/kg/day
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: Daily gavage
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: The study included 5 exposure groups (including control)
	Metric 12:	Exposure Route and Method	High	All Outcomes: Oral gavage
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Medium	All Outcomes: Animal species, strain, age, sex, and commercial source were reported. Starting body weights were not provided, but since animals were randomly assigned, this is unlikely to have an impact on results.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: Animal husbandry conditions (temp, humidity, light/dark cycle, food and water availability) were reported and appropriate. The study noted all aspects of the study were conducted under guidelines of the American Association of Accreditation of Laboratory Animal Care.
	Metric 15:	Number of Animals per Group	Low	All Outcomes: The number of animals per group was not reported; however, appropriate statistical tests were performed indicating enough animals were included for statistical analysis.
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Health Outcome(s):	Neurological/Behavioral; Immune/Hematological;
Reported Health Effect(s):	Neurological/Behavioral: Clinical signs (agitation, lethargy, ataxia); brain organ weight; histology (brain, sciatic nerve); Immune/Hematological: Hematology (RBC, WBC, hemoglobin, hematocrit etc.); Spleen and thymus organ weights; histology (spleen, madibular and mesenteric lymph nodes, bone marrow, thymus);
Duration:	Subchronic (>30-91 days) 90-days
Chemical:	trans-1,2-Dichloroethylene- Isomer: cis-1,2-Dichloroethylene
HERO ID:	5237

Domain	Metric	Rating	Comments
Domain 5: Outcome Assessment			
	Metric 16: Outcome Assessment Methodology	Medium	Neurological/Behavioral: Limited evaluation of organ-system related endpoints. Relative but not absolute organ weights were measured.; Immune/Hematological: Limited evaluation of immunological endpoints. Relative but not absolute organ weights were measured.
	Metric 17: Consistency of Outcome Assessment	High	All Outcomes: Consistent assessment across groups for some endpoints.
	Metric 18: Sampling Adequacy	Medium	All Outcomes: Some endpoints (histology) performed on control and high-dose groups only. The number of animals evaluated/group was not provided.
	Metric 19: Blinding of Assessors	N/A	All Outcomes: Blinding of assessors is not necessary for the outcome evaluated.
	Metric 20: Negative Control Response	High	All Outcomes: The study did not indicate any concerns over control responses for this organ/system.
Domain 6: Confounding / Variable Control			
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	All Outcomes: The study did not report all information to determine confounding. No differences were identified
	Metric 22: Health Outcomes Unrelated to Exposure	Low	All Outcomes: The study summary indicates there were "gavage-related deaths" in the high dose group in the 14-day study, and that there were "gavage-related deaths in both controls and high dose groups in the 90-day study. Although not explicitly stated, it is assumed these are procedural mortalities (due to gavage) and not related to the test substance. It is unclear what confounding effects these deaths may have had on accurately assessing the actual outcome of interest (e.g., it is unclear how many animals in each group died).
	Metric 23: Data Presentation and Analysis	High	All Outcomes: Statistical analysis was described and appropriate for the outcomes of interest.
	Metric 24: Reporting of Data	Medium	Neurological/Behavioral: Histology results were reported in the text-only indicating no significant compound-related changes were observed. Bodyweight measurements were not provided in conjunction with relative organ weights, although the text indicated no differences were observed. Incidence data for clinical observations were not provided.; Immune/Hematological: Histology results were reported in the text-only indicating no significant compound-related changes were observed. Bodyweight measurements were not provided in conjunction with relative organ weights, although the text indicated no differences were observed.

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Domain	Metric	Rating	Comments
Additional Comments:	This study had several reporting deficiencies including the number of animals treated/group and details of the number and sex of animals that died in the control and at the high-dose, which makes interpretation of results difficult. For example, it is unclear how many animals remained in those groups at the end of the study (n = not reported). A discussion as to whether deaths in the control group influenced outcome assessment was not included. Histopathology was performed on control and high-dose animals only; the two groups that reported deaths.		

Overall Quality Determination**High**