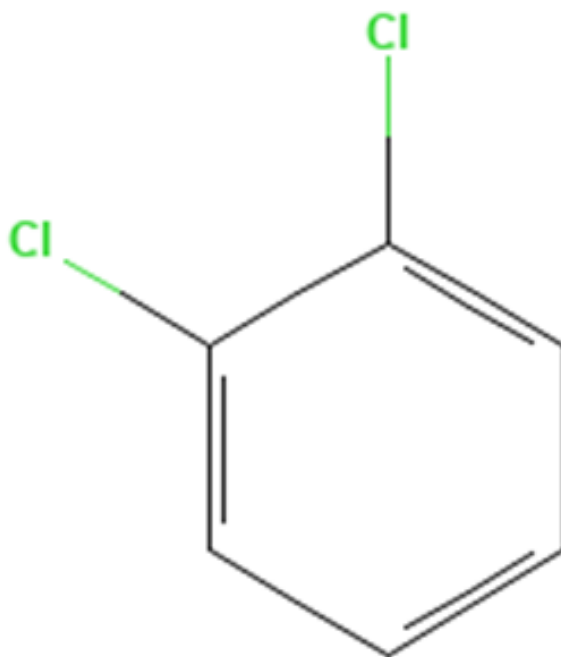

**Data Quality Evaluation Information for
Human Health Hazard Animal Toxicology for
o-Dichlorobenzene**

Systematic Review Support Document for the Draft Risk Evaluation

CASRN: 95-50-1



April 2026

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HERO ID	Reference	Page
o-Dichlorobenzene		
Acute (less than or equal to 24 hr)		
1739054	Ban, M., Hettich, D., Goutet, M., Binet, S. (1998). Serum-borne factor(s) of 1,1-dichloroethylene and 1,2-dichlorobenzene-treated mice inhibited in vitro antibody forming cell response and natural killer cell activity. <i>Toxicology Letters</i> 94(2):93-101.	8
659923	Besten, Den, C., Vet, J., Besselink, H. T., Kiel, G. S., Berkel, van, M., B.J., Beems, R., Bladeren, Van, P. J. (1991). The liver, kidney, and thyroid toxicity of chlorinated benzenes. <i>Toxicology and Applied Pharmacology</i> 111(1):69-81.	14
597571	Brondeau, M. T., Ban, M., Bonnet, P., Guenier, J. P., Ceauriz, de, J. (1986). Concentration-related changes in blood and tissue parameters of hepatotoxicity and their interdependence in rats exposed to bromobenzene and 1,2-dichlorobenzene. <i>Toxicology Letters</i> 31(2):159-166.	20
3119620	Brondeau, M. T., Ban, M., Bonnet, P., Guenier, J. P., Ceauriz, de, J. (1989). Acetone compared to other ketones in modifying the hepatotoxicity of inhaled 1,2-dichlorobenzene in rats and mice. <i>Toxicology Letters</i> 49(1):69-78.	22
200247	Brondeau, M. T., Bonnet, P., Guenier, J. P., De, C. J. (1983). Short-term inhalation test for evaluating industrial hepatotoxicants in rats. <i>Toxicology Letters</i> 19(1-2):139-146.	24
63408	Brondeau, M. T., Bonnet, P., Guenier, J. P., Simon, P., Ceauriz, de, J. (1990). Adrenal-dependent leucopenia after short-term exposure to various airborne irritants in rats. <i>Journal of Applied Toxicology</i> 10(2):83-86.	27
1441241	Ceauriz, De, J., Gagnaire, F., Ban, M., Bonnet, P. (1988). Assessment of the relative hazard involved with airborne irritants with additional hepatotoxic or nephrotoxic properties in mice. <i>Journal of Applied Toxicology</i> 8(6):417-422.	29
68063	Charbonneau, M., Strasser, J., Jr, Lock, E. A., Turner, M. J., Jr, Swenberg, J. A. (1989). Involvement of reversible binding to "alpha"2u-globulin in 1,4-dichlorobenzene-induced nephrotoxicity. <i>Toxicology and Applied Pharmacology</i> 99(1):122-132.	35
5264494	FDRL, (1976). Primary skin irritation studies with rabbits with cover letters.	41
5264501	FDRL, (1976). ortho-Dichlorobenzene: Rabbit eye irritation study.	45
5345264	Gunawardhana, L., Lantz, R. C., Earnest, D. L., Abril, E. R., Sipes, I. G. (1995). Differential production of superoxide by single Kupffer cells isolated from Fischer-344 and Sprague-Dawley rats following administration of the potent hepatotoxicant 1,2-dichlorobenzene. 5:45-47.	47
5345265	Gunawardhana, L., Mobley, S. A., Sipes, I. G. (1993). A role for reactive oxygen species released from kupffer cells in 1,2-dichlorobenzene hepatotoxicity in the fischer-344 rat. 4:403-406.	49
5264631	Haas,, R.a. (1979). Initial submission: Acute parenteral LD50 study with o-dichlorobenzene in rats with cover letter dated 073092. 920005562:#88-920005562.	51
5279930	Haas,, R.a. (1982). Acute toxicity report.	59

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5914598	Haas,, R.a. (1979). Acute toxicity report with attach cover letter.	62
730563	Herr, D. W., Boyes, W. K. (1997). A comparison of the acute neuroactive effects of dichloromethane, 1,3-dichloropropane, and 1,2-dichlorobenzene on rat flash evoked potentials (FEPs). <i>Fundamental and Applied Toxicology</i> 35(1):31-48.	70
2962108	Hollingsworth, R. L., Rowe, V. K., Oyen, F., Torkelson, T. R., Adams, E. M. (1958). Toxicity of o-dichlorobenzene: Studies on animals and industrial experience. <i>AMA Archives of Industrial Health</i> 17(3):180-187.	73
2919019	Kulkarni, S. G., Warbritton, A., Bucci, T. J., Mehendale, H. M. (1997). Antimitotic intervention with colchicine alters the outcome of o-DCB-induced hepatotoxicity in Fischer 344 rats. <i>Toxicology</i> 120(2):79-88.	82
661834	Miyagawa, M., Takasawa, H., Sugiyama, A., Inoue, Y., Murata, T., Uno, Y., Yoshikawa, K. (1995). The in vivo-in vitro replicative DNA synthesis (RDS) test with hepatocytes prepared from male B6C3F1 mice as an early prediction assay for putative nongenotoxic (Ames-negative) mouse hepatocarcinogens. <i>Mutation Research: Genetic Toxicology</i> 343(2-3):157-183.	86
201693	Mohtashampur, E., Triebel, R., Straeter, H., Norpoth, K. (1987). The bone marrow clastogenicity of eight halogenated benzenes in male NMRI mice. <i>Mutagenesis</i> 2(2):111-113.	89
5344757	Sipes, I. G., Gunawardhana, L., Jolley, C. S., Gupta, P., Earnest, D. L., Lantz, R. C. (1995). Correlation of the time course of liver injury and infiltration of inflammatory cells into rat liver following the administration of the potent hepatotoxicant 1,2-dichlorobenzene. <i>CELLS OF THE HEPATIC SINUSOID</i> 5:81-82.	93
4912250	Valentovic, M. A., Ball, J. G., Anestis, D., Madan, E. (1993). Acute hepatic and renal toxicity of dichlorobenzene isomers in Fischer 344 rats. <i>Journal of Applied Toxicology</i> 13(1):7-Jan.	96
5248928	Valentovic, M. A., Ball, J. G., Anestis, D., Madan, E. (1993). Modification of P450 activity and its effect on 1,2-dichlorobenzene toxicity in Fischer 344 rats. <i>Toxicology</i> 79(3):169-180.	99
1994030	Yang, K. H., Peterson, R. E., Fujimoto, J. M. (1979). Increased bile duct-pancreatic fluid flow in benzene and halogenated benzene-treated rats. <i>Toxicology and Applied Pharmacology</i> 47(3):505-514.	105
Short-term (>1-30 days)		
4930792	Ariyoshi, T., Ideguchi, K., Iwasaki, K., Arakaki, M. (1975). Relationship between chemical structure and activity. II. Influences of isomers in dichlorobenzene, trichlorobenzene, and tetrachlorobenzene on the activities of drug-metabolizing enzymes. <i>Chemical and Pharmaceutical Bulletin</i> 23(4):824-830.	109
200247	Brondeau, M. T., Bonnet, P., Guenier, J. P., De, C. J. (1983). Short-term inhalation test for evaluating industrial hepatotoxicants in rats. <i>Toxicology Letters</i> 19(1-2):139-146.	113
68063	Charbonneau, M., Strasser, J., Jr, Lock, E. A., Turner, M. J., Jr, Swenberg, J. A. (1989). Involvement of reversible binding to "alpha"2u-globulin in 1,4-dichlorobenzene-induced nephrotoxicity. <i>Toxicology and Applied Pharmacology</i> 99(1):122-132.	116
5264573	Dow Chemical, (1981). Initial submission: Orthodichlorobenzene: Inhalation teratology probe study in rats and rabbits (final report) with cover letter dated 102591. :Epa/Ots #88-920000044.	119
5279907	Haas,, R.a. (1979). o-Dichlorobenzene myelotoxicity & cytogenetic study in rats. :Order this.	162
5254311	Kulkarni, S. G., Duong, H., Gomila, R., Mehendale, H. M. (1996). Strain differences in tissue repair response to 1,2-dichlorobenzene. <i>Archives of Toxicology</i> 70(11):714-723.	169

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654546	Lehman-McKeeman, L. D., Caudill, D. (1999). Development of an in vitro competitive binding assay to predict α 2u-globulin nephropathy. <i>In Vitro & Molecular Toxicology</i> 12(2):83-95.	171
1944492	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.	174
5099073	Robinson, M., Bercz, J. P., Ringhand, H. P., Condie, L. W., Parnell, M. J. (1991). Ten- and ninety-day toxicity studies of 1,2-dichlorobenzene administered by oral gavage to Sprague-Dawley rats. <i>Drug and Chemical Toxicology</i> 14(1-2):83-112.	187
201742	Zissu, D. (1995). Histopathological changes in the respiratory tract of mice exposed to ten families of airborne chemicals. <i>Journal of Applied Toxicology</i> 15(3):207-213.	192
Subchronic (>30-91 days)		
5264231	Battelle, (1978). Subchronic toxicity study - ortho-dichlorobenzene, Fischer 344 rats. 7820535:#40-7820535.	196
5278656	Battelle, (1978). Subchronic toxicity study - ortho-dichlorobenzene, B6C3F1 mice.	205
13037009	Eun-Sang, C., Yong-Soon, K., Hye-yeon, C., Kyung, R. (2023). Effect of inhaled 1,2-dichlorobenzene on cytochrome P450s and lipid peroxidation in B6C3F1 mice. <i>Journal of Biomedical Translational Research</i> 24(3):67-82.	229
1944492	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.	234
5099073	Robinson, M., Bercz, J. P., Ringhand, H. P., Condie, L. W., Parnell, M. J. (1991). Ten- and ninety-day toxicity studies of 1,2-dichlorobenzene administered by oral gavage to Sprague-Dawley rats. <i>Drug and Chemical Toxicology</i> 14(1-2):83-112.	258
Chronic (>91 days)		
2962108	Hollingsworth, R. L., Rowe, V. K., Oyen, F., Torkelson, T. R., Adams, E. M. (1958). Toxicity of o-dichlorobenzene: Studies on animals and industrial experience. <i>AMA Archives of Industrial Health</i> 17(3):180-187.	263
1944492	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.	270
Reproductive/Developmental		
6331050	Biodynamics, (1989). An inhalation two-generation reproduction study in rats with orthodichlorobenzene, final report [volume I - V].	292
5305322	Dow Chemical, (1982). Orthodichlorobenzene - inhalation teratology study in rats and rabbits with cover letter.	294
503	Hayes, W. C., Hanley, T. R., Jr, Gushow, T. S., Johnson, K. A., John, J. A. (1985). Teratogenic potential of inhaled dichlorobenzenes in rats and rabbits. <i>Toxicological Sciences</i> 5(1):190-202.	298
Mechanistic-Other		
3058574	Hoglen, N. C., Younis, H. S., Hartley, D. P., Gunawardhana, L., Lantz, R. C., Sipes, I. G. (1998). 1,2-dichlorobenzene-induced lipid peroxidation in male Fischer 344 rats is Kupffer cell dependent. <i>Toxicological Sciences</i> 46(2):376-385.	309
Other (specify)		

13006582	HealthCare,, Bayer (2009). o-Dichlorbenzol: Local lymph node assay in mice (LLNA/IMDS).	311

2962108	Hollingsworth, R. L., Rowe, V. K., Oyen, F., Torkelson, T. R., Adams, E. M. (1958). Toxicity of o-dichlorobenzene: Studies on animals and industrial experience. AMA Archives of Industrial Health 17(3):180-187.	313

Isomer: m-dichlorobenzene

Acute (less than or equal to 24 hr)

201693	Mohtashampur, E., Triebel, R., Straeter, H., Norpoth, K. (1987). The bone marrow clastogenicity of eight halogenated benzenes in male NMRI mice. Mutagenesis 2(2):111-113.	316

Short-term (>1-30 days)

4912371	Umemura, T., Saito, M., Takagi, A., Kurokawa, Y. (1996). Isomer-specific acute toxicity and cell proliferation in livers of B6C3F1 mice exposed to dichlorobenzene. Toxicology and Applied Pharmacology 137(2):268-274.	318

Isomer: o-dichlorobenzene

Short-term (>1-30 days)

4912371	Umemura, T., Saito, M., Takagi, A., Kurokawa, Y. (1996). Isomer-specific acute toxicity and cell proliferation in livers of B6C3F1 mice exposed to dichlorobenzene. Toxicology and Applied Pharmacology 137(2):268-274.	320

Isomer: ortho-DCB

Acute (less than or equal to 24 hr)

4930708	Allis, J. W., Simmons, J. E., House, D. E., Robinson, B. L., Berman, E. (1992). The differential hepatotoxicity and cytochrome P450 responses of Fischer-344 rats to the three isomers of dichlorobenzene. Journal of Biochemical Toxicology 7(4):257-264.	322

Isomer: MISSING ISOMER NEED TO FIX

Acute (less than or equal to 24 hr)

4933243	Stine, E. R., Gunawardhana, L., Sipes, I. G. (1991). The acute hepatotoxicity of the isomers of dichlorobenzene in Fischer-344 and Sprague-Dawley rats: Isomer-specific and strain-specific differential toxicity. Toxicology and Applied Pharmacology 109(3):472-481.	324

Mixture: Dichlorobenzene Waste

Acute (less than or equal to 24 hr)

5278523	Biodynamics, (1987). Primary dermal irritation study in rabbits (4- and 24-hour exposure) of dichlorobenzene waste.	326

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'Missing Conf' indicates that the metric is Acceptable, but the confidence rating is missing.'Missing Comment' indicates that the rating was missing a comment.

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5254311 Table: 1 of 1 User:hindman.andrea@epa.gov	171
5099073 Table: 1 of 2 User:Gallagher.Sarah@epa.gov	190
5099073 Table: 2 of 2 User:Gallagher.Sarah@epa.gov	192
5264231 Table: 1 of 3 User:Luz.Anthony@epa.gov	201
5264231 Table: 2 of 3 User:Luz.Anthony@epa.gov	203
5264231 Table: 3 of 3 User:Luz.Anthony@epa.gov	205
5099073 Table: 1 of 2 User:Gallagher.Sarah@epa.gov	261
5099073 Table: 2 of 2 User:Gallagher.Sarah@epa.gov	263
6331050 Table: 1 of 1 User:Surapureddi.Sailesh@epa.gov	294
5305322 Table: 1 of 2 User:Surapureddi.Sailesh@epa.gov	296
4930708 Table: 1 of 1 User:hindman.andrea@epa.gov	324
4933243 Table: 1 of 1 User:Surapureddi.Sailesh@epa.gov	326

Study Citation:	Ban, M., Hettich, D., Goutet, M., Binet, S. (1998). Serum-borne factor(s) of 1,1-dichloroethylene and 1,2-dichlorobenzene-treated mice inhibited in vitro antibody forming cell response and natural killer cell activity. Toxicology Letters 94(2):93-101.			
Health Outcome(s):	Hepatic/Liver			
Reported Health Effect(s):	Hepatic/Liver: Glucose-6- phosphatase activity in liver section			
Duration:	Acute (less than or equal to 24 hr) acute- single administration			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	1739054			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
Metric 1:	Test Substance Identity	High	Test substance identified by nomenclature as 1,2-dichlorobenzene. CASRN not provided.	
Metric 2:	Test Substance Source	Low	Test substance was purchased from Merck. Lot/batch was not provided and chemical identity was not reported as certified or analytically verified.	
Metric 3:	Test Substance Purity	High	Purity reported as 99%.	
Domain 2: Test Design				
Metric 4:	Negative and Vehicle Controls	Low	Concurrent negative control groups were administered vehicle (corn oil) and one control per dose was used. Control animals were sacrificed at the 6 h time point. No control group was used for other time points.	
Metric 5:	Positive Controls	N/A	Not necessary for this study type.	
Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups.	
Domain 3: Exposure Characterization				
Metric 7:	Preparation and Storage of Test Substance	Medium	Test substance was prepared in corn oil and storage was not reported, however, the study was a single dose administration and storage is unlikely to substantially affect results.	
Metric 8:	Consistency of Exposure Administration	Low	Details of exposure administration are insufficiently reported. Gavage volumes were not reported. Timing of exposure administration across treatment groups was not reported.	
Metric 9:	Reporting of Doses/Concentrations	High	Doses were reported without ambiguity.	
Metric 10:	Exposure Frequency and Duration	High	Test substance was administered as a single gavage dose. This is appropriate for an acute study.	
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	The number of exposure groups and dose spacing was not justified by the authors. Dose spacing was insufficient as changes in immune outcomes were seen at all doses including the lowest dose, therefore it is unclear whether the lowest dose is low enough. Dose spacing for liver and kidney effects may also be insufficient, as it is unclear is the highest dose was high enough to observe an adverse effect.	
Metric 12:	Exposure Route and Method	High	Test substance was administered via oral gavage.	
Domain 4: Test Animals				
Metric 13:	Test Animal Characteristics	High	Species, strain, age, starting body weight were reported	
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were not sufficiently reported. The study report states that animals "were group housed (eight animals/cage) for 7 days under controlled environmental conditions, and had free access to food (UAR-Alimentation) and water."	
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Study Citation:	Ban, M., Hettich, D., Goutet, M., Binet, S. (1998). Serum-borne factor(s) of 1,1-dichloroethylene and 1,2-dichlorobenzene-treated mice inhibited in vitro antibody forming cell response and natural killer cell activity. Toxicology Letters 94(2):93-101.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	Hepatic/Liver: Glucose-6- phosphatase activity in liver section
Duration:	Acute (less than or equal to 24 hr) acute- single administration
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	1739054

Domain	Metric	Rating	Comments
	Metric 15: Number of Animals per Group	Medium	8 animals/group were included. This is appropriate for an acute duration study.
Domain 5: Outcome Assessment			
	Metric 16: Outcome Assessment Methodology	Low	Liver assessment was limited to G-6-P staining. Study authors state "close correlation between liver G-6-Pase staining intensity and the logarithmic values of blood enzyme activities" and "enzymatic activity staining also allowed us to recognize tissue degeneration and necrosis." Additional outcomes to assess liver toxicity (e.g., liver weight, gross pathology, histopathology, ALT, AST, etc.) were not evaluated.
	Metric 17: Consistency of Outcome Assessment	Low	Multiple time points (i.e., 6, 16, 24, 48, 74 hours) were evaluated post-exposure. Only 1,2-DCB treated animals were consistently evaluated at all timepoints. Control animals were evaluated only at the 6-hr post-exposure timepoint.
	Metric 18: Sampling Adequacy	High	Livers from all animals (n = 8/group) were evaluated. Liver staining intensity for glucose-6-phosphatase was expressed as a percentage of light absorption (average value of 5 measurements).
	Metric 19: Blinding of Assessors	N/A	Not necessary for this outcome.
	Metric 20: Negative Control Response	High	The biological responses of the negative control group was 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 (or identified only minor 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 (e.g., infection) that could influence the outcome assessment.
	Metric 23: Data Presentation and Analysis	High	Statistical methods were reported and were appropriate for the data set.
	Metric 24: Reporting of Data	High	All data were reported as mean +/- SEM.

Additional Comments: None

Overall Quality Determination**Medium**

Study Citation:	Ban, M., Hettich, D., Goutet, M., Binet, S. (1998). Serum-borne factor(s) of 1,1-dichloroethylene and 1,2-dichlorobenzene-treated mice inhibited in vitro antibody forming cell response and natural killer cell activity. Toxicology Letters 94(2):93-101.			
Health Outcome(s):	Renal/Kidney			
Reported Health Effect(s):	Renal/Kidney: Kidney levels of alkaline phosphatase, microscopy			
Duration:	Acute (less than or equal to 24 hr) acute- single administration			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	1739054			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
Metric 1:	Test Substance Identity	High	Test substance identified by nomenclature as 1,2-dichlorobenzene. CASRN not provided.	
Metric 2:	Test Substance Source	Low	Test substance was purchased from Merck. Lot/batch was not provided and chemical identity was not reported as certified or analytically verified.	
Metric 3:	Test Substance Purity	High	Purity reported as 99%.	
Domain 2: Test Design				
Metric 4:	Negative and Vehicle Controls	Low	Concurrent negative control groups were administered vehicle (corn oil) and one control per dose was used. Control animals were sacrificed at the 6 h time point. No control group was used for other time points.	
Metric 5:	Positive Controls	N/A	Not necessary for this study type.	
Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups.	
Domain 3: Exposure Characterization				
Metric 7:	Preparation and Storage of Test Substance	Medium	Test substance was prepared in corn oil and storage was not reported, however, the study was a single dose administration and storage is unlikely to substantially affect results.	
Metric 8:	Consistency of Exposure Administration	Low	Details of exposure administration are insufficiently reported. Gavage volumes were not reported. Timing of exposure administration across treatment groups was not reported.	
Metric 9:	Reporting of Doses/Concentrations	High	Doses were reported without ambiguity.	
Metric 10:	Exposure Frequency and Duration	High	Test substance was administered as a single gavage dose. This is appropriate for an acute study.	
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	The number of exposure groups and dose spacing was not justified by the authors. Dose spacing was insufficient as changes in immune outcomes were seen at all doses including the lowest dose, therefore it is unclear whether the lowest dose is low enough. Dose spacing for liver and kidney effects may also be insufficient, as it is unclear if the highest dose was high enough to observe an adverse effect.	
Metric 12:	Exposure Route and Method	High	Test substance was administered via oral gavage.	
Domain 4: Test Animals				
Metric 13:	Test Animal Characteristics	High	Species, strain, age, starting body weight were reported.	
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were not sufficiently reported. The study report states that animals "were group housed (eight animals/cage) for 7 days under controlled environmental conditions, and had free access to food (UAR-Alimentation) and water."	
Metric 15:	Number of Animals per Group	Medium	8 animals/group were included. This is appropriate for an acute duration study.	

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Study Citation:	Ban, M., Hettich, D., Goutet, M., Binet, S. (1998). Serum-borne factor(s) of 1,1-dichloroethylene and 1,2-dichlorobenzene-treated mice inhibited in vitro antibody forming cell response and natural killer cell activity. Toxicology Letters 94(2):93-101.		
Health Outcome(s):	Renal/Kidney		
Reported Health Effect(s):	Renal/Kidney: Kidney levels of alkaline phosphatase, microscopy		
Duration:	Acute (less than or equal to 24 hr) acute- single administration		
Chemical:	o-Dichlorobenzene- Parent compound		
HERO ID:	1739054		
Domain	Metric	Rating	Comments
Domain 5: Outcome Assessment			
Metric 16:	Outcome Assessment Methodology	Low	Renal assessment was limited to staining organ sections for alkaline phosphatase and renal proximal tubules were microscopically examined for damage. Other indicators of organ damage (e.g., kidney weight, gross pathology, histopathology, BUN) were not evaluated.
Metric 17:	Consistency of Outcome Assessment	Low	Multiple time points (i.e., 6, 16, 24, 48, 74 hours) were evaluated post-exposure. Only 1,2-DCB treated animals were consistently evaluated at all timepoints. Control animals were evaluated only at the 6-hr post-exposure timepoint.
Metric 18:	Sampling Adequacy	High	Kidneys from all animals (n=8/group) were evaluated. Approximately 300 renal proximal tubules were examined per animal.
Metric 19:	Blinding of Assessors	N/A	Not necessary for this outcome.
Metric 20:	Negative Control Response	High	The biological responses of the negative control group was 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 (or identified only minor 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 (e.g., infection) that could influence the outcome assessment.
Metric 23:	Data Presentation and Analysis	High	Statistical methods were reported and were appropriate for the data set.
Metric 24:	Reporting of Data	Low	Study authors state that 1,2-DCB "did not provoke either damage tubules or an increase in serologic IL-6 level". Data for this outcome is not shown. The study report indicates kidney sections were also stained for alkaline phosphatase, however, results for this outcome are not provided.
Additional Comments: None			

Overall Quality Determination**Uninformative**

Study Citation:	Ban, M., Hettich, D., Goutet, M., Binet, S. (1998). Serum-borne factor(s) of 1,1-dichloroethylene and 1,2-dichlorobenzene-treated mice inhibited in vitro antibody forming cell response and natural killer cell activity. Toxicology Letters 94(2):93-101.			
Health Outcome(s):	Immune/Hematological			
Reported Health Effect(s):	Immune/Hematological: Serum TNF alpha and interleukin-6 levels, antibody forming cell response and NK cytotoxicity			
Duration:	Acute (less than or equal to 24 hr) acute- single administration			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	1739054			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
Metric 1:	Test Substance Identity	High	Test substance identified by nomenclature as 1,2-dichlorobenzene. CASRN not provided.	
Metric 2:	Test Substance Source	Low	Test substance was purchased from Merck. Lot/batch was not provided and chemical identity was not reported as certified or analytically verified.	
Metric 3:	Test Substance Purity	High	Purity reported as 99%.	
Domain 2: Test Design				
Metric 4:	Negative and Vehicle Controls	Low	Concurrent negative control groups were administered vehicle (corn oil) and one control per dose was used. Control animals were sacrificed at the 6 h time point. No control group was used for other time points.	
Metric 5:	Positive Controls	N/A	Not necessary for this study type.	
Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups.	
Domain 3: Exposure Characterization				
Metric 7:	Preparation and Storage of Test Substance	Medium	Test substance was prepared in corn oil and storage was not reported, however, the study was a single dose administration and storage is unlikely to substantially affect results.	
Metric 8:	Consistency of Exposure Administration	Low	Details of exposure administration are insufficiently reported. Gavage volumes were not reported. Timing of exposure administration across treatment groups was not reported.	
Metric 9:	Reporting of Doses/Concentrations	High	Doses were reported without ambiguity.	
Metric 10:	Exposure Frequency and Duration	High	Test substance was administered as a single gavage dose. This is appropriate for an acute study.	
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	The number of exposure groups and dose spacing was not justified by the authors. Dose spacing was insufficient as changes in immune outcomes were seen at all doses including the lowest dose, therefore it is unclear whether the lowest dose is low enough. Dose spacing for liver and kidney effects may also be insufficient, as it is unclear if the highest dose was high enough to observe an adverse effect.	
Metric 12:	Exposure Route and Method	High	Test substance was administered via oral gavage.	
Domain 4: Test Animals				
Metric 13:	Test Animal Characteristics	High	Species, strain, age, starting body weight were reported.	
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were not sufficiently reported. The study report states that animals "were group housed (eight animals/cage) for 7 days under controlled environmental conditions, and had free access to food (UAR-Alimentation) and water."	
Metric 15:	Number of Animals per Group	Medium	8 animals/group were included. This is appropriate for an acute duration study.	

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Study Citation:	Ban, M., Hettich, D., Goutet, M., Binet, S. (1998). Serum-borne factor(s) of 1,1-dichloroethylene and 1,2-dichlorobenzene-treated mice inhibited in vitro antibody forming cell response and natural killer cell activity. Toxicology Letters 94(2):93-101.
Health Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Immune/Hematological: Serum TNF alpha and interleukin-6 levels, antibody forming cell response and NK cytotoxicity
Duration:	Acute (less than or equal to 24 hr) acute- single administration
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	1739054

Domain	Metric	Rating	Comments
Domain 5: Outcome Assessment			
	Metric 16: Outcome Assessment Methodology	Medium	Assessment of serum TNF-alpha and IL-6 were appropriate and evaluation of humoral immunity and NK cytotoxicity were previously cited and briefly described. Immune-related assessments addressed the outcome of interest.
	Metric 17: Consistency of Outcome Assessment	Low	Multiple time points (i.e., 6, 16, 24, 48, 74 hours) were evaluated post-exposure. Only 1,2-DCB treated animals were consistently evaluated at all timepoints. Control animals were evaluated only at the 6-hr post-exposure timepoint.
	Metric 18: Sampling Adequacy	Medium	Serum was sampled from each animal in all treatment groups and was adequate for the outcome of interest. Sampling for immune assay was done in 5 replicates and was adequate for the outcome of interest.
	Metric 19: Blinding of Assessors	N/A	Not necessary for this outcome.
	Metric 20: Negative Control Response	High	The biological responses of the negative control group was 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 (or identified only minor 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 (e.g., infection) that could influence the outcome assessment.
	Metric 23: Data Presentation and Analysis	High	Statistical methods were reported and were appropriate for the data set.
	Metric 24: Reporting of Data	High	Data were presented as mean +/- SEM for all outcomes by exposure group.

Additional Comments: None

Overall Quality Determination**Medium**

Study Citation:	Besten, Den, C., Vet, J., Besselink, H. T., Kiel, G. S., Berkel, van, M., B.J., Beems, R., Bladeren, Van, P. J. (1991). The liver, kidney, and thyroid toxicity of chlorinated benzenes. Toxicology and Applied Pharmacology 111(1):69-81.		
Health Outcome(s):	Hepatic/Liver; Renal/Kidney; Thyroid; Thyroid;		
Reported Health Effect(s):	Hepatic/Liver: Liver weight, histopathology, serum ALT, liver glutathione levels; Renal/Kidney: Kidney weight, histopathology, BUN; Thyroid: Plasma thyroid hormone levels: thyroxine (T4) and triiodothyronine (T3); Thyroid: Plasma thyroid hormone levels: thyroxine (T4) and triiodothyronine (T3);		
Duration:	Acute (less than or equal to 24 hr) Acute- single i.p.		
Chemical:	o-Dichlorobenzene- Parent compound		
HERO ID:	659923		
Domain	Metric	Rating	Comments
Domain 1: Test Substance			
Metric 1:	Test Substance Identity	High	Hepatic/Liver: Test substance was identified as 1,2-dichlorobenzene.; Renal/Kidney: Test substance was identified as 1,2-dichlorobenzene.; Thyroid: Test substance was identified as 1,2-dichlorobenzene.; Thyroid: Test substance was identified as 1,4-dichlorobenzene.
Metric 2:	Test Substance Source	High	All Outcomes: The source of the test substance was Merck (Darmstadt, Germany).
Metric 3:	Test Substance Purity	High	Hepatic/Liver: The purity of the test substance was reported to be >99%.; Renal/Kidney: The purity of the test substance was reported to be >99%.; Thyroid: The purity of the test substance was reported to be >99%.; Thyroid: The purity of the test substance was reported to be >98%.
Domain 2: Test Design			
Metric 4:	Negative and Vehicle Controls	High	All Outcomes: The negative control group was appropriate (vehicle control).
Metric 5:	Positive Controls	N/A	All Outcomes: Not applicable for this study.
Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: The study did not report how animals were allocated.
Domain 3: Exposure Characterization			
Metric 7:	Preparation and Storage of Test Substance	Medium	All Outcomes: Test substance preparation and storage were not fully reported, however since this is a single i.p. injection study, this lack of information is unlikely to have a substantial impact on results. The study did report the vehicle test substance administered with.
Metric 8:	Consistency of Exposure Administration	High	All Outcomes: Exposure was consistent across study groups. The test substance was delivered via i.p. injection; the volume delivered was 3.33 ml/kg.
Metric 9:	Reporting of Doses/Concentrations	High	All Outcomes: Doses were reported without ambiguity (0, 1, 2 or 4 mmol/kg).
Metric 10:	Exposure Frequency and Duration	High	All Outcomes: The exposure frequency and duration were reported and appropriate for the study design.
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	All Outcomes: Selection of doses were not justified by study authors and did not provide a full range of response (both a NOAEL and LOAEL, with at least one dose above the LOAEL).
Metric 12:	Exposure Route and Method	High	All Outcomes: Exposure route and method were appropriate.
Domain 4: Test Animals			
Metric 13:	Test Animal Characteristics	Low	All Outcomes: The study reports 10-14 week of age only male Wistar rats were used. Starting body weight and source of the animals were not reported.
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Study Citation:	Besten, Den, C., Vet, J., Besselink, H. T., Kiel, G. S., Berkel, van, M., B.J., Beems, R., Bladeren, Van, P. J. (1991). The liver, kidney, and thyroid toxicity of chlorinated benzenes. Toxicology and Applied Pharmacology 111(1):69-81.
Health Outcome(s):	Hepatic/Liver; Renal/Kidney; Thyroid; Thyroid;
Reported Health Effect(s):	Hepatic/Liver: Liver weight, histopathology, serum ALT, liver glutathione levels; Renal/Kidney: Kidney weight, histopathology, BUN; Thyroid: Plasma thyroid hormone levels: thyroxine (T4) and triiodothyronine (T3); Thyroid: Plasma thyroid hormone levels: thyroxine (T4) and triiodothyronine (T3);
Duration:	Acute (less than or equal to 24 hr) Acute- single i.p.
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	659923

Domain	Metric	Rating	Comments
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Medium	All Outcomes: Not all husbandry conditions were fully reported. Study states animals were "housed in air-conditioned and light controlled rooms and were allowed food and water ad libitum." The reporting deficiencies are unlikely to substantially impact results.
	Metric 15: Number of Animals per Group	Medium	All Outcomes: The number of animals per study group was adequate (3-4/group).
Domain 5: Outcome Assessment			
	Metric 16: Outcome Assessment Methodology	High	Hepatic/Liver: The outcome assessment methodology addressed the intended outcomes of interest (histopathology, organ weight and serum biochemistry).; Renal/Kidney: The outcome assessment methodology addressed the intended outcomes of interest (histopathology, organ weight and serum biochemistry).; Thyroid: The outcome assessment methodology addressed the intended outcomes of interest.; Thyroid: The outcome assessment methodology addressed the intended outcomes of interest.
	Metric 17: Consistency of Outcome Assessment	High	All Outcomes: Outcomes were assessed consistently across study groups.
	Metric 18: Sampling Adequacy	High	All Outcomes: Sampling was adequate (n=3-4).
	Metric 19: Blinding of Assessors	N/A	All Outcomes: Blinding was not necessary.
	Metric 20: Negative Control Response	High	All Outcomes: The negative control response was appropriate.
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.
	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.
	Metric 23: Data Presentation and Analysis	High	All Outcomes: Statistical analysis was performed and appropriate.
	Metric 24: Reporting of Data	Medium	All Outcomes: Data were presented for most exposure-related findings; however, data is not reported for some time points.

Additional Comments: None

Overall Quality Determination**High**

Study Citation:	Besten, Den, C., Vet, J., Besselink, H. T., Kiel, G. S., Berkel, van, M., B.J., Beems, R., Bladeren, Van, P. J. (1991). The liver, kidney, and thyroid toxicity of chlorinated benzenes. Toxicology and Applied Pharmacology 111(1):69-81.			
Health Outcome(s):	Clinical signs			
Reported Health Effect(s):	Clinical signs: General appearance.			
Duration:	Acute (less than or equal to 24 hr) Acute- single i.p.			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	659923			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1:	Test Substance Identity	High	Test substance was identified as 1,2-dichlorobenzene.
	Metric 2:	Test Substance Source	High	The source of the test substance was Merck (Darmstadt, Germany).
	Metric 3:	Test Substance Purity	High	The purity of the test substance was reported to be >99%.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	The negative control group was appropriate (vehicle control).
	Metric 5:	Positive Controls	N/A	Not applicable for 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	Test substance preparation and storage were not fully reported, however since this is a single i.p. injection study, this lack of information is unlikely to have a substantial impact on results. The study did report the vehicle test substance administered with.
	Metric 8:	Consistency of Exposure Administration	High	Exposure was consistent across study groups. The test substance was delivered via i.p. injection; the volume delivered was 3.33 ml/kg.
	Metric 9:	Reporting of Doses/Concentrations	High	Doses were reported without ambiguity (0, 1, 2 or 4 mmol/kg).
	Metric 10:	Exposure Frequency and Duration	High	The exposure frequency and duration were reported and appropriate for the study design.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	Selection of doses were not justified by study authors and did not provide a full range of response (both a NOAEL and LOAEL, with at least one dose above the LOAEL).
	Metric 12:	Exposure Route and Method	High	Exposure route and method were appropriate.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Low	The study reports 10-14 week of age only male Wistar rats were used. Starting body weight and source of the animals were not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Not all husbandry conditions were fully reported. Study states animals were “housed in air-conditioned and light controlled rooms and were allowed food and water ad libitum.” The reporting deficiencies are unlikely to substantially impact results.
	Metric 15:	Number of Animals per Group	Medium	The number of animals per study group was adequate (3-4/group).
Domain 5: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	High	The outcome assessment methodology addressed the intended outcomes of interest.
	Metric 17:	Consistency of Outcome Assessment	High	Outcomes were assessed consistently across study groups.
	Metric 18:	Sampling Adequacy	Low	No information on number of animals sampled was provided.

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Study Citation:	Besten, Den, C., Vet, J., Besselink, H. T., Kiel, G. S., Berkel, van, M., B.J., Beems, R., Bladeren, Van, P. J. (1991). The liver, kidney, and thyroid toxicity of chlorinated benzenes. Toxicology and Applied Pharmacology 111(1):69-81.			
Health Outcome(s):	Clinical signs			
Reported Health Effect(s):	Clinical signs: General appearance.			
Duration:	Acute (less than or equal to 24 hr) Acute- single i.p.			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	659923			
Domain	Metric	Rating	Comments	
	Metric 19: Blinding of Assessors	N/A	Blinding was not necessary.	
	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	Although the study did not report all information to determine confounding, reported information did not identify differences.	
	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	N/A	Not applicable for this outcome of interest.	
	Metric 24: Reporting of Data	Uninformative	No information is provided on clinical signs of toxicity.	
Additional Comments:	Study reports observing animals for clinical signs but does not report any data or observation made.			
Overall Quality Determination		Uninformative		

Study Citation:	Besten, Den, C., Vet, J., Besselink, H. T., Kiel, G. S., Berkel, van, M., B.J., Beems, R., Bladeren, Van, P. J. (1991). The liver, kidney, and thyroid toxicity of chlorinated benzenes. Toxicology and Applied Pharmacology 111(1):69-81.			
Health Outcome(s):	Nutritional/Metabolic			
Reported Health Effect(s):	Nutritional/Metabolic: Body weight			
Duration:	Acute (less than or equal to 24 hr) Acute- single i.p.			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	659923			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	Test substance was identified as 1,2-dichlorobenzene.	
	Metric 2: Test Substance Source	High	The source of the test substance was Merck (Darmstadt, Germany).	
	Metric 3: Test Substance Purity	High	The purity of the test substance was reported to be >99%.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	The negative control group was appropriate (vehicle control).	
	Metric 5: Positive Controls	N/A	Not applicable for 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	Test substance preparation and storage were not fully reported, however since this is a single i.p. injection study, this lack of information is unlikely to have a substantial impact on results. The study did report the vehicle test substance administered with.	
	Metric 8: Consistency of Exposure Administration	High	Exposure was consistent across study groups. The test substance was delivered via i.p. injection; the volume delivered was 3.33 ml/kg.	
	Metric 9: Reporting of Doses/Concentrations	High	Doses were reported without ambiguity (0, 1, 2 or 4 mmol/kg).	
	Metric 10: Exposure Frequency and Duration	High	The exposure frequency and duration were reported and appropriate for the study design.	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	Medium	Selection of doses were not justified by study authors and did not provide a full range of response (both a NOAEL and LOAEL, with at least one dose above the LOAEL).	
	Metric 12: Exposure Route and Method	High	Exposure route and method were appropriate.	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	Low	The study reports 10-14 week of age only male Wistar rats were used. Starting body weight and source of the animals were not reported.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Medium	Not all husbandry conditions were fully reported. Study states animals were “housed in air-conditioned and light controlled rooms and were allowed food and water ad libitum.” The reporting deficiencies are unlikely to substantially impact results.	
	Metric 15: Number of Animals per Group	Medium	The number of animals per study group was adequate (3-4/group).	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	High	The outcome assessment methodology addressed the intended outcomes of interest.	
	Metric 17: Consistency of Outcome Assessment	High	Outcomes were assessed consistently across study groups.	
	Metric 18: Sampling Adequacy	Low	Number of animals sampled to determine body weight data were not reported.	
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Study Citation:	Besten, Den, C., Vet, J., Besselink, H. T., Kiel, G. S., Berkel, van, M., B.J., Beems, R., Bladeren, Van, P. J. (1991). The liver, kidney, and thyroid toxicity of chlorinated benzenes. Toxicology and Applied Pharmacology 111(1):69-81.
Health Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Nutritional/Metabolic: Body weight
Duration:	Acute (less than or equal to 24 hr) Acute- single i.p.
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	659923

Domain	Metric	Rating	Comments
	Metric 19: Blinding of Assessors	N/A	Blinding was not necessary.
	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	Although the study did not report all information to determine confounding, reported information did not identify differences.
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 performed and appropriate.
Metric 24:	Reporting of Data	Low	Body weight data is not adequately reported. Study states a significant decrease (6-13%) from control but does not provide variability or if decrease was dose related.

Additional Comments: None

Overall Quality Determination**High**

Study Citation:	Brondeau, M. T., Ban, M., Bonnet, P., Guenier, J. P., Ceauriz, de, J. (1986). Concentration-related changes in blood and tissue parameters of hepatotoxicity and their interdependence in rats exposed to bromobenzene and 1,2-dichlorobenzene. Toxicology Letters 31(2):159-166.			
Health Outcome(s):	Hepatic/Liver			
Reported Health Effect(s):	Hepatic/Liver: Increase in activity of serum glutamate dehydrogenase and sorbitol dehydrogenase Decrease in liver Glucose-6-phosphatase activity in the centrolobular areas			
Duration:	Acute (less than or equal to 24 hr) 4hr-inhalation			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	597571			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	Reported as 1,2-dichlorobenzene; CASRN not provided	
	Metric 2: Test Substance Source	High	A commercial source was provided; batch and lot number were not reported.	
	Metric 3: Test Substance Purity	High	Reported as 99% pure	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	Control animals were exposed to filtered-air only	
	Metric 5: Positive Controls	N/A	Not necessary for the study type	
	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	High	Generation of test atmospheres was clearly described. The test substance was vaporized into the inlet pipe using a bubbler.	
	Metric 8: Consistency of Exposure Administration	High	Control groups were concurrently exposed. The time of day of exposure was not reported, but there is no indication that there were any differences in exposure methods across groups	
	Metric 9: Reporting of Doses/Concentrations	Medium	Exposure concentrations were clearly reported, although it was not specified whether these were target, nominal, or analytical concentrations. The study authors did, however, indicated that exposure levels were analyzed twice per exposure via GC, and a table in the study indicates that the chemical exposure levels were the means of 2 or 3 samples (suggesting these were measured concentrations). The error for the measurement is not reported.	
	Metric 10: Exposure Frequency and Duration	High	Exposure frequency and duration were appropriate for the purposes of the study	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	Study included 4 exposure groups plus a control	
	Metric 12: Exposure Route and Method	Medium	Whole body exposure in a dynamic air chamber. The number of air changes/hour was not reported	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	Medium	Species, strain, sex, and initial range of body weights were reported. The animal age was not specified. Animals were obtained from a commercial source	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Medium	Animal husbandry conditions were not reported. Temperature and humidity within the exposure chambers was specified, and animals were not given food or water during exposure, but other details were not provided.	
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Study Citation:	Brondeau, M. T., Ban, M., Bonnet, P., Guenier, J. P., Ceuriz, de, J. (1986). Concentration-related changes in blood and tissue parameters of hepatotoxicity and their interdependence in rats exposed to bromobenzene and 1,2-dichlorobenzene. Toxicology Letters 31(2):159-166.			
Health Outcome(s):	Hepatic/Liver			
Reported Health Effect(s):	Hepatic/Liver: Increase in activity of serum glutamate dehydrogenase and sorbitol dehydrogenase Decrease in liver Glucose-6-phosphatase activity in the centrolobular areas			
Duration:	Acute (less than or equal to 24 hr) 4hr-inhalation			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	597571			
Domain	Metric	Rating	Comments	
	Metric 15:	Number of Animals per Group	Medium	The number of animals (n=10 males/group) was appropriate for the outcomes of interest.
Domain 5: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	Low	The purpose of the study appeared to be to relate blood parameters to hepatotoxicity. The study successfully measured the blood parameters and liver enzymes of interest, but failed to also evaluate other measures of liver damage (e.g., histology, liver weight etc), in order to look at this relationship. The study used liver G6-Pase staining as its measure of hepatotoxicity, which may not be the most sensitive or informative endpoint.
	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	Outcomes were not subjective; blinding was not necessary.
	Metric 20:	Negative Control Response	High	The negative controls parameters appeared to be within the expected values.
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 (or identified only minor differences) among study groups in the above listed confounding factors.
	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 performed and was appropriate for the datasets
	Metric 24:	Reporting of Data	High	Data for all of the outcomes measured were clearly reported as means $\pm$ SE
Additional Comments:	Based on the serum parameters measured. This study could also be considered mechanistic only. The serum parameters accepted/considered to be apical are not well defined; ALT and AST are provided as examples of relevant markers of liver function but were not measured.			

Overall Quality Determination**High**

Study Citation:	Brondeau, M. T., Ban, M., Bonnet, P., Guenier, J. P., Ceaurriz, de, J. (1989). Acetone compared to other ketones in modifying the hepatotoxicity of inhaled 1,2-dichlorobenzene in rats and mice. Toxicology Letters 49(1):69-78.			
Health Outcome(s):	Hepatic/Liver			
Reported Health Effect(s):	Hepatic/Liver: Rat: serum glutamate dehydrogenase activity (as a marker of liver necrosis); liver cytochrome P-450 content and glutathione-S-transferase activityMice: liver glucose-6-phosphatase (no apical effects, mouse study is not further assessed)			
Duration:	Acute (less than or equal to 24 hr) Acute- rat			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	3119620			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
Metric 1:	Test Substance Identity	High	The test substance was definitively identified by name as 1,2-dichlorobenzene. CASRN was not reported.	
Metric 2:	Test Substance Source	Low	The source of the test substance was reported (Merck Schuchard).	
Metric 3:	Test Substance Purity	Low	The purity was not reported.	
Domain 2: Test Design				
Metric 4:	Negative and Vehicle Controls	High	A concurrent control group was exposed to air.	
Metric 5:	Positive Controls	N/A	A positive control was not required for the study type.	
Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated into study groups.	
Domain 3: Exposure Characterization				
Metric 7:	Preparation and Storage of Test Substance	Medium	No information on storage of test substance was reported. Generation of vapor was described adequately.	
Metric 8:	Consistency of Exposure Administration	Medium	Not all details of administration were reported. The number of animals/chamber was not reported.	
Metric 9:	Reporting of Doses/Concentrations	Medium	Actual concentrations were reported. Samples were collected each hour during the 4 hours exposure period, mean concentrations were reported without variance.	
Metric 10:	Exposure Frequency and Duration	High	The exposure duration (4 hours) was appropriate for the aim of the study.	
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	N/A	The study tested a single exposure group known to induce hepatotoxicity. The purpose of the study was not to identify a dose-response.	
Metric 12:	Exposure Route and Method	Medium	Whole-body inhalation chamber was used; the air flow was 10-20 m3/hr in a 200-liter chamber. This would equate to 10-20 air changes/hr.	
Domain 4: Test Animals				
Metric 13:	Test Animal Characteristics	Medium	The study used adult male Sprague-Dawley rats (250-300 g). Animals were obtained from Iffa-Credo France.	
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Housing conditions were not reported; however, the study does say that animals were housed in animal quarters under controlled environmental conditions, suggesting conditions were likely uniform across groups.	
Metric 15:	Number of Animals per Group	Medium	The number of animals/group was sufficient.	
Domain 5: Outcome Assessment				

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Study Citation:	Brondeau, M. T., Ban, M., Bonnet, P., Guenier, J. P., Ceaurriz, de, J. (1989). Acetone compared to other ketones in modifying the hepatotoxicity of inhaled 1,2-dichlorobenzene in rats and mice. Toxicology Letters 49(1):69-78.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	Hepatic/Liver: Rat: serum glutamate dehydrogenase activity (as a marker of liver necrosis); liver cytochrome P-450 content and glutathione-S-transferase activity Mice: liver glucose-6-phosphatase (no apical effects, mouse study is not further assessed)
Duration:	Acute (less than or equal to 24 hr) Acute- rat
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	3119620

Domain	Metric	Rating	Comments
	Metric 16: Outcome Assessment Methodology	Low	The outcome methodology was partially sensitive to the outcome of interest (hepatotoxicity). Only Serum glutamate dehydrogenase activity, liver glutathione-s-transferase activity and liver cytochrome P450 levels were measured. Liver weights, histopathology, or other serum liver enzymes were not assessed. This study was focused on testing the potential for pre-exposures to ketones to potentiate the o-DCB response. Assessing additional measures of hepatotoxicity would have been appropriate.
	Metric 17: Consistency of Outcome Assessment	High	The same protocols were applied to all study groups. Based on the information provided, there is no indication of inconsistencies in outcome assessment.
	Metric 18: Sampling Adequacy	High	Sampling was sufficient. The study reported fining for all rats (5/group).
	Metric 19: Blinding of Assessors	N/A	Blinding was not required for the outcomes of interest.
	Metric 20: Negative Control Response	Medium	The negative control response was appropriate.
Domain 6: Confounding / Variable Control			
	Metric 21: Confounding Variables in Test Design and Procedures	Low	The study did not report information to determine confounding. Body weight and food intake were not reported. The test substance is a respiratory irritant; therefore, respiratory rate should be evaluated.
	Metric 22: Health Outcomes Unrelated to Exposure	Medium	The study did not report any information to support or dismiss there were differences in animal attrition or health unrelated to exposure.
	Metric 23: Data Presentation and Analysis	High	Statistical methods were reported and appropriate.
	Metric 24: Reporting of Data	High	Data are fully reported with means +/- SE and number of animals/group.

Additional Comments: None

Overall Quality Determination**Medium**

Study Citation:	Brondeau, M. T., Bonnet, P., Guenier, J. P., De, C. J. (1983). Short-term inhalation test for evaluating industrial hepatotoxicants in rats. Toxicology Letters 19(1-2):139-146.			
Health Outcome(s):	Hepatic/Liver (Serum enzyme activity for liver damage biomarkers: SDH, GLDH, GOT, and GPT.)			
Reported Health Effect(s):	Hepatic/Liver (Serum enzyme activity for liver damage biomarkers: SDH, GLDH, GOT, and GPT.): Serum enzyme activities (units per ml (U/ml), or nmol per min per ml) of liver hepatotoxicity biomarkers ALT (GPT), AST (GOT), glutamate dehydrogenase (GLDH) and sorbitol dehydrogenase (SHD).			
Duration:	Acute (less than or equal to 24 hr) Acute- 4 hour			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	200247			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	Test substance was identified in nomenclature as o-dichlorobenzene; no CASRN.	
	Metric 2: Test Substance Source	Low	The source of the test substance was Merck. Batch/lot numbers were not provided.Covers the lack of test substance identity in Metric 1 that did not report CASRN or chemical structure without double counting quality metrics.	
	Metric 3: Test Substance Purity	High	The purity of the test substance was reported as >99.0%.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	Negative controls were exposed to clean filtered air.	
	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 if/how animals were allocated.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Low	Preparation and storage are adequately described given the volatility of the test substance.	
	Metric 8: Consistency of Exposure Administration	Medium	Details of exposure were limited; however, this is unlikely to substantially impact results.Unreported why the 6 chemicals tested in the study had different number of doses. Some chemicals tested at 4 doses, one tested at 5, some tested at 6.	
	Metric 9: Reporting of Doses/Concentrations	Medium	Target concentrations were not reported. Chemical concentration levels are means of 3 samples or more with continuous monitoring, with a coefficient of variation of < 13%.	
	Metric 10: Exposure Frequency and Duration	High	Exposure frequency and duration were reported and appropriate. Single 4 hour exposure or 6 hour exposure (2 or 4 days).	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	Single 4 hour: The number of dose groups was appropriate to elicit a full range or responses.	
	Metric 12: Exposure Route and Method	Medium	Dynamic whole body inhalation chambers were used with adjustable air flows of air (10-12 m3/hr).Unknown distribution of test substance in the whole body inhalation chamber, since not reported, despite describing sampling methods. Uncertainty in parameters related to using the whole body inhalation chamber, like the number of air changes (minimum of 10/hr being required), and weather the cages were big enough for the rats and unknown how the rats were caged, possibly with more than one rat per cage.	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	Medium	Age of rats and individual body weights at study initiation were not reported.	
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Study Citation:	Brondeau, M. T., Bonnet, P., Guenier, J. P., De, C. J. (1983). Short-term inhalation test for evaluating industrial hepatotoxicants in rats. Toxicology Letters 19(1-2):139-146.			
Health Outcome(s):	Hepatic/Liver (Serum enzyme activity for liver damage biomarkers: SDH, GLDH, GOT, and GPT.)			
Reported Health Effect(s):	Hepatic/Liver (Serum enzyme activity for liver damage biomarkers: SDH, GLDH, GOT, and GPT.): Serum enzyme activities (units per ml (U/ml), or nmol per min per ml) of liver hepatotoxicity biomarkers ALT (GPT), AST (GOT), glutamate dehydrogenase (GLDH) and sorbitol dehydrogenase (SHD).			
Duration:	Acute (less than or equal to 24 hr) Acute- 4 hour			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	200247			
Domain	Metric	Rating	Comments	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Low	No husbandry conditions were not reported, except that food and water were not available during exposure	
	Metric 15: Number of Animals per Group	Medium	The number of animals treated per group was appropriate (n=8)	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	Low	Histology and organ weight were not assessed (only serum chemistry).	
	Metric 17: Consistency of Outcome Assessment	Low	Details regarding outcome assessment were limited. This is especially uncertain given the only measurements made were serum chemistry with no contextualization from body weights, liver weight, liver histology. The study authors did report that "The choice of seric parameters and sampling time was the result of preliminary experiments conducted to point out the best experimental conditions and not reported here." However, there was no reference or information provided on those parameters, which leaves uncertainty in outcome assessment consistency.	
	Metric 18: Sampling Adequacy	High	Data are means +/- SE for 8 rats in each treatment group for the first, single 4-hour acute exposure. Seems sufficient since serum enzyme activity was the only outcome measure for liver-related biomarkers. Table 1.	
	Metric 19: Blinding of Assessors	N/A	Blinding was not necessary for this study type.	
	Metric 20: Negative Control Response	High	Negative control response was reported and appropriate.The study used a manufacturer kit to measure serum enzyme activity for liver damage biomarkers. The authors stated, "...diagnostic kits purchased from Boehringer Mannheim, France," and "...Quality controls were systematically performed (Precinorm E and S, Boehringer)."GOT and GPT appeared to have high background/values for negative control compared to test substance exposure (Table 1).	
Domain 6: Confounding / Variable Control				
	Metric 21: Confounding Variables in Test Design and Procedures	Low	Study did not report all information to determine confounding, reported information did not identify differences.o-DCB is a respiratory irritant and toxicant, without respiration rate information nor other individual animal information, e.g., body weights, food and water consumption, a low confidence level is most appropriate.(NJ DEH) https://www.nj.gov/health/eoh/rtkweb/documents/fs/0642.pdf (ATSDR) https://wwwn.cdc.gov/TSP/MMG/MMGDetails.aspx?mmgid=1208&toxid=126 (Thermo Fisher) https://www.fishersci.com/store/msds?partNumber=AC396961000&productDescription=1%2C2-DICHLOROBENZENE&vendorId=VN00032119&countryCode=US&language=en	
	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 performed (Student's t-test).	
	Metric 24: Reporting of Data	High	Exposure related stated outcomes of interest were reported.	

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Study Citation:	Brondeau, M. T., Bonnet, P., Guenier, J. P., De, C. J. (1983). Short-term inhalation test for evaluating industrial hepatotoxicants in rats. Toxicology Letters 19(1-2):139-146.
Health Outcome(s):	Hepatic/Liver (Serum enzyme activity for liver damage biomarkers: SDH, GLDH, GOT, and GPT.)
Reported Health Effect(s):	Hepatic/Liver (Serum enzyme activity for liver damage biomarkers: SDH, GLDH, GOT, and GPT.): Serum enzyme activities (units per ml (U/ml), or nmol per min per ml) of liver hepatotoxicity biomarkers ALT (GPT), AST (GOT), glutamate dehydrogenase (GLDH) and sorbitol dehydrogenase (SHD).
Duration:	Acute (less than or equal to 24 hr) Acute- 4 hour
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	200247

Domain	Metric	Rating	Comments
Additional Comments:	This study only evaluated male Sprague-Dawley rats. The two chemicals under active evaluation by EPA, that were evaluated in this study, are 1,2-dichloroethane and o-dichlorobenzene. A major limitation of this study was that both of these test substances are known respiratory irritants and this study did not measure respiration rate of animals to determine if that influenced the serum enzyme activity biomarkers for liver damage. The diagnostic value of the 4 serum biomarkers for liver damage was unclear, especially given there was no concurrent liver weights or liver histology/cytology. the serum enzyme biomarkers for liver damage, GOT and GPT seemed to be the least diagnostic of the 4 serum enzymes measured. There was no individual animal data reported, e.g., initial body weights, weight changes over the course of the study nor food and water consumption.		

Overall Quality Determination**Medium**

Study Citation:	Brondeau, M. T., Bonnet, P., Guenier, J. P., Simon, P., Ceaurriz, de, J. (1990). Adrenal-dependent leucopenia after short-term exposure to various airborne irritants in rats. Journal of Applied Toxicology 10(2):83-86.			
Health Outcome(s):	Immune/Hematological			
Reported Health Effect(s):	Immune/Hematological: Limited hematology parameters			
Duration:	Acute (less than or equal to 24 hr) 4-hr inhalation			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	63408			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1:	Test Substance Identity	High	The test substance was identified as 1,2-dichlorobenzene
	Metric 2:	Test Substance Source	Low	The test substance source was not reported and was not analytically verified by the performing laboratory.
	Metric 3:	Test Substance Purity	Low	
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	Control animals were exposed to clean filtered air
	Metric 5:	Positive Controls	N/A	Not necessary for this study type/outome
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups.
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and Storage of Test Substance	Low	Limited details were provided for atmosphere generation. Dynamic chambers were used with an air-flow of 10-12 min/hr, and the test substance was vaporized by bubbling. Additional methods and equipment used for vapor generation were not specified.
	Metric 8:	Consistency of Exposure Administration	Low	
	Metric 9:	Reporting of Doses/Concentrations	Low	It is unclear whether the concentrations reported are target, nominal or analytical. Based on information in the methods, atmosphere sampling and analysis was performed, but no analytical measurements were reported, and it was not indicated if these were within an acceptable range of nominal. In Figure one, it does indicate that exposure concentrations were means from at least two samples, suggesting analytical measurements may have been used.
	Metric 10:	Exposure Frequency and Duration	High	
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The number of exposure groups and spacing were adequate to show a dose-response for the outcome of interest.
	Metric 12:	Exposure Route and Method	Medium	The exposure route was appropriate for the outcome of interest. Air-flow was reported, but the number of air changes per hour was not specified.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Medium	Species, strain, sex, source, and an initial BW range were provided. The age of the animals was not reported
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Temperature, light cycle, and food and water availability were reported and acceptable. Humidity, housing/bedding information was not reported.
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Study Citation:	Brondeau, M. T., Bonnet, P., Guenier, J. P., Simon, P., Ceaurriz, de, J. (1990). Adrenal-dependent leucopenia after short-term exposure to various airborne irritants in rats. Journal of Applied Toxicology 10(2):83-86.
Health Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Immune/Hematological: Limited hematology parameters
Duration:	Acute (less than or equal to 24 hr) 4-hr inhalation
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	63408

Domain	Metric	Rating	Comments
	Metric 15: Number of Animals per Group	Medium	The number of animals (10/group in one experiment and 5/group in another) were appropriate and sufficient to allow for statistical analysis.
Domain 5: Outcome Assessment			
	Metric 16: Outcome Assessment Methodology	High	Details of outcome assessment methodology were provided and appropriate.
	Metric 17: Consistency of Outcome Assessment	High	Outcome assessment methodology was consistent across all groups.
	Metric 18: Sampling Adequacy	High	All exposed animals were sampled (as specified in the data tables)
	Metric 19: Blinding of Assessors	N/A	The outcomes were not subjected; therefore, blinding was not necessary.
	Metric 20: Negative Control Response	High	The blood cell counts in control animals appeared to be acceptable.
Domain 6: Confounding / Variable Control			
	Metric 21: Confounding Variables in Test Design and Procedures	Low	Respiratory rates were not reported and the test substance was reported to be an irritant.
	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	Data were statistically analyzed by one-way ANOVA.
	Metric 24: Reporting of Data	High	Results from all groups were adequately reported as means (SE) in tables or graphically presented.

Additional Comments: None

Overall Quality Determination**Medium**

Study Citation:	Ceaurriz, De, J., Gagnaire, F., Ban, M., Bonnet, P. (1988). Assessment of the relative hazard involved with airborne irritants with additional hepatotoxic or nephrotoxic properties in mice. Journal of Applied Toxicology 8(6):417-422.			
Health Outcome(s):	Irritation			
Reported Health Effect(s):	Irritation: Respiratory irritation (breathing rate); also relevant to lungs/respiratory			
Duration:	Acute (less than or equal to 24 hr) 15-min nose only inhalation			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	1441241			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	Test substance identified as 1,2-dichlorobenzene; CASRN not provided.	
	Metric 2: Test Substance Source	Low	A commercial source was reported (DCB provided by Merck Schuchardt (Darmstadt, FRG)). The batch and/or lot number were not provided.	
	Metric 3: Test Substance Purity	High	Purity reported as >99%	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	Each animal serves as its own control, appropriate control timepoints (baseline before exposure) are included. Based on the text provided, it suggests baseline measurements were taken from animals restrained in the same manner as during exposure.	
	Metric 5: Positive Controls	N/A	Not necessary for the study type	
	Metric 6: Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	High	Some details of vapor generation are were provided including limited details on equipment. A dynamic chamber was used, airflow was reported.	
	Metric 8: Consistency of Exposure Administration	High	Details of exposure administration were reported and exposures were administered consistently across study groups in a scientifically sound manner	
	Metric 9: Reporting of Doses/Concentrations	High	Analytical measurements were provided. The exposure concentrations reported were the average of three samples taken during the 15-min exposure.	
	Metric 10: Exposure Frequency and Duration	High	The frequency and duration were appropriate for the purposes of the study.	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	The number of exposure groups was acceptable and appropriate for identifying an RD50 value.	
	Metric 12: Exposure Route and Method	High	The exposure route was consistent with standard procedures for taking measurements of respiratory rates; however, the methodology increases the stress of animals which must be taken into consideration. Because the exposure duration was only 15-minutes, the number of air changes per hour is not a necessary parameter.	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	Medium	Animal species, strain, sex, and body weights were reported and appropriate. The age was not provided. Animals were commercially obtained.	

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Study Citation:	Ceaurriz, De, J., Gagnaire, F., Ban, M., Bonnet, P. (1988). Assessment of the relative hazard involved with airborne irritants with additional hepatotoxic or nephrotoxic properties in mice. Journal of Applied Toxicology 8(6):417-422.			
Health Outcome(s):	Irritation			
Reported Health Effect(s):	Irritation: Respiratory irritation (breathing rate); also relevant to lungs/respiratory			
Duration:	Acute (less than or equal to 24 hr) 15-min nose only inhalation			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	1441241			
Domain	Metric	Rating	Comments	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were not sufficiently reported. The text indicates that animals were housed "under controlled environmental conditions," further details were not provided. Food and water were reported to be available ad libitum, except during exposure periods.	
	Metric 15: Number of Animals per Group	Medium	The number of animals per study group was reported, appropriate for the study type and outcome analysis	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	High	The outcome assessment methodology addressed the intended outcome(s) of interest AND the assessment methodology was sensitive and appropriate for the outcomes(s) 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 (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 the outcome of interest.	
	Metric 20: Negative Control Response	High	Each animal served as their own control. Basal respiratory rates were consistent across all groups before exposure.	
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 (or identified only minor differences) among study groups in the above listed confounding factors.	
	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 methods (including any calculations or data transformations) were clearly described or had only minor omissions and were appropriate for the dataset(s).	
	Metric 24: Reporting of Data	High	The data were adequately reported.	
Additional Comments:	The purpose of this part of the study was to determine RD50 values, as an indicator of respiratory irritation. This endpoint is relevant to both lung/respiratory and irritation outcomes. This form 3 is filled out under irritation but also applies to lung/respiratory.			

Overall Quality Determination**High**

Study Citation:	Ceaurriz, De, J., Gagnaire, F., Ban, M., Bonnet, P. (1988). Assessment of the relative hazard involved with airborne irritants with additional hepatotoxic or nephrotoxic properties in mice. Journal of Applied Toxicology 8(6):417-422.			
Health Outcome(s):	Mortality			
Reported Health Effect(s):	Mortality: death			
Duration:	Acute (less than or equal to 24 hr) 4-hr whole body inhalation			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	1441241			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	Test substance identified as 1,2-dichlorobenzene; CASRN not provided.	
	Metric 2: Test Substance Source	Low	A commercial source was reported (DCB provided by Merck Schuchardt (Darmstadt, FRG)). The batch and/or lot number were not provided.	
	Metric 3: Test Substance Purity	High	Purity reported as >99%	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	Control animals were exposed to clean filtered air. Based on the data tables provided, it appears separate concurrent negative control groups were used for each exposure concentration.	
	Metric 5: Positive Controls	N/A	Not necessary for the study type	
	Metric 6: Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	High	Some details of vapor generation are were provided including limited details on equipment. A dynamic chamber was used, airflow was reported.	
	Metric 8: Consistency of Exposure Administration	High	Details of exposure administration were reported and exposures were administered consistently across study groups in a scientifically sound manner.	
	Metric 9: Reporting of Doses/Concentrations	High	Analytical measurements were provided. The exposure concentrations reported were the average of three samples taken during the 4-hr exposure period.	
	Metric 10: Exposure Frequency and Duration	High	The frequency and duration were appropriate for the purposes of the study.	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	The number of exposure groups was acceptable and ranged from 392-976 ppm DCB. No mortality was observed at any dose.	
	Metric 12: Exposure Route and Method	Medium	The number of air changes per hour was not reported, but a dynamic chamber was used.	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	Medium	Animal species, strain, sex, and body weights were reported and appropriate. The age was not provided. Animals were commercially obtained.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were not sufficiently reported. The text indicates that animals were housed "under controlled environmental conditions," further details were not provided. Food and water were reported to be available ad libitum, except during exposure periods.	
	Metric 15: Number of Animals per Group	Medium	The number of animals per study group was reported, appropriate for the study type and outcome analysis	
Domain 5: Outcome Assessment				
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Study Citation:	Ceaurriz, De, J., Gagnaire, F., Ban, M., Bonnet, P. (1988). Assessment of the relative hazard involved with airborne irritants with additional hepatotoxic or nephrotoxic properties in mice. Journal of Applied Toxicology 8(6):417-422.
Health Outcome(s):	Mortality
Reported Health Effect(s):	Mortality: death
Duration:	Acute (less than or equal to 24 hr) 4-hr whole body inhalation
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	1441241

Domain	Metric	Rating	Comments
	Metric 16: Outcome Assessment Methodology	High	The methods did not specify that animals were observed for mortality; however, it was reported in the results that no animals died.
	Metric 17: Consistency of Outcome Assessment	Medium	There were no details regarding outcome assessment, but it was assumed to be consistent as it is stated that no animals died during the experiment.
	Metric 18: Sampling Adequacy	High	Although not explicitly stated, it is assumed at all animals were monitored for mortality
	Metric 19: Blinding of Assessors	N/A	Not necessary for the outcome of interest.
	Metric 20: Negative Control Response	Medium	It was reported that no animals died, although specific results for controls were not separately reported.
Domain 6: Confounding / Variable Control			
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	A previous experiment reported that the test substance is a respiratory irritant and causes changes in respiratory rate. This did not appear to impact mortality.
	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 necessary (negative results)
	Metric 24: Reporting of Data	High	Negative findings were reported qualitatively in the text.
Additional Comments: None			

Overall Quality Determination**High**

Study Citation:	Ceaurriz, De, J., Gagnaire, F., Ban, M., Bonnet, P. (1988). Assessment of the relative hazard involved with airborne irritants with additional hepatotoxic or nephrotoxic properties in mice. Journal of Applied Toxicology 8(6):417-422.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	Hepatic/Liver: G6-phosphate histochemistry in the liver
Duration:	Acute (less than or equal to 24 hr) 4-hr whole body inhalation
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	1441241

Domain	Metric	Rating	Comments
Domain 1: Test Substance			
	Metric 1: Test Substance Identity	High	Test substance identified as 1,2-dichlorobenzene; CASRN not provided.
	Metric 2: Test Substance Source	Low	A commercial source was reported (DCB provided by Merck Schuchardt (Darmstadt, FRG)). The batch and/or lot number were not provided.
	Metric 3: Test Substance Purity	High	Purity reported as >99%
Domain 2: Test Design			
	Metric 4: Negative and Vehicle Controls	High	Control animals were exposed to clean filtered air. Based on the data tables provided, it appears separate concurrent negative control groups were used for each exposure concentration.
	Metric 5: Positive Controls	N/A	Not necessary for the study type
	Metric 6: Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups.
Domain 3: Exposure Characterization			
	Metric 7: Preparation and Storage of Test Substance	High	Some details of vapor generation are were provided including limited details on equipment. A dynamic chamber was used, airflow was reported.
	Metric 8: Consistency of Exposure Administration	High	Details of exposure administration were reported and exposures were administered consistently across study groups in a scientifically sound manner
	Metric 9: Reporting of Doses/Concentrations	High	Analytical measurements were provided. The exposure concentrations reported were the average of three samples taken during the 4-hr exposure period.
	Metric 10: Exposure Frequency and Duration	High	The frequency and duration were appropriate for the purposes of the study.
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	Medium	The number of exposure groups was acceptable, a NOAEL was not identified indicating a lower exposure concentration may have been appropriate.
	Metric 12: Exposure Route and Method	Medium	The number of air changes per hour was not reported, but a dynamic chamber was used.
Domain 4: Test Animals			
	Metric 13: Test Animal Characteristics	Medium	Animal species, strain, sex, and body weights were reported and appropriate. The age was not provided. Animals were commercially obtained.
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were not sufficiently reported. The text indicates that animals were housed "under controlled environmental conditions," further details were not provided. Food and water were reported to be available ad libitum, except during exposure periods.
	Metric 15: Number of Animals per Group	Medium	The number of animals per study group was reported, appropriate for the study type and outcome analysis
Domain 5: Outcome Assessment			

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Study Citation:	Ceaurriz, De, J., Gagnaire, F., Ban, M., Bonnet, P. (1988). Assessment of the relative hazard involved with airborne irritants with additional hepatotoxic or nephrotoxic properties in mice. Journal of Applied Toxicology 8(6):417-422.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	Hepatic/Liver: G6-phosphate histochemistry in the liver
Duration:	Acute (less than or equal to 24 hr) 4-hr whole body inhalation
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	1441241

Domain	Metric	Rating	Comments
	Metric 16: Outcome Assessment Methodology	High	G6-phosphatase histochemistry is not a typical endpoint for evaluating hepatic effects, but the study authors specifically indicated this was a tool used for evaluating endoplasmic reticulum damage in liver cells and it appeared to be a sensitive method.
	Metric 17: Consistency of Outcome Assessment	Medium	The exact time of sacrifice was not explicitly reported.
	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 the outcome of interest.
	Metric 20: Negative Control Response	High	The negative control responses were consistent across all controls.
Domain 6: Confounding / Variable Control			
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	A previous experiment reported that the test substance is a respiratory irritant and causes changes in respiratory rate. Reduced respiratory rate due to reflex bradypnea impacts the received doses of each animal. It is unclear whether this could have an impact on the G6-phosphatase staining in the liver in an acute study.
	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 methods (including any calculations or data transformations) were clearly described or had only minor omissions and were appropriate for the dataset(s).
	Metric 24: Reporting of Data	High	The data were adequately reported and included means and measures of variance.

Additional Comments: None

Overall Quality Determination**High**

Study Citation:	Charbonneau, M., Strasser, J., Jr, Lock, E. A., Turner, M. J., Jr, Swenberg, J. A. (1989). Involvement of reversible binding to "alpha"2u-globulin in 1,4-dichlorobenzene-induced nephrotoxicity. Toxicology and Applied Pharmacology 99(1):122-132.			
Health Outcome(s):	Hepatic/Liver			
Reported Health Effect(s):	Hepatic/Liver: Liver weight (results not reported; no Form 3).No change in chemical content within tissue homogenates measured as relative to liver weight and via globulin binding with chemicals (results were reported; include Form 3). Results reported in Figure 3, Elution Profile of Liver from Male Rats.			
Duration:	Acute (less than or equal to 24 hr) Single exposure - o-DCB			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	68063			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1:	Test Substance Identity	High	The test substance was definitively identified as 1,4-dichlorobenzene.
	Metric 2:	Test Substance Source	High	The source of the test substance was specified (i.e., purchased from a commercial source).
	Metric 3:	Test Substance Purity	High	The purity of the test substance was reported (i.e., >99%); observed effects would be due to the test substance itself.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	Low	Negative controls (e.g., to evaluate kidney histology) were presumably treated with corn oil (as indicated in Table 6 for the 7-day study); however, few details were reported. Negative controls were likely not used or required for all experiments (e.g., radioactivity-based experiments including ADME and assays to evaluate binding to alpha 2u globulin).
	Metric 5:	Positive Controls	Low	The use of positive controls was not applicable to the study type.For kidney endpoints, The use of 2,2,4-trimethylpentane (TMP, a component of unleaded gasoline) was shown in previous experiments by the same group to cause an increase in the metrics used in this study (ADME measures; excreted test chemical (urine) and alpha 2u globulin binding radiological assay). However, there was no indication that TMP was used in the experiments assaying liver tissue.
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups.
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and Storage of Test Substance	Medium	Little information was provided with respect to test substance preparation and/or storage conditions; however, based on the route of exposure (gavage) and study duration (single exposure), these omissions are unlikely to have an impact on the study results. Based on the website for the commercial source from which 1,4-DCB was purchased, the test substance is stable under ambient conditions. SCOPEs documents state that this chemical is miscible in most organic solvents, and PubChem indicate high lipid solubility.
	Metric 8:	Consistency of Exposure Administration	Medium	Details of exposure administration were limited (e.g., it was not explicitly specified that controls were administered the same volume of corn oil as it was for the 7-day study); however, missing information is unlikely to have a substantial impact on the results.
	Metric 9:	Reporting of Doses/Concentrations	High	The study indicated dosing volumes (mmol/kg) and the equivalent doses in mg/kg.
	Metric 10:	Exposure Frequency and Duration	High	The study duration was adequate to evaluate the outcomes of interest, and in line with studies that evaluated the same types of effects for other test substances (as per information included in the introduction).
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Study Citation:	Charbonneau, M., Strasser, J., Jr, Lock, E. A., Turner, M. J., Jr, Swenberg, J. A. (1989). Involvement of reversible binding to "alpha"2u-globulin in 1,4-dichlorobenzene-induced nephrotoxicity. Toxicology and Applied Pharmacology 99(1):122-132.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	Hepatic/Liver: Liver weight (results not reported; no Form 3).No change in chemical content within tissue homogenates measured as relative to liver weight and via globulin binding with chemicals (results were reported; include Form 3). Results reported in Figure 3, Elution Profile of Liver from Male Rats.
Duration:	Acute (less than or equal to 24 hr) Single exposure - o-DCB
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	68063

Domain		Metric	Rating	Comments
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	The study authors did not explicitly justify the doses used in the study; they were presumably chosen because they were higher than those used in cancer bioassays (a longer study that identified similar effects). The doses used in the study were adequate to detect effects on the outcomes of interest.
	Metric 12:	Exposure Route and Method	High	The exposure route and method (i.e., gavage dosing) was well-suited to the test substance; this route/method was used in studies of other chemicals that evaluated similar effects and in cancer bioassays for 1,4-DCB.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Medium	The species/strain of rats used was specified, was the same as that used in the NTP cancer bioassay for 1,4-DCB, and was obtained from a commercial source. Details regarding the animals were sparse (only defined as "sexually mature" and a range of starting body weights reported, which was not differentiated by sex).
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Little to no information was reported on husbandry conditions (other than temp was 21C and there was an artificial 12 hour light/dark cycle); however, there is no reason to believe that husbandry conditions differed among treatment groups.
	Metric 15:	Number of Animals per Group	Medium	Three males and/or females per group were used in the acute study (females used to assess kidney histology and alpha 2u globulin concentrations in the kidney only); however, this number appeared to be sufficient in most cases to detect statistically significant effects on the outcomes of interest. However, no statistically significant effects were seen in liver samples.
Domain 5: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	High	The study evaluated appropriate endpoints to assess alpha 2u globulin-associated kidney and liver effects. Binding to alpha 2u globulin was specifically evaluated by identifying substances that co-eluted with 1,2-DCB or 1,4-DCB using gas chromatography/mass spec. Neither compounds showed alpha 2u binding in their elution profile (figure 3). The authors also state that the addition of SDS did not affect the amount of compound released from tissue, indicating non-reversible covalent bonding of chemicals to liver tissue. These same outcomes measurements were sufficient to find differences in kidney tissues.
	Metric 17:	Consistency of Outcome Assessment	High	The methodological details provided suggested that outcomes were consistently assessed across treatment groups.
	Metric 18:	Sampling Adequacy	Medium	Data were recorded for all rats utilized in the experiments. Note: that scoring of protein droplets was based one section of kidney per animal.

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Study Citation:	Charbonneau, M., Strasser, J., Jr, Lock, E. A., Turner, M. J., Jr, Swenberg, J. A. (1989). Involvement of reversible binding to "alpha"2u-globulin in 1,4-dichlorobenzene-induced nephrotoxicity. Toxicology and Applied Pharmacology 99(1):122-132.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	Hepatic/Liver: Liver weight (results not reported; no Form 3).No change in chemical content within tissue homogenates measured as relative to liver weight and via globulin binding with chemicals (results were reported; include Form 3). Results reported in Figure 3, Elution Profile of Liver from Male Rats.
Duration:	Acute (less than or equal to 24 hr) Single exposure - o-DCB
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	68063

Domain	Metric	Rating	Comments
	Metric 19: Blinding of Assessors	High	The histology evaluations were considered targeted, as the chemical of interest was specifically being evaluated as to its ability to bind a2u globulin and protein droplet formation in the kidney. The study authors reported that histology evaluations were performed without knowledge of treatment group, and severity data were based on mean scores for three analysts.
	Metric 20: Negative Control Response	Medium	A relatively low but detectable level of protein droplet formation was observed in male negative control animals (severity = 1.2, which fell into range of occasional to mild droplet formation); the score for female negative controls was < 1. Negative controls were not used for the other experiments (radioactivity-based experiments).
Domain 6: Confounding / Variable Control			
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	The study did not identify or report differences in study groups that would have confounded the study results.
	Metric 22: Health Outcomes Unrelated to Exposure	Medium	There was no information to support/dismiss differences among groups with respect to health outcomes unrelated to treatment.
	Metric 23: Data Presentation and Analysis	High	Statistical analyses were described adequately. Note: It was unclear if the data for kidney histology after acute exposure were analyzed statistically; however, data were available for independent analyses.
	Metric 24: Reporting of Data	Medium	Data were reported for most but not all outcomes (kidney and liver weights were not reported). Data for the 2.0 mmol/kg (300 mg/kg) group were not reported in their entirety for some of the ancillary endpoints (e.g., ADME, alpha 2u globulin binding). Quantitative data for kidney histology were reported for males; kidney histology data for females and alpha 2u globulin concentrations for males and females were reported qualitatively.

Additional Comments: None

Overall Quality Determination**Medium**

Study Citation:	Charbonneau, M., Strasser, J., Jr, Lock, E. A., Turner, M. J., Jr, Swenberg, J. A. (1989). Involvement of reversible binding to "alpha"2u-globulin in 1,4-dichlorobenzene-induced nephrotoxicity. Toxicology and Applied Pharmacology 99(1):122-132.
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Renal/Kidney: Kidney weight and/or histology (protein droplet formation)Increased chemical content measured within tissue homogenates relative to kidney weight and via globulin binding with chemicals, and/or histology (protein droplet formation)
Duration:	Acute (less than or equal to 24 hr) Single exposure - o-DCB
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	68063

Domain	Metric	Rating	Comments
Domain 1: Test Substance			
	Metric 1: Test Substance Identity	High	The test substance was definitively identified as 1,2-dichlorobenzene.
	Metric 2: Test Substance Source	High	The source of the test substance was specified (i.e., purchased from a commercial source).
	Metric 3: Test Substance Purity	High	The purity of the test substance was reported (i.e., 99%); observed effects would be due to the test substance itself.
Domain 2: Test Design			
	Metric 4: Negative and Vehicle Controls	Low	Negative controls (e.g., to evaluate kidney histology) were presumably treated with corn oil (as indicated in Table 6 for the 7-day study); however, few details were reported. Negative controls were likely not used or required for all experiments (e.g., radioactivity-based experiments to evaluate ADME and alpha 2u globulin binding).
	Metric 5: Positive Controls	Low	The use of positive controls was not applicable to the study type.The use of 2,2,4-trimethylpentane (TMP, a component of unleaded gasoline) was shown in previous experiments by the same group to cause an increase in the metrics used in this study (ADME measures; excreted test chemical (urine) and alpha 2u globulin binding radiological assay).My rating for this is low since the only indication that this was a positive control was from the same lab. More information for the use of TMP in this was should have been provided for higher confidence.
	Metric 6: Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups.
Domain 3: Exposure Characterization			
	Metric 7: Preparation and Storage of Test Substance	Medium	Little information was provided with respect to test substance preparation and/or storage conditions; however, based on the route of exposure (gavage) and study duration (single exposure), these omissions are unlikely to have an impact on the study results. Based on the website for the commercial source from which 1,2-DCB was purchased, the test substance is stable under recommended storage conditions.SCOPEs documents state that this chemical is miscible in most organic solvents, and PubChem indicate high lipid solubility.
	Metric 8: Consistency of Exposure Administration	Medium	Details of exposure administration were limited (e.g., it was not explicitly specified that controls were administered the same volume of corn oil as it was for the 7-day study); however, missing information is unlikely to have a substantial impact on the results.
	Metric 9: Reporting of Doses/Concentrations	Medium	The study indicated dosing volumes (mmol/kg) and the equivalent doses in mg/kg. Data were described in the text for a dose group not specified in the methods section (13.6 mmol/kg; a dose that produced protein droplets).

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Study Citation:	Charbonneau, M., Strasser, J., Jr, Lock, E. A., Turner, M. J., Jr, Swenberg, J. A. (1989). Involvement of reversible binding to "alpha"2u-globulin in 1,4-dichlorobenzene-induced nephrotoxicity. Toxicology and Applied Pharmacology 99(1):122-132.
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Renal/Kidney: Kidney weight and/or histology (protein droplet formation)Increased chemical content measured within tissue homogenates relative to kidney weight and via globulin binding with chemicals, and/or histology (protein droplet formation)
Duration:	Acute (less than or equal to 24 hr) Single exposure - o-DCB
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	68063

Domain		Metric	Rating	Comments
	Metric 10:	Exposure Frequency and Duration	High	The study duration was adequate to evaluate the outcomes of interest, and in line with studies evaluating the same types of effects for other test substances (as per information included in the introduction).
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	The study authors did not explicitly justify the doses used in the study; they were presumably chosen because they were higher than those used in subchronic and chronic studies. The doses used in the study appeared to be adequate to detect effects on the outcomes of interest.
	Metric 12:	Exposure Route and Method	High	The exposure route and method (i.e., gavage dosing) was well-suited to the test substance; this route/method was used in studies of other chemicals that evaluated similar effects and in other studies of 1,2-DCB.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Medium	The species/strain of rats used was specified, was the same as that used in the NTP cancer bioassay for 1,2-DCB, and was obtained from a commercial source. Details regarding the animals were sparse (only defined as "sexually mature" and a range of starting body weights reported, which was not differentiated by sex).
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Little to no information was reported on husbandry conditions (other than temp was 21C and there was an artificial 12 hour light/dark cycle); there is no reason to believe that husbandry conditions differed among treatment groups.
	Metric 15:	Number of Animals per Group	Medium	Three males and/or females per group were used in the acute study (females used only to evaluate kidney histology and alpha 2u globulin concentrations); however, this number appeared to be sufficient in most cases to detect statistically significant effects on the outcomes of interest.
Domain 5: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	High	The study evaluated appropriate endpoints to assess alpha 2u globulin-associated kidney effects. Binding to alpha 2u globulin was specifically evaluated by identifying substances that co-eluted with 1,2-DCB using gas chromatography/mass spec. In addition to evaluating droplet formation histologically, alpha 2u globulin concentrations were quantified by ELISA. Taken together, the apical (kidney histology) and ancillary (alpha 2u globulin binding and the concentration of this protein in the kidney) endpoints specifically evaluated alpha 2u globulin-related kidney effects.
	Metric 17:	Consistency of Outcome Assessment	High	The methodological details provided suggested that outcomes were consistently assessed across treatment groups.
	Metric 18:	Sampling Adequacy	Medium	Data were recorded for all rats utilized in the experiments. Note: that scoring of protein droplets was based one section of kidney per animal.
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Study Citation:	Charbonneau, M., Strasser, J., Jr, Lock, E. A., Turner, M. J., Jr, Swenberg, J. A. (1989). Involvement of reversible binding to "alpha"2u-globulin in 1,4-dichlorobenzene-induced nephrotoxicity. Toxicology and Applied Pharmacology 99(1):122-132.
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Renal/Kidney: Kidney weight and/or histology (protein droplet formation)Increased chemical content measured within tissue homogenates relative to kidney weight and via globulin binding with chemicals, and/or histology (protein droplet formation)
Duration:	Acute (less than or equal to 24 hr) Single exposure - o-DCB
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	68063

Domain	Metric	Rating	Comments
	Metric 19: Blinding of Assessors	High	The histology evaluations were considered targeted, as the chemical of interest was specifically being evaluated as to its ability to bind a2u globulin and protein droplet formation in the kidney. The study authors reported that histology evaluations were performed without knowledge of treatment group, and severity data were based on mean scores for three analysts.
	Metric 20: Negative Control Response	Medium	A relatively low but detectable level of protein droplet formation was observed in male negative control animals (severity = 1.2, which fell into range of occasional to mild droplet formation); the severity was < 1 in female controls. Negative controls were not used for the other experiments (radioactivity-based experiments to evaluate ADME and alpha 2u globulin binding).

Domain 6: Confounding / Variable Control

Metric 21:	Confounding Variables in Test Design and Procedures	Medium	The study did not identify or report differences in study groups that would have confounded the study results.
Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information to support/dismiss differences among groups with respect to health outcomes unrelated to treatment.
Metric 23:	Data Presentation and Analysis	High	Statistical analyses were described adequately. Note: It was unclear if the data for kidney histology after acute exposure was analyzed statistically; however, data were available for independent analyses.
Metric 24:	Reporting of Data	Medium	Data were reported for most but not all outcomes (kidney weights were not reported). Data for kidney histology in males were reported quantitatively; data for kidney histology in females and alpha 2u globulin concentrations in males and females were reported qualitatively. Data for the 13.6 mmol/kg group (not reported in the methods) were reported for some endpoints.

Additional Comments: None

Overall Quality Determination**High**

Study Citation:	FDRL, (1976). Primary skin irritation studies with rabbits with cover letters.			
Health Outcome(s):	Irritation			
Reported Health Effect(s):	Irritation: Skin irritation (Draize scoring for erythema and edema), Eye irritation			
Duration:	Acute (less than or equal to 24 hr) Single instillation into the eye			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	5264494			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1:	Test Substance Identity	High	The test substance was identified by name; a CASRN is provided on the cover page.
	Metric 2:	Test Substance Source	High	The test substance source is reported as Solvay Specialty Chemicals Division. A 9-digit number is reported that could be a batch or lot number, but it isn't clear what this number is. No analytical verification of the test substance identity is described.
	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	N/A	A negative control was not used. Typically, only one eye from animals is treated, leaving the untreated eye as a negative control. This study did not specify whether both or one eye was treated; however, this is not expected to significantly impact the study results.
	Metric 5:	Positive Controls	N/A	Positive controls are not required for the study type.
	Metric 6:	Randomized Allocation of Animals	Low	Healthy, acclimated animals were selected for the study. The method of selection was not specified.
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and Storage of Test Substance	Low	No details on test substance storage or preparation were reported, though the chemical was described as a water-white liquid. It is assumed the test substance was applied neat, as no vehicle was mentioned in the study text but this was not explicitly stated.
	Metric 8:	Consistency of Exposure Administration	Low	Insufficient details about the exposure administration were provided to assess consistency between animals.
	Metric 9:	Reporting of Doses/Concentrations	Uninformative	Insufficient details about exposure administration were provided. Neither the volume nor the dose applied was reported, making the study unusable.
	Metric 10:	Exposure Frequency and Duration	Medium	It is assumed animals received a single instillation, although this was not explicitly reported.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	N/A	The study goal was not to have a dose-dependent effect.
	Metric 12:	Exposure Route and Method	High	The route and method of exposure are appropriate for the study type
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Low	The authors only report the species and strain of the test animal. Sex, source, and starting body weight are not reported. The animals were described as being young adults.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Animal husbandry conditions were not reported.

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Study Citation:	FDRL, (1976). Primary skin irritation studies with rabbits with cover letters.			
Health Outcome(s):	Irritation			
Reported Health Effect(s):	Irritation: Skin irritation (Draize scoring for erythema and edema), Eye irritation			
Duration:	Acute (less than or equal to 24 hr) Single instillation into the eye			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	5264494			
Domain	Metric	Rating	Comments	
	Metric 15:	Number of Animals per Group	Medium	The number of animals is reported and is acceptable for the study design.
Domain 5: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	Medium	The outcome assessment methodology was partially described. The study provided its own scoring criteria, but details of how the eyes were examined were not provided. Animals were observed through 7 days, although reversal for conjunctivae scores was not reached. Typically, 21 days of observation are recommended.
	Metric 17:	Consistency of Outcome Assessment	High	The time points of examination were reported. Based on the information provided, all animals were consistently examined.
	Metric 18:	Sampling Adequacy	High	There are no concerns regarding sampling for the study design.
	Metric 19:	Blinding of Assessors	Low	Grading ocular irritation is necessarily subjective; OECD TG 405 indicates that personnel performing the observations need to be adequately trained in the scoring system used. The study did not specify whether this was the case.
	Metric 20:	Negative Control Response	N/A	The study did not require a control, so no negative control response could be evaluated.
Domain 6: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	The authors did not report all of the information required to evaluate confounding, but the influence of these unmeasured factors is likely to be minimal.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was little information to either support or dismiss the possibility of attrition.
	Metric 23:	Data Presentation and Analysis	N/A	Statistical analysis was not required for the study design.
	Metric 24:	Reporting of Data	High	Full data for exposure related findings were reported with severity scores.
Additional Comments: None				
Overall Quality Determination			Uninformative	

Study Citation:	FDRL, (1976). Primary skin irritation studies with rabbits with cover letters.			
Health Outcome(s):	Irritation			
Reported Health Effect(s):	Irritation: Skin irritation (Draize scoring for erythema and edema), Eye irritation			
Duration:	Acute (less than or equal to 24 hr) 24-hour skin irritation			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	5264494			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
Metric 1:	Test Substance Identity	High	The test substance was identified by name; a CASRN is provided on the cover page.	
Metric 2:	Test Substance Source	High	The test substance source is reported as Solvay Specialty Chemicals Division. A 9-digit number is reported that could be a batch or lot number, but it isn't clear what this number is. No analytical verification of the test substance identity is described.	
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	N/A	A negative control was not used, but negative controls aren't required for skin irritation studies. Generally, sites where the test substance is not applied act as a negative control.	
Metric 5:	Positive Controls	N/A	Positive controls are not required for the study type.	
Metric 6:	Randomized Allocation of Animals	Low	Healthy, acclimated animals were selected for the study. The method of selection was not specified.	
Domain 3: Exposure Characterization				
Metric 7:	Preparation and Storage of Test Substance	Low	No details on test substance storage or preparation were reported, though the chemical was described as a water-white liquid. It is assumed the test substance was applied neat, as no vehicle was mentioned in the study text.	
Metric 8:	Consistency of Exposure Administration	Medium	Several exposure administration details are missing. A constant 0.5mL volume was applied to each site underneath surgical gauze. It was not specified when the backs of animals were shaved in relation to the time of application, and the exposure area was not reported. The study did not report how the surgical tape was held in place (e.g., occlusion was not mentioned). The information that is provided does not suggest any inconsistency between animals	
Metric 9:	Reporting of Doses/Concentrations	Medium	The study reported that "the material (0.5mL or 0.5g) was introduced..." It is assumed that the text indicates that 0.5mL is used for liquids (as in this case), or, if the chemicals tested were a solid, then 0.5g would be used.	
Metric 10:	Exposure Frequency and Duration	High	The duration of exposure (24 hrs) is appropriate and consistent with similar study types.	
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	N/A	The study goal was not to have a dose-dependent effect.	
Metric 12:	Exposure Route and Method	High	The route and method of exposure are appropriate for measuring dermal irritation.	
Domain 4: Test Animals				
Metric 13:	Test Animal Characteristics	Low	The authors only report the species and strain of the test animal. Sex, source, and starting body weight are not reported. The animals were described as being adults.	
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Animal husbandry conditions were not reported.	
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Study Citation:	FDRL, (1976). Primary skin irritation studies with rabbits with cover letters.			
Health Outcome(s):	Irritation			
Reported Health Effect(s):	Irritation: Skin irritation (Draize scoring for erythema and edema), Eye irritation			
Duration:	Acute (less than or equal to 24 hr) 24-hour skin irritation			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	5264494			
Domain		Metric	Rating	Comments
	Metric 15:	Number of Animals per Group	Medium	The number of animals is reported and is acceptable for the study design.
Domain 5: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	Low	The outcome assessment methodology deviates from current guidelines. Skin was examined at 24 and 72 hours only. Typically, observations should be done at 60 min, 24, 48, and 72 hrs, and then up to 14 days to assess reversibility.
	Metric 17:	Consistency of Outcome Assessment	High	Details of the outcome assessment are reported in adequate detail and are consistent between animals.
	Metric 18:	Sampling Adequacy	High	There are no concerns regarding sampling for the study design.
	Metric 19:	Blinding of Assessors	N/A	Grading of skin is necessarily subjective; however, OECD TG 404 does not require blinded assessments. Additionally, the Draize scale was used which facilitates more consistent scoring.
	Metric 20:	Negative Control Response	N/A	The study did not require a control, so no negative control response could be evaluated.
Domain 6: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	The authors did not report all of the information required to evaluate confounding, but the influence of these unmeasured factors is likely to be minimal.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was little information to either support or dismiss the possibility of attrition.
	Metric 23:	Data Presentation and Analysis	N/A	Statistical analysis was not required for the study design.
	Metric 24:	Reporting of Data	High	Full data for exposure related findings were reported with severity scores.
Additional Comments:	None			

Overall Quality Determination**Medium**

Study Citation:	FDRL, (1976). ortho-Dichlorobenzene: Rabbit eye irritation study.			
Health Outcome(s):	Irritation (Ocular/Eye)			
Reported Health Effect(s):	Irritation (Ocular/Eye): Dichlorobenzene is a mild eye irritant as indicated by effects in the conjunctiva of the treated eye.			
Duration:	Acute (less than or equal to 24 hr) Acute eye irritation			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	5264501			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	The test substance was identified definitively by name.	
	Metric 2: Test Substance Source	Low	The source of the test substance was not identified or analytically verified by the performing laboratory.	
	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	Low	Details regarding the negative control group were not reported.	
	Metric 5: Positive Controls	N/A	Positive controls are not included in this type of study.	
	Metric 6: Randomized Allocation of Animals	Low	The study did not report that the animals were randomly allocated into the treatment group, but they did ensure that the eyes were normal and followed the procedure outlined in 16 CFT 1500.42	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Low	Information on preparation was not reported. Information on storage was not provided, however, it is not likely to impact the results because it is an acute exposure study.	
	Metric 8: Consistency of Exposure Administration	Medium	Details of exposure administration are incompletely reported, but the missing information is unlikely to have a substantial impact on results.	
	Metric 9: Reporting of Doses/Concentrations	Low	The exposure volume was not reported.	
	Metric 10: Exposure Frequency and Duration	High	The exposure frequency and duration of exposure were appropriate for this study type.	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	N/A	The study goal was not to have a dose-dependent effect.	
	Metric 12: Exposure Route and Method	High	The route and method of exposure were reported and were appropriate for the study type.	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	Medium	The source and sex of the test animals was not reported. However, the sex of the animals in unlikely to impact the results, and the albino rabbit is an appropriate choice for an eye irritation study.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Medium	The husbandry conditions were not completely reported and therefore, the appropriateness of the conditions can not be comprehensively evaluated.	
	Metric 15: Number of Animals per Group	Medium	The number of animals per test group was appropriate.	
Domain 5: Outcome Assessment				
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Study Citation:	FDRL, (1976). ortho-Dichlorobenzene: Rabbit eye irritation study.			
Health Outcome(s):	Irritation (Ocular/Eye)			
Reported Health Effect(s):	Irritation (Ocular/Eye): Dichlorobenzene is a mild eye irritant as indicated by effects in the conjunctiva of the treated eye.			
Duration:	Acute (less than or equal to 24 hr) Acute eye irritation			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	5264501			
Domain	Metric	Rating	Comments	
	Metric 16: Outcome Assessment Methodology	Medium	According to the newer OECD guideline 405, the effects on the eye should be documented until they dissipate. For this study, they were still observed 7 days later, which was the last day of observation.	
	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 all study groups.	
	Metric 18: Sampling Adequacy	High	Reported information indicates the study used adequate sampling.	
	Metric 19: Blinding of Assessors	N/A	While the study did not report blinding of the assessors, the outcome is not likely to be impacted.	
	Metric 20: Negative Control Response	Low	The results for the untreated eye were not reported.	
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, it was unlikely to have an impact.	
	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 that could influence the outcome assessment.	
	Metric 23: Data Presentation and Analysis	N/A	Statistical analysis was not necessary.	
	Metric 24: Reporting of Data	High	Data for exposure-related findings were presented for all outcomes.	
Additional Comments:	The most concerning aspects of this study was lack of reporting on the untreated eye used as the negative control, and the details of the rabbits housing and feeding conditions were not adequately described.			

Overall Quality Determination**High**

Study Citation:	Gunawardhana, L., Lantz, R. C., Earnest, D. L., Abril, E. R., Sipes, I. G. (1995). Differential production of superoxide by single Kupffer cells isolated from Fischer-344 and Sprague-Dawley rats following administration of the potent hepatotoxicant 1,2-dichlorobenzene. 5:45-47.			
Health Outcome(s):	Hepatic/Liver			
Reported Health Effect(s):	Hepatic/Liver: Serum chemistry (ALT only), superoxide production by Kupffer cells,			
Duration:	Acute (less than or equal to 24 hr) Single ip injection			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	5345264			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
Metric 1:	Test Substance Identity	High	Test substance was identified by a common name, 1,2-dichlorobenzene. CASRN was not provided	
Metric 2:	Test Substance Source	High	Test substance was purchased from Aldrich Chemical Company Inc. (Milwaukee, WI). Batch/Lot # were not provided.	
Metric 3:	Test Substance Purity	Low	Purity and/or grade of test substance were not reported.	
Domain 2: Test Design				
Metric 4:	Negative and Vehicle Controls	High	An appropriate vehicle (corn oil) control was included and was appropriate.	
Metric 5:	Positive Controls	N/A	Not necessary for this study type.	
Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups.	
Domain 3: Exposure Characterization				
Metric 7:	Preparation and Storage of Test Substance	Medium	Study authors state "The dosing solutions were prepared on the day they were used. Appropriate amounts of 1,2-DCB were dissolved in corn oil (Mazola) to prepare dosing solutions so that each animal received 2 ml/kg of the respective dosing solutions via intraperitoneal injection." Methods for mixing test substance were not provided, nor was homogeneity confirmed.	
Metric 8:	Consistency of Exposure Administration	High	Rats were administered a single ip injection of test substance at a volume of 2 ml/kg.	
Metric 9:	Reporting of Doses/Concentrations	High	Doses were reported in units of mmol/kg without ambiguity.	
Metric 10:	Exposure Frequency and Duration	High	A single ip injection was appropriate for this acute study type.	
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	A control and 5 treatment groups were included and a full range of responses were observed.	
Metric 12:	Exposure Route and Method	High	IP injection was appropriate for this study.	
Domain 4: Test Animals				
Metric 13:	Test Animal Characteristics	Medium	"Male Fischer-344 (F344) and Sprague-Dawley (SD) rats, 9-10 week old, were purchased from Harlan Sprague Dawley Inc. Indianapolis, IN." Staring body weight was not reported.	
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Animal husbandry conditions were not reported.	
Metric 15:	Number of Animals per Group	Low	3 animals were included per group. Acute studies typically require 5 animals/group.	

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Study Citation:	Gunawardhana, L., Lantz, R. C., Earnest, D. L., Abril, E. R., Sipes, I. G. (1995). Differential production of superoxide by single Kupffer cells isolated from Fischer-344 and Sprague-Dawley rats following administration of the potent hepatotoxicant 1,2-dichlorobenzene. 5:45-47.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	Hepatic/Liver: Serum chemistry (ALT only), superoxide production by Kupffer cells,
Duration:	Acute (less than or equal to 24 hr) Single ip injection
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	5345264

Domain	Metric	Rating	Comments
Domain 5: Outcome Assessment			
Metric 16:	Outcome Assessment Methodology	Low	The outcome assessment methodology partially addressed the reported outcome. Serum ALT was measured as a marker of liver toxicity. Liver weight, other serum chemistry parameters (e.g., ALP, AST), and histopathology were not measured.
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	All animals in each test group were evaluated for the outcomes of interest.
Metric 19:	Blinding of Assessors	N/A	Not necessary for this study type. No subjective outcomes were reported.
Metric 20:	Negative Control Response	High	The biological response of the negative control group was adequate.
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.
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	Low	"Statistical differences were determined by analysis of variance (ANOVA). Differences were considered significant at p<0.05." No information on the post-hoc analysis used for pairwise comparisons was provided.
Metric 24:	Reporting of Data	Medium	ALT measurements were shown graphically as mean+/- SEM. Background superoxide production in rats treated with 1,2-DCB was not shown.

Additional Comments: None

Overall Quality Determination**Medium**

Study Citation:	Gunawardhana, L., Mobley, S. A., Sipes, I. G. (1993). A role for reactive oxygen species released from kupffer cells in 1,2-dichlorobenzene hepatotoxicity in the fischer-344 rat. 4:403-406.			
Health Outcome(s):	Hepatic/Liver			
Reported Health Effect(s):	Hepatic/Liver: Increased plasma ALT and observed changes to liver histopathology.			
Duration:	Acute (less than or equal to 24 hr) Acute liver toxicity			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	5345265			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	Reported as 1,2-dichlorobenzene; CASRN not provided	
	Metric 2: Test Substance Source	High	The source of the material was provided but not the batch/lot. However, this is unlikely to lead to differences in the results.	
	Metric 3: Test Substance Purity	Low	No report of the purity of the test substance.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	Authors reported appropriate negative control	
	Metric 5: Positive Controls	N/A	No need for positive controls for this study.	
	Metric 6: Randomized Allocation of Animals	Low	No reports of random allocation of animals.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Missing Conf	The preparation of the test substance was adequately described. The storage conditions were not reported, but as this is an acute study, it is unlikely to impact the results.	
	Metric 8: Consistency of Exposure Administration	High	Details of exposure were adequately reported.	
	Metric 9: Reporting of Doses/Concentrations	High	Doses were reported without ambiguity	
	Metric 10: Exposure Frequency and Duration	High	The duration and exposure were appropriate for an acute study	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	Appropriate doses of o-DCB and methyl palmitate appear to be based on prior reported literature that is cited in the article.	
	Metric 12: Exposure Route and Method	High	Appropriate for test substance, 1,2-dichlorobenzene was administered by i.p. but this substance is volatile.	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	Medium	Starting body weight was not reported.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Low	Animal husbandry conditions were not reported at all.	
	Metric 15: Number of Animals per Group	Medium	The number of rats per group was reported, but the number of animals per group greatly varied (from 3 to 18). However, there was enough animal per group to determine means and standard error.	
Domain 5: Outcome Assessment				
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Study Citation:	Gunawardhana, L., Mobley, S. A., Sipes, I. G. (1993). A role for reactive oxygen species released from kupffer cells in 1,2-dichlorobenzene hepatotoxicity in the fischer-344 rat. 4:403-406.			
Health Outcome(s):	Hepatic/Liver			
Reported Health Effect(s):	Hepatic/Liver: Increased plasma ALT and observed changes to liver histopathology.			
Duration:	Acute (less than or equal to 24 hr) Acute liver toxicity			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	5345265			
Domain	Metric	Rating	Comments	
	Metric 16: Outcome Assessment Methodology	Medium	The main focus of the paper was determine the role of Kupffer cells in the propagation of hepatic injury after exposure to o-DCB. For this reason, they never treated the animals with o-DCB and corn oil alone. The rats were either pre-treated with 0.2% Tween-20 and 5% dextrose or with i.v. saline and then o-DCB was administered. As these are inert vehicle substances, it is unlikely they cause injury without o-DCB exposure. The evidence for these substances to be unlikely to cause injury comes from the paper's negative control data for methyl palmitate in vehicle + corn oil and corn oil + superoxide dismutase (conjugated to polyethylene glycol) reconstituted in saline to the appropriate dose. The results for the controls shows no significant increase in plasma ALT activity levels compared to corn oil alone or corn oil in saline. However, representative liver sections of these controls were not shown in the paper.	
	Metric 17: Consistency of Outcome Assessment	High	Outcomes were assessed adequately	
	Metric 18: Sampling Adequacy	High	The study used adequate sampling for the outcome of interest.	
	Metric 19: Blinding of Assessors	N/A	No need to blind assessors. Initial histopathology review was done.	
	Metric 20: Negative Control Response	High	The biological responses of the negative control group were adequate.	
Domain 6: Confounding / Variable Control				
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	The study did not report enough information to determine confounding. However, the test substance was administered by injection and the rats were killed 24 h later. It is unlikely that confounding variables would be impact the results.	
	Metric 22: Health Outcomes Unrelated to Exposure	Medium	There was no information to either support or dismiss the suggestion that health outcomes unrelated to exposure could influence the outcome assessment.	
	Metric 23: Data Presentation and Analysis	High	Statistical methods were clearly described.	
	Metric 24: Reporting of Data	Medium	Data for plasma ALT activity were shown in a figure but not reported in the text. Although representative images of the liver sections were shown in a figure, the exact number of rats that exhibited signs of necrosis after treatment compared to control were not reported.	
Additional Comments:	The biggest limitations of this paper are the lack of reporting animal husbandry conditions, and the hepatotoxicity of 3.6 mmol/kg o-DCB in corn oil alone was never assessed.			
Overall Quality Determination		High		

Study Citation:	Haas,, R.a. (1979). Initial submission: Acute parenteral LD50 study with o-dichlorobenzene in rats with cover letter dated 073092. 920005562:#88-920005562.			
Health Outcome(s):	Nutritional/Metabolic; Lung/Respiratory;			
Reported Health Effect(s):	Nutritional/Metabolic: Body weights; Lung/Respiratory: Gross necropsy;			
Duration:	Acute (less than or equal to 24 hr) Single subcutaneous dose			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	5264631			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	All Outcomes: The test material was identified as 1,2-dichlorobenzene, CASRN 99-50-1	
	Metric 2: Test Substance Source	High	All Outcomes: The test substance was sourced from Aldrich with a batch/lot number: 101867.	
	Metric 3: Test Substance Purity	High	All Outcomes: Test substance purity/grade was reported as 98% technical grade.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	N/A	All Outcomes: Although negative controls are not required for this study type, a vehicle control (olive oil) group was included	
	Metric 5: Positive Controls	N/A	All Outcomes: A positive control is not required for this study type.	
	Metric 6: Randomized Allocation of Animals	Low	All Outcomes: The method of allocation of animals into study groups was not specified.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Low	All Outcomes: There is a lack of information regarding test substance preparation/storage conditions. Although this is an acute study, the test substance is considered a volatile compound and these missing details could have a substantial impact on the study results.	
	Metric 8: Consistency of Exposure Administration	Low	All Outcomes: In acute toxicity up-and-down test, the volumes administered subcutaneously were not adequately described. In cases where the test substance was dispersed in olive oil, the study indicates that animals were given “a constant volume of 3.88 g/kg”, which is clearly a reporting error. Due to the missing information the consistency of exposure administration cannot be determined.	
	Metric 9: Reporting of Doses/Concentrations	Medium	All Outcomes: Individual nominal doses ranging from 0.04 to 74.0 g/kg (which is excessive) were clearly reported. Analytical measurements were not performed, but this is unlikely to have a substantial impact on results.	
	Metric 10: Exposure Frequency and Duration	High	All Outcomes: Animals were administered single subcutaneous doses. The study generally followed a step-up-and-down procedure where 4 dose groups were administered on day 1, two higher doses were administered on day 2, and finally, two intermediate doses were administered on day 3.	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	Medium	All Outcomes: This was reported to be a rang-finding study. The doses selected were not justified by the study authors, and several dose groups exceed the recommended dose for a limit test. The spacing used resulted in data showing either 100% mortality or 0% mortality, therefore, additional groups in between those doses would have been warranted.	

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Study Citation:	Haas,, R.a. (1979). Initial submission: Acute parenteral LD50 study with o-dichlorobenzene in rats with cover letter dated 073092. 920005562:#88-920005562.			
Health Outcome(s):	Nutritional/Metabolic; Lung/Respiratory;			
Reported Health Effect(s):	Nutritional/Metabolic: Body weights; Lung/Respiratory: Gross necropsy;			
Duration:	Acute (less than or equal to 24 hr) Single subcutaneous dose			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	5264631			
Domain	Metric	Rating	Comments	
	Metric 12:	Exposure Route and Method	High	All Outcomes: The route (subcutaneous) was acceptable and suitable for the test substance.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Medium	All Outcomes: Test animal sex, strain, species (male, CRCD, rat) and starting body weight were reported. The animal source and age were not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	All Outcomes: Animal husbandry conditions and procedures were not reported. No guidelines were provided to account for the lack of detailed husbandry conditions.
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: 3 animals/dose group were used in a study generally following a step-up-and-down procedure, which is more that required based on current guidelines (OECD 425)
Domain 5: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	High	Nutritional/Metabolic: The outcome assessment methodology effectively addressed the outcome of interest in this study.; Lung/Respiratory: All animals were subjected to gross necropsy. Although gross examinations are generally not considered to be the most sensitive endpoint for this outcome, other endpoints (e.g., organ weights, histopathology) are not required for this study type. Therefore, gross examinations is considered appropriate for the purposes of the study.
	Metric 17:	Consistency of Outcome Assessment	High	All Outcomes: Details of the outcome assessment were not described in the text but could generally be determined based on the tables provided. It appears that all groups were observed consistently daily post-dosing and all animals were necropsied either upon death or at the end of the 14-day observation period.
	Metric 18:	Sampling Adequacy	High	All Outcomes: Sampling was adequate for the outcomes of interest and the number of evaluations, as incidences were reported.
	Metric 19:	Blinding of Assessors	N/A	Nutritional/Metabolic: Blinding was not reported, but the outcome of interest (body weight) is not subjective in nature.; Lung/Respiratory: Blinding was not reported, but blinding is generally not required for pathology in an acute toxicity study (as per OECD 425)
	Metric 20:	Negative Control Response	High	Nutritional/Metabolic: A negative control is not required for this study type, but a vehicle control was included. The negative control response was adequate, as there were no deaths, clinical signs or treatment-related effects.; Lung/Respiratory: Incidences and severity of lung pathology were clearly reported for all groups.
Domain 6: Confounding / Variable Control				
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Study Citation:	Haas., R.a. (1979). Initial submission: Acute parenteral LD50 study with o-dichlorobenzene in rats with cover letter dated 073092. 920005562:#88-920005562.
Health Outcome(s):	Nutritional/Metabolic; Lung/Respiratory;
Reported Health Effect(s):	Nutritional/Metabolic: Body weights; Lung/Respiratory: Gross necropsy;
Duration:	Acute (less than or equal to 24 hr) Single subcutaneous dose
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	5264631

Domain	Metric	Rating	Comments
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	All Outcomes: There was some variation in the mean starting body weights of animals across groups (124 -153 g), but this is not expected to have had a significant effect on the outcome of interest. Other data to determine confounding (food/water intake) were not reported.
	Metric 22: Health Outcomes Unrelated to Exposure	High	All Outcomes: Qualitative or quantitative results were reported for all prespecified outcomes. The mortalities observed were considered to be treatment related. There is no indication that any of the outcomes were unrelated to exposure.
	Metric 23: Data Presentation and Analysis	N/A	All Outcomes: Generally, for acute toxicity studies, statistical analysis of other endpoints (e.g., incidences of clinical signs, body weights, or pathology) is not required/conducted because these study types do not include controls. Data are adequately reported for this study if statistical analysis is desired.
	Metric 24: Reporting of Data	Low	All Outcomes: Initial and final mean body weight measurements for each group were reported in the absence of measures of variance. Terminal body weights were not recorded for animals that died.

Additional Comments: None

Overall Quality Determination**Medium**

Study Citation:	Haas,, R.a. (1979). Initial submission: Acute parenteral LD50 study with o-dichlorobenzene in rats with cover letter dated 073092. 920005562:#88-920005562.			
Health Outcome(s):	Mortality			
Reported Health Effect(s):	Mortality: Mortality, LD50			
Duration:	Acute (less than or equal to 24 hr) Single subcutaneous dose			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	5264631			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1:	Test Substance Identity	High	The test material was identified as 1,2-dichlorobenzene, CASRN 99-50-1
	Metric 2:	Test Substance Source	High	The test substance was sourced from Aldrich with a batch/lot number: 101867.
	Metric 3:	Test Substance Purity	High	Test substance purity/grade was reported as 98% technical grade.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	N/A	Although negative controls are not required for this study type, a vehicle control (olive oil) group was included
	Metric 5:	Positive Controls	N/A	A positive control is not required for this study type.
	Metric 6:	Randomized Allocation of Animals	Low	The method of allocation of animals into study groups was not specified.
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and Storage of Test Substance	Low	There is a lack of information regarding test substance preparation/storage conditions. Although this is an acute study, the test substance is considered a volatile compound and these missing details could have a substantial impact on the study results.
	Metric 8:	Consistency of Exposure Administration	Low	In acute toxicity up-and-down test, the volumes administered subcutaneously were not adequately described. In cases where the test substance was dispersed in olive oil, the study indicates that animals were given “a constant volume of 3.88 g/kg”, which is clearly a reporting error. Due to the missing information the consistency of exposure administration cannot be determined.
	Metric 9:	Reporting of Doses/Concentrations	Medium	Individual nominal doses ranging from 0.04 to 74.0 g/kg (which is excessive) were clearly reported. Analytical measurements were not performed, but this is unlikely to have a substantial impact on results.
	Metric 10:	Exposure Frequency and Duration	High	Animals were administered single subcutaneous doses. The study generally followed a step-up-and-down procedure where 4 dose groups were administered on day 1, two higher doses were administered on day 2, and finally, two intermediate doses were administered on day 3.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	This was reported to be a rang-finding study. The doses selected were not justified by the study authors, and several dose groups exceed the recommended dose for a limit test. The spacing used resulted in data showing either 100% mortality or 0% mortality, therefore, additional groups in between those doses would have been warranted.
	Metric 12:	Exposure Route and Method	High	The route (subcutaneous) was acceptable and suitable for the test substance.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Medium	Test animal sex, strain, species (male, CRCD, rat) and starting body weight were reported. The animal source and age were not reported.
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Study Citation:	Haas,, R.a. (1979). Initial submission: Acute parenteral LD50 study with o-dichlorobenzene in rats with cover letter dated 073092. 920005562:#88-920005562.
Health Outcome(s):	Mortality
Reported Health Effect(s):	Mortality: Mortality, LD50
Duration:	Acute (less than or equal to 24 hr) Single subcutaneous dose
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	5264631

Domain	Metric	Rating	Comments
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Low	Animal husbandry conditions and procedures were not reported. No guidelines were provided to account for the lack of detailed husbandry conditions.
	Metric 15: Number of Animals per Group	Medium	3 animals/dose group were used in a study generally following a step-up-and-down procedure, which is more that required based on current guidelines (OECD 425)
Domain 5: Outcome Assessment			
	Metric 16: Outcome Assessment Methodology	High	The outcome assessment methodology effectively addressed the outcome of interest in this study.
	Metric 17: Consistency of Outcome Assessment	High	Details of the outcome assessment were not described in the text but could generally be determined based on the tables provided. It appears that all groups were observed consistently daily post-dosing and all animals were necropsied either upon death or at the end of the 14-day observation period.
	Metric 18: Sampling Adequacy	High	Sampling was adequate for the outcomes of interest and the number of evaluations, as incidences were reported.
	Metric 19: Blinding of Assessors	N/A	Blinding was not reported, but the outcome of interest (mortality) is not subjective in nature.
	Metric 20: Negative Control Response	High	A negative control is not required for this study type, but a vehicle control was included. The negative control response was adequate, as there were no deaths, clinical signs or treatment-related effects.
Domain 6: Confounding / Variable Control			
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	There was some variation in the mean starting body weights of animals across groups (124 -153 g), but this is not expected to have had a significant effect on the outcome of interest. Other data to determine confounding (food/water intake) were not reported.
	Metric 22: Health Outcomes Unrelated to Exposure	High	Qualitative or quantitative results were reported for all prespecified outcomes. The mortalities observed were considered to be treatment related. There is no indication that any of the outcomes were unrelated to exposure.
	Metric 23: Data Presentation and Analysis	High	The method of LD50 determination was not specified; however, incidences of mortality are clearly reported to allow for independent analysis.
	Metric 24: Reporting of Data	High	The number of animals that died and the timing of deaths in each group were clearly reported. The LD50 was reported as a range between 5 and 10 g/kg.
Additional Comments: None			

Overall Quality Determination**High**

Study Citation:	Haas,, R.a. (1979). Initial submission: Acute parenteral LD50 study with o-dichlorobenzene in rats with cover letter dated 073092. 920005562:#88-920005562.			
Health Outcome(s):	Neurological/Behavioral			
Reported Health Effect(s):	Neurological/Behavioral: CNS specific clinical signs			
Duration:	Acute (less than or equal to 24 hr) Single subcutaneous dose			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	5264631			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1:	Test Substance Identity	High	The test material was identified as 1,2-dichlorobenzene, CASRN 99-50-1
	Metric 2:	Test Substance Source	High	The test substance was sourced from Aldrich with a batch/lot number: 101867.
	Metric 3:	Test Substance Purity	High	Test substance purity/grade was reported as 98% technical grade.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	N/A	Although negative controls are not required for this study type, a vehicle control (olive oil) group was included
	Metric 5:	Positive Controls	N/A	A positive control is not required for this study type.
	Metric 6:	Randomized Allocation of Animals	Low	The method of allocation of animals into study groups was not specified.
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and Storage of Test Substance	Low	There is a lack of information regarding test substance preparation/storage conditions. Although this is an acute study, the test substance is considered a volatile compound and these missing details could have a substantial impact on the study results.
	Metric 8:	Consistency of Exposure Administration	Low	In acute toxicity up-and-down test, the volumes administered subcutaneously were not adequately described. In cases where the test substance was dispersed in olive oil, the study indicates that animals were given “a constant volume of 3.88 g/kg”, which is clearly a reporting error. Due to the missing information the consistency of exposure administration cannot be determined.
	Metric 9:	Reporting of Doses/Concentrations	Medium	Individual nominal doses ranging from 0.04 to 74.0 g/kg (which is excessive) were clearly reported. Analytical measurements were not performed, but this is unlikely to have a substantial impact on results.
	Metric 10:	Exposure Frequency and Duration	High	Animals were administered single subcutaneous doses. The study generally followed a step-up-and-down procedure where 4 dose groups were administered on day 1, two higher doses were administered on day 2, and finally, two intermediate doses were administered on day 3.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	This was reported to be a rang-finding study. The doses selected were not justified by the study authors, and several dose groups exceed the recommended dose for a limit test. The spacing used resulted in data showing either 100% mortality or 0% mortality, therefore, additional groups in between those doses would have been warranted.
	Metric 12:	Exposure Route and Method	High	The route (subcutaneous) was acceptable and suitable for the test substance.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Medium	Test animal sex, strain, species (male, CRCD, rat) and starting body weight were reported. The animal source and age were not reported.

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Study Citation:	Haas,, R.a. (1979). Initial submission: Acute parenteral LD50 study with o-dichlorobenzene in rats with cover letter dated 073092. 920005562:#88-920005562.			
Health Outcome(s):	Neurological/Behavioral			
Reported Health Effect(s):	Neurological/Behavioral: CNS specific clinical signs			
Duration:	Acute (less than or equal to 24 hr) Single subcutaneous dose			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	5264631			
Domain		Metric	Rating	Comments
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Animal husbandry conditions and procedures were not reported. No guidelines were provided to account for the lack of detailed husbandry conditions.
	Metric 15:	Number of Animals per Group	Medium	3 animals/dose group were used in a study generally following a step-up-and-down procedure, which is more that required based on current guidelines (OECD 425)
Domain 5: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	High	The outcome assessment methodology effectively addressed the outcome of interest in this study. Although clinical signs are generally not considered to be the most sensitive endpoint for a neurotoxicity outcome, it is consistent with the types of evaluations performed in an acute toxicity study, and therefore was considered to be appropriate.
	Metric 17:	Consistency of Outcome Assessment	High	Details of the outcome assessment were not described in the text but could generally be determined based on the tables provided. It appears that all groups were observed consistently daily post-dosing and all animals were necropsied either upon death or at the end of the 14-day observation period.
	Metric 18:	Sampling Adequacy	High	Sampling was adequate for the outcomes of interest and the number of evaluations, as incidences were reported.
	Metric 19:	Blinding of Assessors	Low	Blinding was not reported and the outcomes (neurotoxicity-related clinical signs) are subjective in nature.
	Metric 20:	Negative Control Response	High	A negative control is not required for this study type, but a vehicle control was included. The negative control response was adequate, as there were no deaths, clinical signs or treatment-related effects.
Domain 6: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	There was some variation in the mean starting body weights of animals across groups (124 -153 g), but this is not expected to have had a significant effect on the outcome of interest. Other data to determine confounding (food/water intake) were not reported.
	Metric 22:	Health Outcomes Unrelated to Exposure	High	Qualitative or quantitative results were reported for all prespecified outcomes. The mortalities observed were considered to be treatment related. There is no indication that any of the outcomes were unrelated to exposure.
	Metric 23:	Data Presentation and Analysis	N/A	Generally, for acute toxicity studies, statistical analysis of other endpoints (e.g., incidences of clinical signs, body weights, or pathology) is not required/conducted because these study types do not include controls. Data are adequately reported for this study if statistical analysis is desired.
	Metric 24:	Reporting of Data	High	Neurotoxicity related clinical signs were recorded in detail for each dose group, including the time of onset and recovery.
Additional Comments:	None			

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Study Citation:	Haas,, R.a. (1979). Initial submission: Acute parenteral LD50 study with o-dichlorobenzene in rats with cover letter dated 073092. 920005562:#88-920005562.		
Health Outcome(s):	Neurological/Behavioral		
Reported Health Effect(s):	Neurological/Behavioral: CNS specific clinical signs		
Duration:	Acute (less than or equal to 24 hr) Single subcutaneous dose		
Chemical:	o-Dichlorobenzene- Parent compound		
HERO ID:	5264631		
Domain	Metric	Rating	Comments
Overall Quality Determination		High	

Study Citation:	Haas,, R.a. (1982). Acute toxicity report.			
Health Outcome(s):	Immune/Hematological; Missing target organ; Skin/Connective Tissue; Mortality; body weight; body weight; Thymus; Missing target organ; Hepatic/Liver; Missing target organ;			
Reported Health Effect(s):	Immune/Hematological: A slight increase in mean white blood cell was observed in animals treated with o-DCB at 1 g/kg/day at day 8.; Missing target organ: missing health effects; Skin/Connective Tissue: On the basis of range finding in rabbits, this substance is considered to be practically non-toxic by a single dermal application. The rabbit dermal LD50 estimate greater than 5 g/kg.; Mortality: For range finding in rats, mortality was observed in all animals receiving test article at dose levels of 10 mg/kg or higher (within 4 days of dosing), and the LD50 was reported to be between 5 and 10 g/kg. In the 16 day myelotoxicity study, increased mortality was also reported following 1g/kg/day, though statistical significance was not reported.; body weight: Animals treated with o-DCB at 1 g/kg/day exhibited a slight decrease in mean body weight through day 7 after which a slight increase in body weight occurred through day 16.; body weight: Animals treated with o-DCB at 1 g/kg/day exhibited a slight decrease in mean body weight through day 7 after which a slight increase in body weight occurred through day 16.; Thymus: A less pronounced decrease occurred in the high dose o-OCB treated animals in absolute thymus weights.; Missing target organ: missing health effects; Hepatic/Liver: There was an increase in mean absolute liver weights in the control and all o-DCB groups with growth of the rats. Statistically significant increases in relativeliver weights were observed in the high and mid-dose o-DCB treated animals.; Missing target organ: missing health effects;			
Duration:	Acute (less than or equal to 24 hr) Acute subcutaneous intra-scapular injection toxicity study			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	5279930			

Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	All Outcomes: The test substance was identified	
	Metric 2: Test Substance Source	High	All Outcomes: The source of the test substance was reported as a manufacturer or the production process was specifically identified	
	Metric 3: Test Substance Purity	High	All Outcomes: 98% purity was reported	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	All Outcomes: negative control group with all conditions equal except chemical exposure	
	Metric 5: Positive Controls	Medium	All Outcomes: A positive control was used and a positive response was observed	
	Metric 6: Randomized Allocation of Animals	Medium	All Outcomes: animals were randomly allocated	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	High	All Outcomes: the study characterizes the test substance preparation	
	Metric 8: Consistency of Exposure Administration	High	All Outcomes: Details of exposure administration were reported (this a non repeated dose)	
	Metric 9: Reporting of Doses/Concentrations	High	All Outcomes: doses were reported without ambiguity	
	Metric 10: Exposure Frequency and Duration	High	All Outcomes: Animals were injected	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: dose range finding was performed	
	Metric 12: Exposure Route and Method	High	All Outcomes: the route and method of exposure reported and suited to the test substance	
Domain 4: Test Animals				

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Study Citation:	Haas., R.a. (1982). Acute toxicity report.			
Health Outcome(s):	Immune/Hematological; Missing target organ; Skin/Connective Tissue; Mortality; body weight; body weight; Thymus; Missing target organ; Hepatic/Liver; Missing target organ;			
Reported Health Effect(s):	Immune/Hematological: A slight increase in mean white blood cell was observed in animals treated with o-DCB at 1 g/kg/day at day 8.; Missing target organ: missing health effects; Skin/Connective Tissue: On the basis of range finding in rabbits, this substance is considered to be practically non-toxic by a single dermal application. The rabbit dermal LD50 estimate greater than 5 g/kg.; Mortality: For range finding in rats, mortality was observed in all animals receiving test article at dose levels of 10 mg/kg or higher (within 4 days of dosing), and the LD50 was reported to be between 5 and 10 g/kg. In the 16 day myelotoxicity study, increased mortality was also reported following 1g/kg/day, though statistical significance was not reported.; body weight: Animals treated with o-DCB at 1 g/kg/day exhibited a slight decrease in mean body weight through day 7 after which a slight increase in body weight occurred through day 16.; body weight: Animals treated with o-DCB at 1 g/kg/day exhibited a slight decrease in mean body weight through day 7 after which a slight increase in body weight occurred through day 16.; Thymus: A less pronounced decrease occurred in the high dose o-OCB treated animals in absolute thymus weights.; Missing target organ: missing health effects; Hepatic/Liver: There was an increase in mean absolute liver weights in the control and all o-DCB groups with growth of the rats. Statistically significant increases in relativeliver weights were observed in the high and mid-dose o-DCB treated animals.; Missing target organ: missing health effects;			
Duration:	Acute (less than or equal to 24 hr) Acute subcutaneous intra-scapular injection toxicity study			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	5279930			
Domain	Metric	Rating	Comments	
	Metric 13: Test Animal Characteristics	High	All Outcomes: the test animal species, strain, sex, age, and starting body weight were reported	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Medium	All Outcomes: Animal husbandry conditions reported	
	Metric 15: Number of Animals per Group	Medium	All Outcomes: The number of animals per study group was reported	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	High	All Outcomes: outcome assessment methodology addressed or reported the intended outcomes of interest	
	Metric 17: Consistency of Outcome Assessment	High	All Outcomes: 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 outcomes of interest	
	Metric 19: Blinding of Assessors	High	All Outcomes: the study explicitly reported that investigators assessing subjective outcomes were blinded to treatment group	
	Metric 20: Negative Control Response	High	All Outcomes: The biological responses of the negative control groups were adequate	
Domain 6: Confounding / Variable Control				
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	Immune/Hematological: Missing Comment ; Missing target organ: Missing Comment ; Skin/Connective Tissue: Missing Comment ; Mortality: Missing Comment ; body weight: Missing Comment ; body weight: Missing Comment ; Thymus: Missing Comment ; Missing target organ: Missing Comment ; Hepatic/Liver: Missing Comment ; Missing target organ: Missing Comment	
	Metric 22: Health Outcomes Unrelated to Exposure	Medium	All Outcomes: No information either to support or dismiss the suggestion that could influence the outcome assessment	
	Metric 23: Data Presentation and Analysis	High	All Outcomes: statistical significance between-an experimental valueand a control value was described	
	Metric 24: Reporting of Data	High	All Outcomes: the data for all outcomes were presented	

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Study Citation:	Haas., R.a. (1982). Acute toxicity report.
Health Outcome(s):	Immune/Hematological; Missing target organ; Skin/Connective Tissue; Mortality; body weight; body weight; Thymus; Missing target organ; Hepatic/Liver; Missing target organ;
Reported Health Effect(s):	Immune/Hematological: A slight increase in mean white blood cell was observed in animals treated with o-DCB at 1 g/kg/day at day 8.; Missing target organ: missing health effects; Skin/Connective Tissue: On the basis of range finding in rabbits, this substance is considered to be practically non-toxic by a single dermal application. The rabbit dermal LD50 estimate greater than 5 g/kg.; Mortality: For range finding in rats, mortality was observed in all animals receiving test article at dose levels of 10 mg/kg or higher (within 4 days of dosing), and the LD50 was reported to be between 5 and 10 g/kg. In the 16 day myelotoxicity study, increased mortality was also reported following 1g/kg/day, though statistical significance was not reported.; body weight: Animals treated with o-DCB at 1 g/kg/day exhibited a slight decrease in mean body weight through day 7 after which a slight increase in body weight occurred through day 16.; body weight: Animals treated with o-DCB at 1 g/kg/day exhibited a slight decrease in mean body weight through day 7 after which a slight increase in body weight occurred through day 16.; Thymus: A less pronounced decrease occurred in the high dose o-OCB treated animals in absolute thymus weights.; Missing target organ: missing health effects; Hepatic/Liver: There was an increase in mean absolute liver weights in the control and all o-DCB groups with growth of the rats. Statistically significant increases in relativeliver weights were observed in the high and mid-dose o-DCB treated animals.; Missing target organ: missing health effects;
Duration:	Acute (less than or equal to 24 hr) Acute subcutaneous intra-scapular injection toxicity study
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	5279930

Domain	Metric	Rating	Comments
Additional Comments: None			

Overall Quality Determination**High**

*** 'Missing Conf' indicates that the metric is Acceptable, but the confidence rating is missing. This evaluation needs to be QC'd.

Study Citation:	Haas,, R.a. (1979). Acute toxicity report with attach cover letter.			
Health Outcome(s):	Mortality (Neurological and irritation); Neurological/Behavioral (Mortality and irritation);			
Reported Health Effect(s):	Mortality (Neurological and irritation): LD50; Neurological/Behavioral (Mortality and irritation): Ataxia;			
Duration:	Acute (less than or equal to 24 hr) Acute dermal toxicity			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	5914598			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1:	Test Substance Identity	High	All Outcomes: The test substance is identified definitively by name. A CASRN is not reported.
	Metric 2:	Test Substance Source	High	All Outcomes: The test substance source is reported. No batch or lot number is reported, but "Aldrich 101867" and "TD No. 78-293", which may serve as additional information regarding test substance source. No analytical confirmation of the test substance identity was performed.
	Metric 3:	Test Substance Purity	High	All Outcomes: The test substance purity is reported and is sufficient to rule out significant influence of potential impurities.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	N/A	All Outcomes: As an acute dermal toxicity study, a negative control was not required.
	Metric 5:	Positive Controls	N/A	All Outcomes: A positive control was not required for the chosen study design.
	Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: Details on allocation into the two dose groups were not described.
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and Storage of Test Substance	Medium	All Outcomes: Details on test substance storage and preparation are reported but are lacking. The authors indicate that the test substance was applied to animals "as received" or dispersed in corn oil and the authors report how the test substance was dermally applied. These deficiencies are unlikely to have a large impact on the results due to the acute nature of the study design.
	Metric 8:	Consistency of Exposure Administration	Low	All Outcomes: The authors disclose that animals in the two groups were dosed at different times, and that the observational period of the 5.0 g/kg was cut short by 4 days due to a holiday. The authors do not report whether the dosing occurred at the same time of day on different days or not. These uncertainties may be concerning for the quality of the results. The volume of test material applied was not reported.
	Metric 9:	Reporting of Doses/Concentrations	Medium	All Outcomes: A nominal dose is reported with mean animal body weights. This is enough information to determine administered dose, but the lack of analytic measurements may have a minor impact on the study's data quality.
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: The exposure frequency and duration were reported and are appropriate for acute dermal toxicity assays.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	N/A	All Outcomes: This study is a range-finding study meant to inform future studies. As such the goal was not determine a dose-dependent effect, even though two doses were used.
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Study Citation:	Haas,, R.a. (1979). Acute toxicity report with attach cover letter.			
Health Outcome(s):	Mortality (Neurological and irritation); Neurological/Behavioral (Mortality and irritation);			
Reported Health Effect(s):	Mortality (Neurological and irritation): LD50; Neurological/Behavioral (Mortality and irritation): Ataxia;			
Duration:	Acute (less than or equal to 24 hr) Acute dermal toxicity			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	5914598			
Domain	Metric	Rating	Comments	
	Metric 12:	Exposure Route and Method	Medium	All Outcomes: The method of dermal exposure is described as an "impervious cuff in 24-hour contact with clipped skin", which seems to be appropriate, but some details are not described, such as whether a porous gauze was used or whether the animal was immobilized.
Domain 4: Test Animals	Metric 13:	Test Animal Characteristics	Medium	All Outcomes: Test animal species, strain, sex and body weight were reported. Test animal source and starting age were omitted.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	All Outcomes: No information regarding animal husbandry conditions were reported.
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: Number of animals per group are reported and are appropriate for the study design.
Domain 5: Outcome Assessment	Metric 16:	Outcome Assessment Methodology	Medium	All Outcomes: The outcome assessment methodology addressed the intended outcomes, but some details were omitted
	Metric 17:	Consistency of Outcome Assessment	Medium	All Outcomes: The authors indicate that animals were monitored for 10 days in the 5 g/kg group and for 14 days in the 3.27 g/kg group. This difference in outcome assessment is unlikely to influence the results as animals had recovered from clinical signs in the 5 g/kg group by day 3.
	Metric 18:	Sampling Adequacy	High	All Outcomes: There appear to be no concerns regarding sampling as all outcomes were measured in all animals.
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: OECD guidelines for acute dermal studies do not typically require blinding.
	Metric 20:	Negative Control Response	N/A	All Outcomes: No negative control was required for the chosen study design.
Domain 6: Confounding / Variable Control	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: The study did not report all the information required to determine confounding, but the reported information on body weights suggested that confounding is unlikely to be a major concern.
	Metric 22:	Health Outcomes Unrelated to Exposure	High	All Outcomes: The authors report information on clinical signs and gross necropsy, indicating that attrition was unlikely.
	Metric 23:	Data Presentation and Analysis	N/A	All Outcomes: Statistical analysis was not possible and not necessary for the study design.
	Metric 24:	Reporting of Data	High	All Outcomes: Quantitative data for exposure related findings were presented for all outcomes.
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Study Citation:	Haas., R.a. (1979). Acute toxicity report with attach cover letter.
Health Outcome(s):	Mortality (Neurological and irritation); Neurological/Behavioral (Mortality and irritation);
Reported Health Effect(s):	Mortality (Neurological and irritation); LD50; Neurological/Behavioral (Mortality and irritation); Ataxia;
Duration:	Acute (less than or equal to 24 hr) Acute dermal toxicity
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	5914598

Domain	Metric	Rating	Comments
Additional Comments:	None		

Overall Quality Determination**Medium**

Study Citation:	Haas,, R.a. (1979). Acute toxicity report with attach cover letter.			
Health Outcome(s):	Nutritional/Metabolic			
Reported Health Effect(s):	Nutritional/Metabolic: Body weight			
Duration:	Acute (less than or equal to 24 hr) Acute dermal toxicity			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	5914598			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	The test substance is identified definitively by name. A CASRN is not reported.	
	Metric 2: Test Substance Source	High	The test substance source is reported. No batch or lot number is reported, but "Aldrich 101867" and "TD No. 78-293", which may serve as additional information regarding test substance source. No analytical confirmation of the test substance identity was performed.	
	Metric 3: Test Substance Purity	High	The test substance purity is reported and is sufficient to rule out significant influence of potential impurities.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	N/A	As an acute dermal toxicity study, a negative control was not required.	
	Metric 5: Positive Controls	N/A	A positive control was not required for the chosen study design.	
	Metric 6: Randomized Allocation of Animals	Low	Details on allocation into the two dose groups were not described.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Medium	Details on test substance storage and preparation are reported but are lacking. The authors indicate that the test substance was applied to animals "as received" or dispersed in corn oil and the authors report how the test substance was dermally applied. These deficiencies are unlikely to have a large impact on the results due to the acute nature of the study design.	
	Metric 8: Consistency of Exposure Administration	Low	The authors disclose that animals in the two groups were dosed at different times, and that the observational period of the 5.0 g/kg was cut short by 4 days due to a holiday. The authors do not report whether the dosing occurred at the same time of day on different days or not. These uncertainties may be concerning for the quality of the results. The volume of test material applied was not reported.	
	Metric 9: Reporting of Doses/Concentrations	Medium	A nominal dose is reported with mean animal body weights. This is enough information to determine administered dose, but the lack of analytic measurements may have a minor impact on the study's data quality.	
	Metric 10: Exposure Frequency and Duration	High	The exposure frequency and duration were reported and are appropriate for acute dermal toxicity assays.	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	N/A	This study is a range-finding study meant to inform future studies. As such the goal was not determine a dose-dependent effect, even though two doses were used.	
	Metric 12: Exposure Route and Method	Medium	The method of dermal exposure is described as an "impervious cuff in 24-hour contact with clipped skin", which seems to be appropriate, but some details are not described, such as whether a porous gauze was used or whether the animal was immobilized.	
Domain 4: Test Animals				
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Study Citation:	Haas,, R.a. (1979). Acute toxicity report with attach cover letter.			
Health Outcome(s):	Nutritional/Metabolic			
Reported Health Effect(s):	Nutritional/Metabolic: Body weight			
Duration:	Acute (less than or equal to 24 hr) Acute dermal toxicity			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	5914598			
Domain	Metric	Rating	Comments	
	Metric 13: Test Animal Characteristics	Medium	Test animal species, strain, sex and body weight were reported. Test animal source and starting age were omitted.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Low	No information regarding animal husbandry conditions were reported.	
	Metric 15: Number of Animals per Group	Medium	Number of animals per group are reported and are appropriate for the study design.	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	Medium	The outcome assessment methodology addressed the intended outcomes, but some details were omitted	
	Metric 17: Consistency of Outcome Assessment	Medium	The authors indicate that animals were monitored for 10 days in the 5 g/kg group and for 14 days in the 3.27 g/kg group. This difference in outcome assessment is unlikely to influence the results as animals had recovered from clinical signs in the 5 g/kg group by day 3.	
	Metric 18: Sampling Adequacy	High	There appear to be no concerns regarding sampling as all outcomes were measured in all animals.	
	Metric 19: Blinding of Assessors	N/A	OECD guidelines for acute dermal studies do not typically require blinding.	
	Metric 20: Negative Control Response	N/A	No negative control was required for the chosen study design.	
Domain 6: Confounding / Variable Control				
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	The study did not report all the information required to determine confounding, but the reported information on body weights suggested that confounding is unlikely to be a major concern.	
	Metric 22: Health Outcomes Unrelated to Exposure	High	The authors report information on clinical signs and gross necropsy, indicating that attrition was unlikely.	
	Metric 23: Data Presentation and Analysis	N/A	Statistical analysis was not possible and not necessary for the study design.	
	Metric 24: Reporting of Data	Low	Mean body weights are reported without measures of variability.	
Additional Comments:	None			

Overall Quality Determination**Medium**

Study Citation:	Haas,, R.a. (1979). Acute toxicity report with attach cover letter.			
Health Outcome(s):	Irritation (Mortality and neurological/behavioral); Gross necropsy (Gross lesions);			
Reported Health Effect(s):	Irritation (Mortality and neurological/behavioral): Skin irritation; Gross necropsy (Gross lesions): Gross necropsy;			
Duration:	Acute (less than or equal to 24 hr) Acute dermal toxicity			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	5914598			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1:	Test Substance Identity	High	All Outcomes: The test substance is identified definitively by name. A CASRN is not reported.
	Metric 2:	Test Substance Source	High	All Outcomes: The test substance source is reported. No batch or lot number is reported, but "Aldrich 101867" and "TD No. 78-293", which may serve as additional information regarding test substance source. No analytical confirmation of the test substance identity was performed.
	Metric 3:	Test Substance Purity	High	All Outcomes: The test substance purity is reported and is sufficient to rule out significant influence of potential impurities.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	N/A	All Outcomes: As an acute dermal toxicity study, a negative control was not required.
	Metric 5:	Positive Controls	N/A	All Outcomes: A positive control was not required for the chosen study design.
	Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: Details on allocation into the two dose groups were not described.
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and Storage of Test Substance	Medium	All Outcomes: Details on test substance storage and preparation are reported but are lacking. The authors indicate that the test substance was applied to animals "as received" or dispersed in corn oil and the authors report how the test substance was dermally applied. These deficiencies are unlikely to have a large impact on the results due to the acute nature of the study design.
	Metric 8:	Consistency of Exposure Administration	Low	All Outcomes: The authors disclose that animals in the two groups were dosed at different times, and that the observational period of the 5.0 g/kg was cut short by 4 days due to a holiday. The authors do not report whether the dosing occurred at the same time of day on different days or not. These uncertainties may be concerning for the quality of the results. The volume of test material applied was not reported.
	Metric 9:	Reporting of Doses/Concentrations	Medium	All Outcomes: A nominal dose is reported with mean animal body weights. This is enough information to determine administered dose, but the lack of analytic measurements may have a minor impact on the study's data quality.
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: The exposure frequency and duration were reported and are appropriate for acute dermal toxicity assays.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	N/A	All Outcomes: This study is a range-finding study meant to inform future studies. As such the goal was not determine a dose-dependent effect, even though two doses were used.
	Metric 12:	Exposure Route and Method	Medium	All Outcomes: The method of dermal exposure is described as an "impervious cuff in 24-hour contact with clipped skin", which seems to be appropriate, but some details are not described, such as whether a porous gauze was used or whether the animal was immobilized.

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Study Citation:	Haas,, R.a. (1979). Acute toxicity report with attach cover letter.			
Health Outcome(s):	Irritation (Mortality and neurological/behavioral); Gross necropsy (Gross lesions);			
Reported Health Effect(s):	Irritation (Mortality and neurological/behavioral): Skin irritation; Gross necropsy (Gross lesions): Gross necropsy;			
Duration:	Acute (less than or equal to 24 hr) Acute dermal toxicity			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	5914598			
Domain	Metric	Rating	Comments	
Domain 4: Test Animals				
Metric 13:	Test Animal Characteristics	Medium	All Outcomes: Test animal species, strain, sex and body weight were reported. Test animal source and starting age were omitted.	
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	All Outcomes: No information regarding animal husbandry conditions were reported.	
Metric 15:	Number of Animals per Group	Medium	All Outcomes: Number of animals per group are reported and are appropriate for the study design.	
Domain 5: Outcome Assessment				
Metric 16:	Outcome Assessment Methodology	Medium	All Outcomes: The outcome assessment methodology addressed the intended outcomes, but some details were omitted	
Metric 17:	Consistency of Outcome Assessment	Medium	All Outcomes: The authors indicate that animals were monitored for 10 days in the 5 g/kg group and for 14 days in the 3.27 g/kg group. This difference in outcome assessment is unlikely to influence the results as animals had recovered from clinical signs in the 5 g/kg group by day 3.	
Metric 18:	Sampling Adequacy	High	All Outcomes: There appear to be no concerns regarding sampling as all outcomes were measured in all animals.	
Metric 19:	Blinding of Assessors	N/A	All Outcomes: OECD guidelines for acute dermal studies do not typically require blinding.	
Metric 20:	Negative Control Response	N/A	All Outcomes: No negative control was required for the chosen study design.	
Domain 6: Confounding / Variable Control				
Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: The study did not report all the information required to determine confounding, but the reported information on body weights suggested that confounding is unlikely to be a major concern.	
Metric 22:	Health Outcomes Unrelated to Exposure	High	All Outcomes: The authors report information on clinical signs and gross necropsy, indicating that attrition was unlikely.	
Metric 23:	Data Presentation and Analysis	N/A	All Outcomes: Statistical analysis was not possible and not necessary for the study design.	
Metric 24:	Reporting of Data	Medium	Irritation (Mortality and neurological/behavioral): Qualitative data for erythema and edema were reported, but severity scores and incidence were not reported.; Gross necropsy (Gross lesions): Gross lesions were reported as negative in text.	
Additional Comments:	None			

Overall Quality Determination**Medium**

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Study Citation:	Haas,, R.a. (1979). Acute toxicity report with attach cover letter.
Health Outcome(s):	Irritation (Mortality and neurological/behavioral); Gross necropsy (Gross lesions);
Reported Health Effect(s):	Irritation (Mortality and neurological/behavioral); Skin irritation; Gross necropsy (Gross lesions); Gross necropsy;
Duration:	Acute (less than or equal to 24 hr) Acute dermal toxicity
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	5914598

Domain	Metric	Rating	Comments

Study Citation:	Herr, D. W., Boyes, W. K. (1997). A comparison of the acute neuroactive effects of dichloromethane, 1,3-dichloropropane, and 1,2-dichlorobenzene on rat flash evoked potentials (FEPs). Fundamental and Applied Toxicology 35(1):31-48.		
Health Outcome(s):	Neurological/Behavioral (Changes in FEP peaks)		
Reported Health Effect(s):	Neurological/Behavioral (Changes in FEP peaks): Changes in peak Flash Evoked Potentials (FEPs)		
Duration:	Acute (less than or equal to 24 hr) acute		
Chemical:	o-Dichlorobenzene- Parent compound		
HERO ID:	730563		
Domain	Metric	Rating	Comments
Domain 1: Test Substance			
	Metric 1: Test Substance Identity	High	CAS No.95-50-1 was provided
	Metric 2: Test Substance Source	Low	Source is Aldrich Chemical Company. Lot # was not provided
	Metric 3: Test Substance Purity	High	Authors reported purity as 99% pure
Domain 2: Test Design			
	Metric 4: Negative and Vehicle Controls	High	Appropriate vehicle control (corn oil)
	Metric 5: Positive Controls	N/A	Positive control not applicable for study type
	Metric 6: Randomized Allocation of Animals	Medium	Animals were randomly assigned to treatments. Randomization protocol was not described.
Domain 3: Exposure Characterization			
	Metric 7: Preparation and Storage of Test Substance	Low	Preparation and storage were not described
	Metric 8: Consistency of Exposure Administration	Medium	Details of exposure administration are incompletely reported, but the missing information is unlikely to have a substantial impact on results
	Metric 9: Reporting of Doses/Concentrations	High	All doses were reported
	Metric 10: Exposure Frequency and Duration	Medium	Acute study; details of the IP treatment were not provided
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	Doses were based on LD50 experiments/data
	Metric 12: Exposure Route and Method	Medium	IP injection was appropriate.
Domain 4: Test Animals			
	Metric 13: Test Animal Characteristics	Medium	Animal species, age, number, sex were provided. Body weight information was not available. The animal facility was AAALAC approved, and all experiments were approved in advance by the National Health and Environmental Effects Research Laboratory Animal Care Committee of U.S. E.P.A. that requires compliance with NIH guidelines.
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were reported and were adequate and the same for control animals. Animals were housed singly and allowed to acclimate to the animal colony (12:12 hr light:dark cycle, lights on 0600 hr; 22 ± 2°C; 40 ± 20% relative humidity) and had free access to food (Purina Lab Chow, St. Louis, MO) and tap water for at least 1 week before surgery.
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Study Citation:	Herr, D. W., Boyes, W. K. (1997). A comparison of the acute neuroactive effects of dichloromethane, 1,3-dichloropropane, and 1,2-dichlorobenzene on rat flash evoked potentials (FEPs). Fundamental and Applied Toxicology 35(1):31-48.			
Health Outcome(s):	Neurological/Behavioral (Changes in FEP peaks)			
Reported Health Effect(s):	Neurological/Behavioral (Changes in FEP peaks): Changes in peak Flash Evoked Potentials (FEPs)			
Duration:	Acute (less than or equal to 24 hr) acute			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	730563			
Domain	Metric	Rating	Comments	
	Metric 15: Number of Animals per Group	Medium	Number of animals in the DCB experiment was provided for each treatment group (page 7: 0 (n = 18), 53 (n = 15), 105 (n = 19), 210 (n = 15), or 420 mg/kg (n = 17), which represent 0, 0.0625, 0.125, 0.25, or 0.5 of published LD50 values. This was comparable to the number of animals, 14-16 per group used in the experiments for other solvents in the study.	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	High	The outcome assessment methodology addressed the intended outcome(s) of interest AND the assessment methodology were sensitive and appropriate to assess changes in FEP, i.e., decreases of both peak N30 and N160 amplitudes in a dose- and time-related manner.	
	Metric 17: Consistency of Outcome Assessment	High	Same protocol was used in treatment vs control animals: baseline FEP Test, followed by ip injection with either corn oil and o-DCB, and then retesting 0.5, 1, 2, 4 and 24 hr after treatment.	
	Metric 18: Sampling Adequacy	Medium	Sampling was adequate to detect changes in FEP potential and colonic temperatures. However, body weight information was not provided.	
	Metric 19: Blinding of Assessors	N/A	Blinding was not applicable to study type as no subjective outcomes were assessed	
	Metric 20: Negative Control Response	High	Control response was appropriate	
Domain 6: Confounding / Variable Control				
	Metric 21: Confounding Variables in Test Design and Procedures	Low	Body weight information was not provided	
	Metric 22: Health Outcomes Unrelated to Exposure	Medium	No information provided to support or dismiss outcomes unrelated to exposure	
	Metric 23: Data Presentation and Analysis	High	Amplitudes and latencies for the baseline FEP (Time 0) and the postinjection waveforms were statistically analyzed using a repeated measures analysis of variance (ANOVA) (SAS Institute Inc., 1989). Degrees of freedom for within-subject factors and their interactions were adjusted using a Greenhouse-Geisser correction factor (Geisser and Greenhouse, 1958; Greenhouse and Geisser, 1959; Keselman and Rogan, 1980). Six peak amplitudes and latencies were quantified in each FEP average. Significant treatment by time interactions were further analyzed using step-down ANOVAs at each time point, which used Bonferroni corrections to maintain a familywise $\alpha \leq 0.05$.	
	Metric 24: Reporting of Data	High	All data were reported for control and treated groups.	
Additional Comments:	none			

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Study Citation:	Herr, D. W., Boyes, W. K. (1997). A comparison of the acute neuroactive effects of dichloromethane, 1,3-dichloropropane, and 1,2-dichlorobenzene on rat flash evoked potentials (FEPs). Fundamental and Applied Toxicology 35(1):31-48.		
Health Outcome(s):	Neurological/Behavioral (Changes in FEP peaks)		
Reported Health Effect(s):	Neurological/Behavioral (Changes in FEP peaks): Changes in peak Flash Evoked Potentials (FEPs)		
Duration:	Acute (less than or equal to 24 hr) acute		
Chemical:	o-Dichlorobenzene- Parent compound		
HERO ID:	730563		
Domain	Metric	Rating	Comments
Overall Quality Determination		High	

Study Citation:	Hollingsworth, R. L., Rowe, V. K., Oyen, F., Torkelson, T. R., Adams, E. M. (1958). Toxicity of o-dichlorobenzene: Studies on animals and industrial experience. AMA Archives of Industrial Health 17(3):180-187.			
Health Outcome(s):	all studies (Acute inhalation - Organ injury experiments: Organ weights (liver, kidney), gross and microscopic examinations (liver and kidney).)			
Reported Health Effect(s):	all studies (Acute inhalation - Organ injury experiments: Organ weights (liver, kidney), gross and microscopic examinations (liver and kidney).): Acute inhalation - Lethality experiments: Mortality; "gross response" (drowsiness, unsteadiness, eye irritation, difficulty breathing, anaesthesia); weight loss.Acute inhalation - Organ injury experiments: Organ weights (liver, kidney), gross and microscopic examinations (liver and kidney).Inhalation Chronic experiments: Mortality, observations of gross appearance and behavior, growth/body weights, organ weights (lungs, heart, liver, kidney, spleen, testes), hematology (rabbits and monkeys), urine tests (blood, sugar, albumin, sediment in females), serum BUN (female guinea pig and rabbits), gross and microscopic examinations. Acute oral: mortality, body weight gain.Oral chronic: mortality, body weights, organ weights (heart, liver, kidney, spleen), gross and microscopic examinations.Eye irritation: eye irritation.			
Duration:	Acute (less than or equal to 24 hr) Acute inhalation (0.5 to 6.5 hrs)- organ injury			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	2962108			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	The test substance was identified by name as o-dichlorobenzene. Physical chemical properties were provided. A CASRN was not reported.	
	Metric 2: Test Substance Source	Low	The original source was not described; the test substance was a re-distillation of a commercial product and was not analytically verified by the performing laboratory.	
	Metric 3: Test Substance Purity	High	The purity was ≥99% based on physical properties	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	A set of acute inhalation experiments was conducted that looked at organ weights and histopathological changes. These experiments used suitable matched groups of air-exposed animals. The study reported generally that control animals were "well matched with experimental animals in respect to number, age, sex, and body weight."	
	Metric 5: Positive Controls	N/A	Positive controls are not required for the study type	
	Metric 6: Randomized Allocation of Animals	Low	The study did not report how animals were allocated into study groups.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Medium	The methods of atmosphere generation were briefly described with further details in a cited reference (Adams et al., 1951), which was viewed for this review. The method of vapor generation was appropriate.	
	Metric 8: Consistency of Exposure Administration	Low	Details of the exposure chamber were provided in a cited reference (Adams et al., 1951). Air flow rates were between 15 and 30 liters/min in the cited reference, but it is difficult to know whether all of the details were similar in the current study. The number of animals per cage was not reported. Animals were consistently exposed in glass-walled chambers of 160 L capacity.	

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Study Citation:	Hollingsworth, R. L., Rowe, V. K., Oyen, F., Torkelson, T. R., Adams, E. M. (1958). Toxicity of o-dichlorobenzene: Studies on animals and industrial experience. AMA Archives of Industrial Health 17(3):180-187.			
Health Outcome(s):	all studies (Acute inhalation - Organ injury experiments: Organ weights (liver, kidney), gross and microscopic examinations (liver and kidney).)			
Reported Health Effect(s):	all studies (Acute inhalation - Organ injury experiments: Organ weights (liver, kidney), gross and microscopic examinations (liver and kidney).): Acute inhalation - Lethality experiments: Mortality; "gross response" (drowsiness, unsteadiness, eye irritation, difficulty breathing, anaesthesia); weight loss.Acute inhalation - Organ injury experiments: Organ weights (liver, kidney), gross and microscopic examinations (liver and kidney).Inhalation Chronic experiments: Mortality, observations of gross appearance and behavior, growth/body weights, organ weights (lungs, heart, liver, kidney, spleen, testes), hematology (rabbits and monkeys), urine tests (blood, sugar, albumin, sediment in females), serum BUN (female guinea pig and rabbits), gross and microscopic examinations. Acute oral: mortality, body weight gain.Oral chronic: mortality, body weights, organ weights (heart, liver, kidney, spleen), gross and microscopic examinations.Eye irritation: eye irritation.			
Duration:	Acute (less than or equal to 24 hr) Acute inhalation (0.5 to 6.5 hrs)- organ injury			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	2962108			
Domain	Metric	Rating	Comments	
	Metric 9: Reporting of Doses/Concentrations	Medium	Vapor concentrations were analytically determined "by combustion of samples of the chamber atmosphere, absorption of combustion products in dilute sodium carbonate-sodium formate solution, and titration of the chloride by the micro Volhard method. " This is an antiquated method, but it was likely appropriate, and all that was available at the time the study was published (1958). The frequency of measurements was not explicitly reported, but the number of samples was indicated, and it was noted that concentrations were "checked repeatedly at intervals during the experimental period." It was not specified where the air samples were taken from. The study reported nominal concentrations, and measured concentrations were reported as a range and as an average.	
	Metric 10: Exposure Frequency and Duration	Low	Animals from one dose group were exposed for 0.5 hrs or for 1 hr, and the other exposure group was exposed for 3 hrs or 6.5 hrs. The lack of consistency makes it difficult to interpret the data results.	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	Low	For acute exposures focused on assessing changes in organ weights and histology, two exposure concentrations were tested in independent experiments, precluding the ability to identify a dose-response. No justification for the concentration tested was provided.	
	Metric 12: Exposure Route and Method	Low	Animals were exposed, whole body, to the vaporized test material. The number of air changes per hour was not reported; however, the flow rate was indicated, suggesting a dynamic chamber was used. The referenced study noted using 160-liter capacity chambers, it is unclear whether this was appropriate for the number of animals.	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	Low	Details were provided in a citation (Spencer et al. 1951). The animals (rats) were from in-house colonies, although the original source of rats was also specified. Strains, initial body weights, and age were not reported. Based on the text, it appears that only male rats were used. No justification was provided.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were not sufficiently reported.	
	Metric 15: Number of Animals per Group	Medium	The test suggests that there were 20 animals per group, which is sufficient for the study type.	
Domain 5: Outcome Assessment				
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Study Citation:	Hollingsworth, R. L., Rowe, V. K., Oyen, F., Torkelson, T. R., Adams, E. M. (1958). Toxicity of o-dichlorobenzene: Studies on animals and industrial experience. AMA Archives of Industrial Health 17(3):180-187.			
Health Outcome(s):	all studies (Acute inhalation - Organ injury experiments: Organ weights (liver, kidney), gross and microscopic examinations (liver and kidney).)			
Reported Health Effect(s):	all studies (Acute inhalation - Organ injury experiments: Organ weights (liver, kidney), gross and microscopic examinations (liver and kidney).): Acute inhalation - Lethality experiments: Mortality; "gross response" (drowsiness, unsteadiness, eye irritation, difficulty breathing, anaesthesia); weight loss.Acute inhalation - Organ injury experiments: Organ weights (liver, kidney), gross and microscopic examinations (liver and kidney).Inhalation Chronic experiments: Mortality, observations of gross appearance and behavior, growth/body weights, organ weights (lungs, heart, liver, kidney, spleen, testes), hematology (rabbits and monkeys), urine tests (blood, sugar, albumin, sediment in females), serum BUN (female guinea pig and rabbits), gross and microscopic examinations. Acute oral: mortality, body weight gain.Oral chronic: mortality, body weights, organ weights (heart, liver, kidney, spleen), gross and microscopic examinations.Eye irritation: eye irritation.			
Duration:	Acute (less than or equal to 24 hr) Acute inhalation (0.5 to 6.5 hrs)- organ injury			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	2962108			
Domain		Metric	Rating	Comments
	Metric 16:	Outcome Assessment Methodology	Medium	These experiments were focused on assessing "organic injury." The only endpoints described are select organ weights (liver and kidney), and microscopic examinations of those same tissues. Methodological details (e.g., tissue fixation, histology methods) were not provided, but the endpoints are generally sensitive for the outcomes of interest.
	Metric 17:	Consistency of Outcome Assessment	Medium	The text indicated that in each group, half of the animals were killed within 24 hrs of the last exposure, while the other half were killed 3 days after the last exposure.
	Metric 18:	Sampling Adequacy	Low	The study did not report whether any animals died, and the results were qualitatively described in the text; sample sizes were not specified.
	Metric 19:	Blinding of Assessors	N/A	Blinding is not required for the outcomes of interest.
	Metric 20:	Negative Control Response	Medium	Control responses for organ weights (reported as means with no measures of variance) seemed appropriate. Histological examinations were qualitatively described, and control responses were not mentioned.
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 (or identified only minor differences) among study groups in the above listed confounding factors.
	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	Uninformative	The study specified using T-tests in the methods; however, all results were qualitatively described in the text, and it was not specified whether any of the findings were statistically analyzed; an independent analysis cannot be done.
	Metric 24:	Reporting of Data	Uninformative	The qualitative description of results does not distinguish between exposure scenarios (concentration and duration of exposure) or sacrifice times.
Additional Comments:	None			

Overall Quality Determination**Uninformative**

Study Citation:	Hollingsworth, R. L., Rowe, V. K., Oyen, F., Torkelson, T. R., Adams, E. M. (1958). Toxicity of o-dichlorobenzene: Studies on animals and industrial experience. AMA Archives of Industrial Health 17(3):180-187.
Health Outcome(s):	all studies (Acute Oral - Lethality experiments: mortality, body weight gain)
Reported Health Effect(s):	all studies (Acute Oral - Lethality experiments: mortality, body weight gain): Acute inhalation - Lethality experiments: Mortality; "gross response" (drowsiness, unsteadiness, eye irritation, difficulty breathing, anaesthesia); weight loss. Acute inhalation - Organ injury experiments: Organ weights (liver, kidney), gross and microscopic examinations (liver and kidney). Inhalation Chronic experiments: Mortality, observations of gross appearance and behavior, growth/body weights, organ weights (lungs, heart, liver, kidney, spleen, testes), hematology (rabbits and monkeys), urine tests (blood, sugar, albumin, sediment in females), serum BUN (female guinea pig and rabbits), gross and microscopic examinations. Acute oral: mortality, body weight gain. Oral chronic: mortality, body weights, organ weights (heart, liver, kidney, spleen), gross and microscopic examinations. Eye irritation: eye irritation.
Duration:	Acute (less than or equal to 24 hr) Acute oral - single dose
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	2962108

Domain	Metric	Rating	Comments
Domain 1: Test Substance			
	Metric 1: Test Substance Identity	High	The test substance was identified by name as o-dichlorobenzene. Physical chemical properties were provided. A CASRN was not reported.
	Metric 2: Test Substance Source	Low	The original source was not described; the test substance was a re-distillation of a commercial product and was not analytically verified by the performing laboratory.
	Metric 3: Test Substance Purity	High	The purity was $\geq 99\%$ based on physical properties
Domain 2: Test Design			
	Metric 4: Negative and Vehicle Controls	N/A	Controls were not described in what appears to be an oral acute lethality study. This is appropriate and consistent with similar study types.
	Metric 5: Positive Controls	N/A	Positive controls are not required for the study type
	Metric 6: Randomized Allocation of Animals	Low	The study did not report how animals were allocated into study groups.
Domain 3: Exposure Characterization			
	Metric 7: Preparation and Storage of Test Substance	Low	Preparation and storage details were not provided. The test substance was delivered as a 50% solution in olive oil.
	Metric 8: Consistency of Exposure Administration	Low	Animals were dosed via gavage. The gavage volume was not reported.
	Metric 9: Reporting of Doses/Concentrations	Low	Two mg/kg doses were reported. It was not specified whether these were target or nominal doses. It was not reported whether concentrations of the test substance in the test solutions were analytically verified. No animal body weights were provided.
	Metric 10: Exposure Frequency and Duration	High	Animals were dosed via a single gavage, which is appropriate for the test substance and the study type.
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	Medium	Two dose groups were included. The doses and dose spacing were not justified by the authors. The highest dose, 2,000 mg/kg, killed all animals, and the second dose (800 mg/kg) killed no animals.
	Metric 12: Exposure Route and Method	High	Animals were dosed via gavage, which is an appropriate exposure method for the test substance.
Domain 4: Test Animals			

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Study Citation:	Hollingsworth, R. L., Rowe, V. K., Oyen, F., Torkelson, T. R., Adams, E. M. (1958). Toxicity of o-dichlorobenzene: Studies on animals and industrial experience. AMA Archives of Industrial Health 17(3):180-187.			
Health Outcome(s):	all studies (Acute Oral - Lethality experiments: mortality, body weight gain)			
Reported Health Effect(s):	all studies (Acute Oral - Lethality experiments: mortality, body weight gain): Acute inhalation - Lethality experiments: Mortality; "gross response" (drowsiness, unsteadiness, eye irritation, difficulty breathing, anaesthesia); weight loss.Acute inhalation - Organ injury experiments: Organ weights (liver, kidney), gross and microscopic examinations (liver and kidney).Inhalation Chronic experiments: Mortality, observations of gross appearance and behavior, growth/body weights, organ weights (lungs, heart, liver, kidney, spleen, testes), hematology (rabbits and monkeys), urine tests (blood, sugar, albumin, sediment in females), serum BUN (female guinea pig and rabbits), gross and microscopic examinations. Acute oral: mortality, body weight gain.Oral chronic: mortality, body weights, organ weights (heart, liver, kidney, spleen), gross and microscopic examinations.Eye irritation: eye irritation.			
Duration:	Acute (less than or equal to 24 hr) Acute oral - single dose			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	2962108			
Domain	Metric	Rating	Comments	
	Metric 13: Test Animal Characteristics	Low	Details were provided in a citation (Spencer et al. 1951). The animals (guinea pigs) were from in-house colonies. Strains, initial body weights, and age were not reported. These experiments used "mixed sex."	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were not sufficiently reported.	
	Metric 15: Number of Animals per Group	Medium	10 animals total of mixed sex were used in each group. The number is appropriate for the study type.	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	Medium	Mortality and weight loss were the only outcomes described. The frequency of observations or measurements was not reported. Animals were observed for "about two weeks", which is consistent with current guidelines for acute lethality studies.	
	Metric 17: Consistency of Outcome Assessment	Low	Details of outcome assessment methods were limited. The frequencies of observations were not provided, so consistency across groups is unclear.	
	Metric 18: Sampling Adequacy	Medium	The text suggests that all animals were observed for mortality. Weight loss was qualitatively described and sample sizes were not specified.	
	Metric 19: Blinding of Assessors	N/A	Blinding is not required for the outcomes of interest.	
	Metric 20: Negative Control Response	N/A	Controls were not included in acute lethality experiments.	
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 (or identified only minor differences) among study groups in the above listed confounding factors.	
	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 is not required (no control group). Sufficient information about mortality is provided to potentially calculate an LD50 value.	
	Metric 24: Reporting of Data	Low	Mortality incidences were adequately described; however, the time and causes of death were not provided. Animal body weight loss was qualitatively described.	
Additional Comments:	None			

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Study Citation:	Hollingsworth, R. L., Rowe, V. K., Oyen, F., Torkelson, T. R., Adams, E. M. (1958). Toxicity of o-dichlorobenzene: Studies on animals and industrial experience. AMA Archives of Industrial Health 17(3):180-187.
Health Outcome(s):	all studies (Acute Oral - Lethality experiments: mortality, body weight gain)
Reported Health Effect(s):	all studies (Acute Oral - Lethality experiments: mortality, body weight gain): Acute inhalation - Lethality experiments: Mortality; "gross response" (drowsiness, unsteadiness, eye irritation, difficulty breathing, anaesthesia); weight loss.Acute inhalation - Organ injury experiments: Organ weights (liver, kidney), gross and microscopic examinations (liver and kidney).Inhalation Chronic experiments: Mortality, observations of gross appearance and behavior, growth/body weights, organ weights (lungs, heart, liver, kidney, spleen, testes), hematology (rabbits and monkeys), urine tests (blood, sugar, albumin, sediment in females), serum BUN (female guinea pig and rabbits), gross and microscopic examinations. Acute oral: mortality, body weight gain.Oral chronic: mortality, body weights, organ weights (heart, liver, kidney, spleen), gross and microscopic examinations.Eye irritation: eye irritation.
Duration:	Acute (less than or equal to 24 hr) Acute oral - single dose
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	2962108

Domain	Metric	Rating	Comments
Overall Quality Determination		Medium	

Study Citation:	Hollingsworth, R. L., Rowe, V. K., Oyen, F., Torkelson, T. R., Adams, E. M. (1958). Toxicity of o-dichlorobenzene: Studies on animals and industrial experience. AMA Archives of Industrial Health 17(3):180-187.			
Health Outcome(s):	all studies (Acute inhalation - Lethality experiments: Mortality; "gross response" (drowsiness, unsteadiness, eye irritation, difficulty breathing, anaesthesia); weight loss.)			
Reported Health Effect(s):	all studies (Acute inhalation - Lethality experiments: Mortality; "gross response" (drowsiness, unsteadiness, eye irritation, difficulty breathing, anaesthesia); weight loss.): Acute inhalation - Lethality experiments: Mortality; "gross response" (drowsiness, unsteadiness, eye irritation, difficulty breathing, anaesthesia); weight loss.Acute inhalation - Organ injury experiments: Organ weights (liver, kidney), gross and microscopic examinations (liver and kidney).Inhalation Chronic experiments: Mortality, observations of gross appearance and behavior, growth/body weights, organ weights (lungs, heart, liver, kidney, spleen, testes), hematology (rabbits and monkeys), urine tests (blood, sugar, albumin, sediment in females), serum BUN (female guinea pig and rabbits), gross and microscopic examinations. Acute oral: mortality, body weight gain.Oral chronic: mortality, body weights, organ weights (heart, liver, kidney, spleen), gross and microscopic examinations.Eye irritation: eye irritation.			
Duration:	Acute (less than or equal to 24 hr) Acute inhalation (0.5 to 10 hrs)-lethality			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	2962108			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	The test substance was identified by name as o-dichlorobenzene. Physical chemical properties were provided. A CASRN was not reported.	
	Metric 2: Test Substance Source	Low	The original source was not described; the test substance was a re-distillation of a commercial product and was not analytically verified by the performing laboratory.	
	Metric 3: Test Substance Purity	High	The purity was ≥99% based on physical properties	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	N/A	Control animals were not included in the acute lethality experiments reporting on mortality and clinical signs, and this is appropriate and consistent with similar study types.	
	Metric 5: Positive Controls	N/A	Positive controls are not required for the study type	
	Metric 6: Randomized Allocation of Animals	Low	The study did not report how animals were allocated into study groups.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Medium	The methods of atmosphere generation were briefly described with further details in a cited reference (Adams et al., 1951), which was viewed for this review. The method of vapor generation was appropriate.	
	Metric 8: Consistency of Exposure Administration	Low	Details of the exposure chamber were provided in a cited reference (Adams et al., 1951). Air flow rates were between 15 and 30 liters/min in the cited reference, but it is difficult to know whether all of the details were similar in the current study. The number of animals per cage was not reported. Animals were consistently exposed in glass-walled chambers of 160 L capacity.	
	Metric 9: Reporting of Doses/Concentrations	Medium	Vapor concentrations were analytically determined "by combustion of samples of the chamber atmosphere, absorption of combustion products in dilute sodium carbonate-sodium formate solution, and titration of the chloride by the micro Volhard method. " This is an antiquated method, but it was likely appropriate, and all that was available at the time the study was published (1958). The frequency of measurements was not explicitly reported, but the number of samples was indicated, and it was noted that concentrations were "checked repeatedly at intervals during the experimental period." It was not specified where the air samples were taken from. The study reported nominal concentrations, and measured concentrations were reported as a range and as an average.	
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Study Citation:	Hollingsworth, R. L., Rowe, V. K., Oyen, F., Torkelson, T. R., Adams, E. M. (1958). Toxicity of o-dichlorobenzene: Studies on animals and industrial experience. AMA Archives of Industrial Health 17(3):180-187.			
Health Outcome(s):	all studies (Acute inhalation - Lethality experiments: Mortality; "gross response" (drowsiness, unsteadiness, eye irritation, difficulty breathing, anaesthesia); weight loss.)			
Reported Health Effect(s):	all studies (Acute inhalation - Lethality experiments: Mortality; "gross response" (drowsiness, unsteadiness, eye irritation, difficulty breathing, anaesthesia); weight loss.): Acute inhalation - Lethality experiments: Mortality; "gross response" (drowsiness, unsteadiness, eye irritation, difficulty breathing, anaesthesia); weight loss.Acute inhalation - Organ injury experiments: Organ weights (liver, kidney), gross and microscopic examinations (liver and kidney).Inhalation Chronic experiments: Mortality, observations of gross appearance and behavior, growth/body weights, organ weights (lungs, heart, liver, kidney, spleen, testes), hematology (rabbits and monkeys), urine tests (blood, sugar, albumin, sediment in females), serum BUN (female guinea pig and rabbits), gross and microscopic examinations. Acute oral: mortality, body weight gain.Oral chronic: mortality, body weights, organ weights (heart, liver, kidney, spleen), gross and microscopic examinations.Eye irritation: eye irritation.			
Duration:	Acute (less than or equal to 24 hr) Acute inhalation (0.5 to 10 hrs)-lethality			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	2962108			
Domain	Metric	Rating	Comments	
	Metric 10:	Exposure Frequency and Duration	Low	Animals from different exposure groups were exposed over a wide range of durations (1 hour to 10 hours), many of which are not consistent with a standard acute lethality inhalation study. Although some durations were shared across some groups, the lack of consistency makes it difficult to interpret the data results.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	All together 4 exposure concentrations were independently tested in acute duration exposures. No justification for the concentrations tested was provided.
	Metric 12:	Exposure Route and Method	Low	Animals were exposed, whole body, to the vaporized test material. The number of air changes per hour was not reported; however, the flow rate was indicated, suggesting a dynamic chamber was used. The referenced study noted using 160-liter capacity chambers, it is unclear whether this was appropriate for the number of animals.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Low	Details were provided in a citation (Spencer et al. 1951). The animals (rats) were from in-house colonies, although the original source of rats was also specified. Strains, initial body weights, and age were not reported. Based on the text, it appears that only male rats were used. No justification was provided.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were not sufficiently reported.
	Metric 15:	Number of Animals per Group	Medium	The number of animals used in each acute exposure experiment ranged from 5 to 20. It is unclear why some exposure scenarios used more rats than others, but the numbers were appropriate for assessing lethality.
Domain 5: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	Medium	Outcomes assessed were limited to mortality, "gross response" (clinical signs), and body weights, and it is reported that animals were observed for 14 days, which is consistent with current guidelines for acute lethality studies.
	Metric 17:	Consistency of Outcome Assessment	Low	Insufficient details were provided to determine consistency in outcome assessments. Details on the frequencies of observations were not provided.
	Metric 18:	Sampling Adequacy	Medium	All animals were assessed for mortality. For other endpoints, results are qualitatively described, and sample sizes were not specified.
	Metric 19:	Blinding of Assessors	N/A	Blinding is not required for the outcomes of interest.
	Metric 20:	Negative Control Response	N/A	Controls were not included in acute lethality experiments.

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Study Citation:	Hollingsworth, R. L., Rowe, V. K., Oyen, F., Torkelson, T. R., Adams, E. M. (1958). Toxicity of o-dichlorobenzene: Studies on animals and industrial experience. AMA Archives of Industrial Health 17(3):180-187.
Health Outcome(s):	all studies (Acute inhalation - Lethality experiments: Mortality; "gross response" (drowsiness, unsteadiness, eye irritation, difficulty breathing, anaesthesia); weight loss.)
Reported Health Effect(s):	all studies (Acute inhalation - Lethality experiments: Mortality; "gross response" (drowsiness, unsteadiness, eye irritation, difficulty breathing, anaesthesia); weight loss.): Acute inhalation - Lethality experiments: Mortality; "gross response" (drowsiness, unsteadiness, eye irritation, difficulty breathing, anaesthesia); weight loss. Acute inhalation - Organ injury experiments: Organ weights (liver, kidney), gross and microscopic examinations (liver and kidney). Inhalation Chronic experiments: Mortality, observations of gross appearance and behavior, growth/body weights, organ weights (lungs, heart, liver, kidney, spleen, testes), hematology (rabbits and monkeys), urine tests (blood, sugar, albumin, sediment in females), serum BUN (female guinea pig and rabbits), gross and microscopic examinations. Acute oral: mortality, body weight gain. Oral chronic: mortality, body weights, organ weights (heart, liver, kidney, spleen), gross and microscopic examinations. Eye irritation: eye irritation.
Duration:	Acute (less than or equal to 24 hr) Acute inhalation (0.5 to 10 hrs)-lethality
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	2962108

Domain	Metric	Rating	Comments
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 (or identified only minor differences) among study groups in the above listed confounding factors.
	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	Data were not statistically analyzed. Although quantitative mortality data were provided, the study was not properly designed to allow for identification of an LC50. Statistical analysis is not applicable to the other endpoints because a control group was not included.
	Metric 24: Reporting of Data	Low	Mortality results for acute exposures were quantitatively reported. Clinical signs were generally reported in the text, but was not defined by test group or duration. The study merely indicated that the "intensity of the responses were dependent on the concentration and the duration of exposure." Similarly, it was noted that "survivors generally suffered from temporary body weight loss," but no further information about specific groups/conditions was provided.

Additional Comments: None

Overall Quality Determination**Low**

Study Citation:	Kulkarni, S. G., Warbritton, A., Bucci, T. J., Mehendale, H. M. (1997). Antimitotic intervention with colchicine alters the outcome of o-DCB-induced hepatotoxicity in Fischer 344 rats. Toxicology 120(2):79-88.			
Health Outcome(s):	Hepatic/Liver			
Reported Health Effect(s):	Hepatic/Liver: Increase in plasma ALT and SDH levels; liver histopathology, increase in thymidine incorporation and cell proliferation after treatment as a marker of tissue repair			
Duration:	Acute (less than or equal to 24 hr) Acute liver injury and mortality			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	2919019			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	Test substance was identified as 1,2-dichlorobenzene, but the CASRN was not reported.	
	Metric 2: Test Substance Source	High	The source of the test substance was Aldrich Chem Co (Milwaukee, WI). The batch/lot number was not reported, but this is should have limited impact on the results.	
	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	High	Details regarding the negative control group were reported. Study states “Appropriate control group of rats receiving corn oil + distilled water and corn oil + CLC were also maintained.”	
	Metric 5: Positive Controls	N/A	Not applicable for this study.	
	Metric 6: Randomized Allocation of Animals	Low	Study does not state how animals were allocated.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Medium	Test substance preparation and storage were not adequately described given the volatility of the test substance. However, this is an acute study and the storage is unlikely to impact the results.	
	Metric 8: Consistency of Exposure Administration	High	Test substance was delivered consistently across study groups.	
	Metric 9: Reporting of Doses/Concentrations	Low	There is some ambiguity around the dose used in this study. For instance, under 2.2 Treatment in the Materials and Methods section, the authors state that the dose used to determine liver injury and changes to enzyme activity was 0.6 mL/kg 1,2-dichlorobenzene (o-DCB) but was administered in corn oil (3:1; o-DCB:corn oil). Based on this information, the correct dose of o-DCB would be calculated as 0.45 mL/kg. The authors also make no mention in the figures or results sections for the biochemical assays or observation of liver injury of the actual dose that was administered. However, for the lethality studies, they clearly state in the Materials and Methods and in Table 1, the dose of o-DCB used was 0.6 mL/kg. Therefore, it is not clear if the actual dose was different based on the experiment, or if the same dose was used consistently throughout all experiments (e.g. lethality and acute liver injury).	
	Metric 10: Exposure Frequency and Duration	High	The exposure frequency and duration were appropriate.	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	Medium	Only one dose was tested, and it was based on prior references that reported the LD50. However, in the context of the study aim, this is unlikely to substantially impact results.	
	Metric 12: Exposure Route and Method	High	The exposure route and method were appropriate.	

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Study Citation:	Kulkarni, S. G., Warbritton, A., Bucci, T. J., Mehendale, H. M. (1997). Antimitotic intervention with colchicine alters the outcome of o-DCB-induced hepatotoxicity in Fischer 344 rats. Toxicology 120(2):79-88.			
Health Outcome(s):	Hepatic/Liver			
Reported Health Effect(s):	Hepatic/Liver: Increase in plasma ALT and SDH levels; liver histopathology, increase in thymidine incorporation and cell proliferation after treatment as a marker of tissue repair			
Duration:	Acute (less than or equal to 24 hr) Acute liver injury and mortality			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	2919019			
Domain	Metric	Rating	Comments	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	High	Animal test characteristics were adequately reported.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Medium	Temperature and humidity were not reported.	
	Metric 15: Number of Animals per Group	Medium	The number of animals per groups was equal to 4 as stated in the figures of the paper.	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	High	Outcome assessment methodology was appropriate for intended outcomes of interest.	
	Metric 17: Consistency of Outcome Assessment	Low	Information regarding outcome assessment of the negative controls group is not reported. It is not clear if this group was assessed in the same manner as the dosed group.	
	Metric 18: Sampling Adequacy	High	The sampling was adequate for the outcomes of interest.	
	Metric 19: Blinding of Assessors	N/A	Blinding was not necessary.	
	Metric 20: Negative Control Response	Low	The negative control responses were not reported.	
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 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	Statistical analysis was performed and appropriate.	
	Metric 24: Reporting of Data	Medium	Data on histology and PCNA proliferation are not fully reported. The differences in enzyme activity and thymidine incorporation over time are presented as mean ± SE for four rats in each group. It is impossible to conclude that thymidine incorporation and cell proliferation was increased due to treatment because there is no comparison to a negative control.	
Additional Comments:	The major limitation for this study is that the results of the negative control group were not reported. Although increases to enzyme activity due to treatment were reported over time (from 0 h to 96 h), the comparison to the negative control was not reported or presented. Although data was reported regarding tissue repair after treatment, the the lack of negative control data precludes the unequivocal conclusion that the observed increase in thymidine incorporation and cell proliferation was due to 1,2-dichlorobenzene exposure.			

Overall Quality Determination**Medium**

Study Citation:	Kulkarni, S. G., Warbritton, A., Bucci, T. J., Mehendale, H. M. (1997). Antimitotic intervention with colchicine alters the outcome of o-DCB-induced hepatotoxicity in Fischer 344 rats. Toxicology 120(2):79-88.			
Health Outcome(s):	Mortality			
Reported Health Effect(s):	Mortality: Lethality study (observation for 14 days following single i.p. dose)			
Duration:	Acute (less than or equal to 24 hr) Acute liver injury and mortality			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	2919019			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	Test substance was identified as 1,2-dichlorobenzene.	
	Metric 2: Test Substance Source	High	The source of the test substance was Aldrich Chem Co (Milwaukee, WI). The batch/lot number was not reported, but this is unlikely impact the results.	
	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	N/A	Not necessary for this acute lethality study.	
	Metric 5: Positive Controls	N/A	Not applicable for this study.	
	Metric 6: Randomized Allocation of Animals	Low	Study does not state how animals were allocated into treatment groups.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Medium	Test substance preparation and storage were not adequately described given the volatility of the test substance, but this was an acute study and the storage is unlikely to affect the results.	
	Metric 8: Consistency of Exposure Administration	High	Test substance was delivered consistently across study groups.	
	Metric 9: Reporting of Doses/Concentrations	Low	There is some ambiguity around the dose used in this study. For instance, under 2.2 Treatment in the Materials and Methods section, the authors state that the dose used to determine liver injury and changes to enzyme activity was 0.6 mL/kg 1,2-dichlorobenzene (o-DCB) but was administered in corn oil (3:1; o-DCB:corn oil). Based on this information, the correct dose of o-DCB would be calculated as 0.45 mL/kg. The authors also make no mention in the figures or results sections for the biochemical assays or observation of liver injury of the actual dose that was administered. However, for the lethality studies, they clearly state in the Materials and Methods and in Table 1, the dose of o-DCB used was 0.6 mL/kg. Therefore, it is not clear if the actual dose was different based on the experiment or if the same dose was used consistently throughout.	
	Metric 10: Exposure Frequency and Duration	High	The exposure frequency and duration were appropriate.	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	Only one dose was tested, and it was chosen based on reference studies that reported an LD50.	
	Metric 12: Exposure Route and Method	High	The exposure route and method were appropriate.	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	High	Animal test characteristics were adequately reported.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Medium	Temperature and humidity were not reported.	
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Study Citation:	Kulkarni, S. G., Warbritton, A., Bucci, T. J., Mehendale, H. M. (1997). Antimitotic intervention with colchicine alters the outcome of o-DCB-induced hepatotoxicity in Fischer 344 rats. Toxicology 120(2):79-88.
Health Outcome(s):	Mortality
Reported Health Effect(s):	Mortality: Lethality study (observation for 14 days following single i.p. dose)
Duration:	Acute (less than or equal to 24 hr) Acute liver injury and mortality
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	2919019

Domain	Metric	Rating	Comments
	Metric 15: Number of Animals per Group	Medium	Number of animals were reported and appropriate.

Domain 5: Outcome Assessment

Metric 16:	Outcome Assessment Methodology	High	Outcome assessment methodology was appropriate for intended outcomes of interest.
Metric 17:	Consistency of Outcome Assessment	High	Outcome was assessed consistently across study groups.
Metric 18:	Sampling Adequacy	High	Sampling was adequate.
Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary.
Metric 20:	Negative Control Response	N/A	Negative control was not included for lethality.

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 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	Sufficient data were provided to conduct independent statistical analysis.
Metric 24:	Reporting of Data	High	Data were adequately reported. The number of animals in the group, the dose used, and the % lethality was reported.

Additional Comments: None

Overall Quality Determination**High**

Study Citation:	Miyagawa, M., Takasawa, H., Sugiyama, A., Inoue, Y., Murata, T., Uno, Y., Yoshikawa, K. (1995). The in vivo-in vitro replicative DNA synthesis (RDS) test with hepatocytes prepared from male B6C3F1 mice as an early prediction assay for putative nongenotoxic (Ames-negative) mouse hepatocarcinogens. Mutation Research: Genetic Toxicology 343(2-3):157-183.			
Health Outcome(s):	Mortality			
Reported Health Effect(s):	Mortality: Determination of MTD (set at half the LD50)			
Duration:	Acute (less than or equal to 24 hr) Single gavage dose			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	661834			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	The test substance was definitively identified as o-dichlorobenzene; CASRN 95-50-1	
	Metric 2: Test Substance Source	High	The test substance source was reported (Wako Pure Chemical Industries, Osaka). A lot or batch number was not provided.	
	Metric 3: Test Substance Purity	Low	The test substance purity was not provided, and the chemical could not be identified on the supplier website.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	N/A	Negative control mice are not required for acute toxicity studies focused on identifying an LD50	
	Metric 5: Positive Controls	N/A	Positive controls are not required for this study type	
	Metric 6: Randomized Allocation of Animals	Low	The method of distribution of animals into study groups was not specified	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Low	Details on preparation of the test substance are limited. The test substance was dissolved in a corn oil vehicle, no further information was provided. No details on storage were included; however, since animals were treated with a single gavage, if solutions were prepared fresh, storage conditions may not be relevant for this study. Because the test substance is volatile, the lack of information on preparation and storage could have a significant impact on the study results.	
	Metric 8: Consistency of Exposure Administration	Low	Details of exposure administration were limited. Gavage volumes were not reported, therefore, it cannot be determined whether the volumes were excessive, or if there was consistency across groups.	
	Metric 9: Reporting of Doses/Concentrations	Uninformative	Doses used to determine an LD50 were not reported.	
	Metric 10: Exposure Frequency and Duration	High	Animals were administered a single gavage, which was appropriate for the purposes of the study.	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	Uninformative	The number of exposure groups for the acute toxicity test was not specified.	
	Metric 12: Exposure Route and Method	High	The exposure route (oral) and method (gavage) were suited to the test substance and appropriate for the purposes of the study.	
Domain 4: Test Animals				
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Study Citation:	Miyagawa, M., Takasawa, H., Sugiyama, A., Inoue, Y., Murata, T., Uno, Y., Yoshikawa, K. (1995). The in vivo-in vitro replicative DNA synthesis (RDS) test with hepatocytes prepared from male B6C3F1 mice as an early prediction assay for putative nongenotoxic (Ames-negative) mouse hepatocarcinogens. Mutation Research: Genetic Toxicology 343(2-3):157-183.			
Health Outcome(s):	Mortality			
Reported Health Effect(s):	Mortality: Determination of MTD (set at half the LD50)			
Duration:	Acute (less than or equal to 24 hr) Single gavage dose			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	661834			
Domain	Metric	Rating	Comments	
	Metric 13: Test Animal Characteristics	Medium	Animal species, strain, age, and sex were reported, and the strain used was justified by the study authors. Animals were obtained from a commercial source. Starting body weights were not reported.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	High	The study provided sufficient animal husbandry details including room temperature, humidity, light cycle, food and water availability and the number of animals per cage.	
	Metric 15: Number of Animals per Group	Low	The number animals per group for acute toxicity testing was not clearly specified. The study text indicated that testing was conducted using 4-5 mice, but it is unclear if this was the number of mice per group, or if 4-5 doses were tested on single mice.	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	Low	Details of outcome assessment methodology, including how long animals were observed and how the LD50 was determined were not provided.	
	Metric 17: Consistency of Outcome Assessment	Low	Details regarding execution of the study protocol for outcome assessment were not reported.	
	Metric 18: Sampling Adequacy	Medium	Details regarding sampling for were not reported, it is assumed that all animals were monitored for mortality in order to determine an LD50.	
	Metric 19: Blinding of Assessors	N/A	Blinding is not required for this type of study	
	Metric 20: Negative Control Response	N/A	A negative control was not used for the acute toxicity text.	
Domain 6: Confounding / Variable Control				
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	The study did not report information required to determine confounding (body weights, food and water intake); however, given the short duration of the study, it is not expected that there would be confounding variables that would significantly impact the study results.	
	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	Low	The method used to calculate LD50 values were not reported and mortality incidences by dose were not provided.	
	Metric 24: Reporting of Data	Low	Deaths were not reported. The study did not report LD50 values. A maximum tolerated dose (MTD) was reported, which was described as being set at “about half the LD50”	
Additional Comments:	The LD50 was not reported and cannot be accurately determined. The reported MTD was ”about half the LD50” which was not considered to be precise enough to upgrade this endpoint.			

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Study Citation:	Miyagawa, M., Takasawa, H., Sugiyama, A., Inoue, Y., Murata, T., Uno, Y., Yoshikawa, K. (1995). The in vivo-in vitro replicative DNA synthesis (RDS) test with hepatocytes prepared from male B6C3F1 mice as an early prediction assay for putative nongenotoxic (Ames-negative) mouse hepatocarcinogens. Mutation Research: Genetic Toxicology 343(2-3):157-183.		
Health Outcome(s):	Mortality		
Reported Health Effect(s):	Mortality: Determination of MTD (set at half the LD50)		
Duration:	Acute (less than or equal to 24 hr) Single gavage dose		
Chemical:	o-Dichlorobenzene- Parent compound		
HERO ID:	661834		
Domain	Metric	Rating	Comments
Overall Quality Determination		Uninformative	

Study Citation:	Mohtashamipur, E., Triebel, R., Straeter, H., Norpoth, K. (1987). The bone marrow clastogenicity of eight halogenated benzenes in male NMRI mice. <i>Mutagenesis</i> 2(2):111-113.			
Health Outcome(s):	Clastogenicity (micronuclei) (in vivo genotoxicity); Clastogenicity (micronuclei) (in vivo genotoxicity);			
Reported Health Effect(s):	Clastogenicity (micronuclei) (in vivo genotoxicity): In vivo micronuclei assay; Clastogenicity (micronuclei) (in vivo genotoxicity): In vivo micronuclei assay;			
Duration:	Acute (less than or equal to 24 hr) 1 or 2 doses within 24 hrs			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	201693			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	All Outcomes: Test substance is clearly identified by name (isoform specified)	
	Metric 2: Test Substance Source	Low	All Outcomes: The test substance was commercially obtained. A batch or lot number were not provided.	
	Metric 3: Test Substance Purity	High	All Outcomes: Synthetic grade, purity 99%	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	All Outcomes: A corn oil vehicle control was included.	
	Metric 5: Positive Controls	Medium	All Outcomes: An appropriate positive control was used and gave the expected response	
	Metric 6: Randomized Allocation of Animals	Low	All Outcomes: Allocation of animals was not specified	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Medium	All Outcomes: There are limited details on preparation and storage of the test substance, but these are unlikely to have a substantial impact on results.	
	Metric 8: Consistency of Exposure Administration	Low	All Outcomes: Limited details of exposure administration were provided. Injection volume was not reported.	
	Metric 9: Reporting of Doses/Concentrations	High	All Outcomes: Doses were clearly reported and justified by the study authors.	
	Metric 10: Exposure Frequency and Duration	High	All Outcomes: Animals were administered 2 doses at 0 and 24 hrs. This is consistent with current guidelines for this study type	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	Medium	All Outcomes: The study included an acceptable number of dose groups, and the high dose was justified by the study author. However, even the low dose group gave a positive response. In fact, all of the chemicals tested in this study gave positive results in all dose groups tested indicating that the lowest dosing group may not have been appropriate.	
	Metric 12: Exposure Route and Method	Low	All Outcomes: Animals were dosed i.p., this is a PECO relevant route of exposure, however, i.p. injections are generally not recommended for micronucleus assays unless justified.	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	Medium	All Outcomes: Animal species, strain, sex, age, and source were provided. Initial body weights were not reported.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Medium	All Outcomes: All animal husbandry conditions were not reported. It was only specified that animals were housed 5/cage with free access to food and water; no other details were provided. This is unlikely to have a major impact on an acute study.	

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Study Citation:	Mohtashamipur, E., Triebel, R., Straeter, H., Norpoth, K. (1987). The bone marrow clastogenicity of eight halogenated benzenes in male NMRI mice. <i>Mutagenesis</i> 2(2):111-113.
Health Outcome(s):	Clastogenicity (micronuclei) (in vivo genotoxicity); Clastogenicity (micronuclei) (in vivo genotoxicity);
Reported Health Effect(s):	Clastogenicity (micronuclei) (in vivo genotoxicity): In vivo micronuclei assay; Clastogenicity (micronuclei) (in vivo genotoxicity): In vivo micronuclei assay;
Duration:	Acute (less than or equal to 24 hr) 1 or 2 doses within 24 hrs
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	201693

Domain	Metric	Rating	Comments
	Metric 15: Number of Animals per Group	Medium	All Outcomes: The number of animals per group is consistent with current guidelines.
Domain 5: Outcome Assessment			
	Metric 16: Outcome Assessment Methodology	Low	All Outcomes: The sampling time was earlier than current recommendations. In the study, a single sample was taken 30hrs after the first injection (only 6 hours after the last injection). The current guideline recommends sampling between 18-24 hours following the final treatment.
	Metric 17: Consistency of Outcome Assessment	High	All Outcomes: Some Details regarding the execution of the study protocol for outcome assessment were reported and were consistent across groups
	Metric 18: Sampling Adequacy	High	All Outcomes: Sampling was adequate for the outcome of interest
	Metric 19: Blinding of Assessors	Medium	All Outcomes: Blinding was not explicitly reported, but slides were coded and examined by two different examiners
	Metric 20: Negative Control Response	High	All Outcomes: The negative control response was as expected
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 (or identified only minor differences) among study groups in the above listed confounding factors.
	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 analysis was performed using the Student T-test
	Metric 24: Reporting of Data	Medium	All Outcomes: Data were presented as means $\pm$ SD of micronuclei/1000 PCE
Additional Comments:	This form is for the m-dichlorobenzene isomer Generally in vivo micronucleus assays should also report on animal toxicity and clinical signs. This was not included in this study.		

Overall Quality Determination**Medium**

Study Citation:	Mohtashamipur, E., Triebel, R., Straeter, H., Norpoth, K. (1987). The bone marrow clastogenicity of eight halogenated benzenes in male NMRI mice. <i>Mutagenesis</i> 2(2):111-113.			
Health Outcome(s):	Mortality			
Reported Health Effect(s):	Mortality: LD50 values			
Duration:	Acute (less than or equal to 24 hr) 1 or 2 doses within 24 hrs			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	201693			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	Test substance is clearly identified by name (isoform specified)	
	Metric 2: Test Substance Source	Low	The test substance was commercially obtained. A batch or lot number were not provided.	
	Metric 3: Test Substance Purity	High	Synthetic grade, purity 99%	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	N/A	Negative controls are not required for acute toxicity studies	
	Metric 5: Positive Controls	N/A	Not required for study type	
	Metric 6: Randomized Allocation of Animals	Low	Allocation of animals was not specified	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Medium	There are limited details on preparation and storage of the test substance, but these are unlikely to have a substantial impact on results.	
	Metric 8: Consistency of Exposure Administration	Low	Details of exposure administration were not reported (cited to other publications). These publications were not available for review. Injection volumes were not reported.	
	Metric 9: Reporting of Doses/Concentrations	Low	Doses were not reported. It is unclear if the LD50 value reported was one of the dose groups, or if it was a calculated LD50 value. However, the main purpose of the acute study was to determine the LD50 value, and that is provided.	
	Metric 10: Exposure Frequency and Duration	High	Single dose acute toxicity study	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	N/A	Not applicable to an acute toxicity study	
	Metric 12: Exposure Route and Method	High	Animals were dosed i.p., this is a PECO relevant route of exposure	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	Medium	Animal species, strain, sex, age, and source were provided. Initial body weights were not reported.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Low	All animal husbandry conditions were not reported. It was only specified that animals were housed 5/cage with free access to food and water; no other details were provided. This is unlikely to have a major impact on an acute study.	
	Metric 15: Number of Animals per Group	Low	It was reported that 25-30 mice were used, but it is unclear if these mice were split between chemicals tested, or if that was the number per group.	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	Low	The outcome assessment methodology was not reported (e.g., how long animals were monitored for mortality post-dosing).	
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Study Citation:	Mohtashamipur, E., Triebel, R., Straeter, H., Norpoth, K. (1987). The bone marrow clastogenicity of eight halogenated benzenes in male NMRI mice. Mutagenesis 2(2):111-113.
Health Outcome(s):	Mortality
Reported Health Effect(s):	Mortality: LD50 values
Duration:	Acute (less than or equal to 24 hr) 1 or 2 doses within 24 hrs
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	201693

Domain		Metric	Rating	Comments
	Metric 17:	Consistency of Outcome Assessment	Low	Details regarding the execution of the study protocol for outcome assessment (e.g., timing of assessment across groups) were not reported, and these deficiencies are likely to have a substantial impact on results.
	Metric 18:	Sampling Adequacy	Low	Details regarding sampling of outcomes were not reported
	Metric 19:	Blinding of Assessors	N/A	not necessary for this outcome of interest
	Metric 20:	Negative Control Response	N/A	Not applicable for the 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 (or identified only minor differences) among study groups in the above listed confounding factors.
	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	not necessary for the outcome of interest
	Metric 24:	Reporting of Data	Medium	LD50 values were reported, but it is not specified how many mortalities were observed.

Additional Comments: The form 3's for the mortality outcome are identical for all three isomers.

Overall Quality Determination

Medium

Study Citation:	Sipes, I. G., Gunawardhana, L., Jolley, C. S., Gupta, P., Earnest, D. L., Lantz, R. C. (1995). Correlation of the time course of liver injury and infiltration of inflammatory cells into rat liver following the administration of the potent hepatotoxicant 1,2-dichlorobenzene. CELLS OF THE HEPATIC SINUSOID 5:81-82.			
Health Outcome(s):	Hepatic/Liver			
Reported Health Effect(s):	Hepatic/Liver: Changes to liver histopathology, specifically, necrosis in the centrilobular region at 24 h after treatment, increased ICAM-1 staining of endothelial cells, and an increase in plasma alanine transaminase activity.			
Duration:	Acute (less than or equal to 24 hr) Acute hepatotoxicity			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	5344757			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	The test substance was identified as 1,2, but the CASRN was not reported. However, this is unlikely to impact the overall results.	
	Metric 2: Test Substance Source	Low	The source of the test substance was not reported and the test identity was not analytically verified by the laboratory.	
	Metric 3: Test Substance Purity	Low	Purity and grade of the test substance were not reported.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	The authors stated that they used corn oil as the negative control. This is an appropriate negative control for this study.	
	Metric 5: Positive Controls	N/A	A positive control is not needed for this experiment	
	Metric 6: Randomized Allocation of Animals	Low	The study did not report how the animals were allocated into control versus treatment groups.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Low	Details for the preparation of the test substance for i.p injection were not reported, and it may impact the results. 1,2-Dichlorobenzene is volatile, and this may affect its administration. There were no details provided about the storage of the test substance. However, this is an acute study so storage details may not be as important.	
	Metric 8: Consistency of Exposure Administration	Medium	Details of the exposure were reported and they were administered consistently as one single dose. However, the amount of corn oil administered was not reported nor was the mL/kg of 1,2-dichlorobenzene.	
	Metric 9: Reporting of Doses/Concentrations	High	The dose of 1,2-dichlorobenzene used was reported without ambiguity.	
	Metric 10: Exposure Frequency and Duration	High	The exposure frequency and duration was appropriate for a single dose acute toxicity study.	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	The chosen dose appears to be based on prior studies that is cited by the authors.	
	Metric 12: Exposure Route and Method	Low	The route of administration for the negative control was not reported. It is unclear if it was the same route as the test substance. However, i.p injection is suitable method for a volatile compound, such as 1,2-dichlorobenzene.	
Domain 4: Test Animals				
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Study Citation:	Sipes, I. G., Gunawardhana, L., Jolley, C. S., Gupta, P., Earnest, D. L., Lantz, R. C. (1995). Correlation of the time course of liver injury and infiltration of inflammatory cells into rat liver following the administration of the potent hepatotoxicant 1,2-dichlorobenzene. CELLS OF THE HEPATIC SINUSOID 5:81-82.			
Health Outcome(s):	Hepatic/Liver			
Reported Health Effect(s):	Hepatic/Liver: Changes to liver histopathology, specifically, necrosis in the centrilobular region at 24 h after treatment, increased ICAM-1 staining of endothelial cells, and an increase in plasma alanine transaminase activity.			
Duration:	Acute (less than or equal to 24 hr) Acute hepatotoxicity			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	5344757			
Domain	Metric	Rating	Comments	
	Metric 13: Test Animal Characteristics	Medium	The starting body weight of the animals was not reported, but this is unlikely to impact the results since it was an acute study.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were not reported for the Fischer rats with no mention of temperature, light/dark cycle, humidity, diet, or water availability in the Materials and Methods. There is no way to evaluate the adequacy of the conditions.	
	Metric 15: Number of Animals per Group	Low	The number of animals per study group was not reported.	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	High	Changes to the histopathology and in serum chemistry were reported as outcomes, which is appropriate for this type of study.	
	Metric 17: Consistency of Outcome Assessment	High	It is stated in the abstract that the negative control (corn oil), and the treatment group were assessed at the same time points.	
	Metric 18: Sampling Adequacy	High	The sampling was adequate to detect the intended changes for the purpose of this study.	
	Metric 19: Blinding of Assessors	N/A	Blinding of assessors is not necessary	
	Metric 20: Negative Control Response	High	A representative image was shown for the vehicle in the periportal region, and although there were no statistics reported for the negative control, from the the reported number for alanine transaminase activity, it appeared adequate.	
Domain 6: Confounding / Variable Control				
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	The authors did not report all information to determine confounding, but this is an acute study with administration via intraperitoneal injection.	
	Metric 22: Health Outcomes Unrelated to Exposure	Medium	There was no information to either support or dismiss the suggestion that there were differences among groups due to infection. However, this is an acute study, and liver toxicity was still observed.	
	Metric 23: Data Presentation and Analysis	Uninformative	Data enabling an independent statistical analysis were not provided. Although, a statistical method was described for ED2 quantification, the method used for the plasma alanine transferase activity assay was not described. Also, the reviewer could not determine the numbers themselves because individual data points were not reported nor where the number of animals in each group.	
	Metric 24: Reporting of Data	Low	The number of animals that developed necrosis of the liver was not reported. An increase in ALT activity for treated rats versus control was reported as a marker of liver necrosis and numbers were reported for control rats versus treated. However, it was unclear if these numbers were presented as an average, and there was no standard deviation or standard error reported. The number of animals in each treatment group or control group was also not provided.For the mechanistic studies, the result from the staining for ED1, ICAM-1, and HIS48 were not reported.	

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Study Citation:	Sipes, I. G., Gunawardhana, L., Jolley, C. S., Gupta, P., Earnest, D. L., Lantz, R. C. (1995). Correlation of the time course of liver injury and infiltration of inflammatory cells into rat liver following the administration of the potent hepatotoxicant 1,2-dichlorobenzene. CELLS OF THE HEPATIC SINUSOID 5:81-82.		
Health Outcome(s):	Hepatic/Liver		
Reported Health Effect(s):	Hepatic/Liver: Changes to liver histopathology, specifically, necrosis in the centrilobular region at 24 h after treatment, increased ICAM-1 staining of endothelial cells, and an increase in plasma alanine transaminase activity.		
Duration:	Acute (less than or equal to 24 hr) Acute hepatotoxicity		
Chemical:	o-Dichlorobenzene- Parent compound		
HERO ID:	5344757		
Domain	Metric	Rating	Comments
Additional Comments:	Major limitations for this paper are that the number of animals per study group and the route of administration for the negative control were not reported . Also, the number of animals that developed liver necrosis was not reported. The other marker of liver injury used was an increase in alanine transaminase (ALT) activity, but the details of the results was not adequately reported to draw an accurate conclusion. The standard deviation or standard error and the number of rats in each group were not reported with the activity measurements.		

Overall Quality Determination**Uninformative**

Study Citation:	Valentovic, M. A., Ball, J. G., Anestis, D., Madan, E. (1993). Acute hepatic and renal toxicity of dichlorobenzene isomers in Fischer 344 rats. Journal of Applied Toxicology 13(1):7-Jan.			
Health Outcome(s):	Renal/Kidney; Hepatic/Liver;			
Reported Health Effect(s):	Renal/Kidney: kidney weight, histological examination (morphological changes of kidney), BUN levels, renal cortical slice accumulation of PAH, PAH in the presence of lactate, and TEA; Hepatic/Liver: liver weight, plasma ALT/GPT, histological changes (necrosis) of liver;			
Duration:	Acute (less than or equal to 24 hr) 24h			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	4912250			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
Metric 1:	Test Substance Identity	High	All Outcomes: The test substance was identified as 1,2-DCB.CASRN was not listed.	
Metric 2:	Test Substance Source	High	All Outcomes: The test substance was purchased from Aldrich Chemical Company (Milwaukee, WI).	
Metric 3:	Test Substance Purity	Medium	All Outcomes: 1,2-DCB purity is listed at 99%.	
Domain 2: Test Design				
Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Authors indicate that an appropriate negative control (vehicle = corn oil) was used and the control group was pair-fed to eliminate food intake variability.	
Metric 5:	Positive Controls	N/A	All Outcomes: Positive control not listed.	
Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: Rats were reported to be randomly divided into treated and control groups.	
Domain 3: Exposure Characterization				
Metric 7:	Preparation and Storage of Test Substance	Medium	All Outcomes: Authors do not provide details on how the test substance was prepared or stored. Single-dose administration per experiment.	
Metric 8:	Consistency of Exposure Administration	High	All Outcomes: Time of day injection administered and i.p. injection volume was consistent across groups.	
Metric 9:	Reporting of Doses/Concentrations	High	All Outcomes: Doses are reported without ambiguity.	
Metric 10:	Exposure Frequency and Duration	High	All Outcomes: A single IP dose was administered.	
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	Renal/Kidney: In terms of daily urine output, kidney weight, BUN levels for 1,2-DCB, there are no significant results reported, so there should be more doses added for a satisfactory LOAEL. The PAH and TEA accumulation analysis are missing more dosing levels for a full range of exposure groups. Histological/morphological analysis of kidney only shows control and results after 24h. Urine output over time, food consumption over time, organ/body weight over time, and PAH and TEA accumulation over time show that more duration points would prove to be valuable for a solid NOAEL and LOAEL.; Hepatic/Liver: In terms of liver weight for 1,2-DCB, there are no significant results reported, so there should be more doses added for a satisfactory LOAEL. Alternatively, ALT/GPT activities were significant at both doses, leaving a NOAEL to be desired. All other endpoints (i.e food consumption and organ/body weight over time, histological changes (necrosis) of liver) are missing more dosing levels for a full range of exposure groups.	
Metric 12:	Exposure Route and Method	High	All Outcomes: I.p. injection is a suitable administration method for volatile substances.	

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Study Citation:	Valentovic, M. A., Ball, J. G., Anestis, D., Madan, E. (1993). Acute hepatic and renal toxicity of dichlorobenzene isomers in Fischer 344 rats. Journal of Applied Toxicology 13(1):7-Jan.			
Health Outcome(s):	Renal/Kidney; Hepatic/Liver;			
Reported Health Effect(s):	Renal/Kidney: kidney weight, histological examination (morphological changes of kidney), BUN levels, renal cortical slice accumulation of PAH, PAH in the presence of lactate, and TEA; Hepatic/Liver: liver weight, plasma ALT/GPT, histological changes (necrosis) of liver;			
Duration:	Acute (less than or equal to 24 hr) 24h			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	4912250			
Domain	Metric	Rating	Comments	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	Medium	All Outcomes: Test animal species, strain, weight, and sex were reported; animals derived from in-laboratory colony. Age not reported, but is unlikely to have a substantial impact on results.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: Rats were individually placed in stainless-steel metabolism racks, permitted same food and water ad libitum during the initial 24h acclimation period and after hour 4 from initial exposure period. Humidity not reported, but unlikely to affect results.	
	Metric 15: Number of Animals per Group	Medium	All Outcomes: Each group contained 4 rats.	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	High	Renal/Kidney: Daily urine output, BUN levels, kidney weight, renal cortical slice accumulation of PAH and TEA, histological/morphological examination, outputted for 1,2-DCB listed.; Hepatic/Liver: Liver weight, plasma ALT/GPT over dose and time, histological changes (necrosis) of liver, food consumption and organ/body weight over time, outputted for 1,2-DCB listed.	
	Metric 17: Consistency of Outcome Assessment	High	All Outcomes: Assessment protocol was reported and there is no indication of differences in outcome evaluation across treatment 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	Low	All Outcomes: Blinding not needed for most tests, however no blinded was mentioned to be used for histological examination.	
	Metric 20: Negative Control Response	High	All Outcomes: The biological responses of the negative control groups were adequate.	
Domain 6: Confounding / Variable Control				
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	All Outcomes: Reported information did not identify differences among the groups.	
	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.	
	Metric 23: Data Presentation and Analysis	High	All Outcomes: Used ANOVA and Dunnett’s test at 95% confidence interval for differences within groups. ANOVA and Newman-Keuls test for differences between treated and pair-fed control groups. Values reported as means $\pm$ SE.	
	Metric 24: Reporting of Data	High	All Outcomes: Data for all exposure groups were adequately reported.	
Additional Comments:	None			

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Study Citation:	Valentovic, M. A., Ball, J. G., Anestis, D., Madan, E. (1993). Acute hepatic and renal toxicity of dichlorobenzene isomers in Fischer 344 rats. Journal of Applied Toxicology 13(1):7-Jan.
Health Outcome(s):	Renal/Kidney; Hepatic/Liver;
Reported Health Effect(s):	Renal/Kidney: kidney weight, histological examination (morphological changes of kidney), BUN levels, renal cortical slice accumulation of PAH, PAH in the presence of lactate, and TEA; Hepatic/Liver: liver weight, plasma ALT/GPT, histological changes (necrosis) of liver;
Duration:	Acute (less than or equal to 24 hr) 24h
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	4912250

Domain	Metric	Rating	Comments

Overall Quality Determination**Medium**

Study Citation:	Valentovic, M. A., Ball, J. G., Anestis, D., Madan, E. (1993). Modification of P450 activity and its effect on 1,2-dichlorobenzene toxicity in Fischer 344 rats. Toxicology 79(3):169-180.
Health Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Nutritional/Metabolic: Body weight decreased after treatment; food consumption and water intake
Duration:	Acute (less than or equal to 24 hr) Rats treated with a single injection of 1,2-DCB
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	5248928

Domain	Metric	Rating	Comments
Domain 1: Test Substance			
Metric 1:	Test Substance Identity	High	The test substance was identified as 1,2-dichlorobenzene. No CASRN or structure were provided.
Metric 2:	Test Substance Source	Low	The source of the test substance was not reported, and the identity was not analytically verified by the performing laboratory.
Metric 3:	Test Substance Purity	Low	Purity and grade of the test substance were not reported.
Domain 2: Test Design			
Metric 4:	Negative and Vehicle Controls	High	Appropriate negative controls were included.
Metric 5:	Positive Controls	N/A	A positive control is not needed for this study.
Metric 6:	Randomized Allocation of Animals	Medium	The study reported that the animals were randomly distributed into study groups.
Domain 3: Exposure Characterization			
Metric 7:	Preparation and Storage of Test Substance	Low	Information on the preparation of test substances or storage conditions were not reported.
Metric 8:	Consistency of Exposure Administration	Low	The amount of corn oil used for the control was not reported. It is not possible to compare amounts of vehicle to amount of test substance administered.
Metric 9:	Reporting of Doses/Concentrations	High	Doses were reported as vehicle (corn oil), 2 or 3 mmol/kg of 1,2-DCB (2 ml/kg).
Metric 10:	Exposure Frequency and Duration	High	The exposure frequency and duration were appropriate for an acute study.
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	Two dose groups were included (2 and 3 mmol/kg 1,2-DCB). Study authors did not justify dose selection. Effects on rat body weight, and evidence of liver and kidney toxicity were observed at both dose levels, therefore the lowest dose was not low enough to identify a NOAEL.
Metric 12:	Exposure Route and Method	Low	Although the authors reported that the rats were injected with 2 mmol/kg or 3 mmol/kg 1,2 DCA or corn oil as the control, the details of the site of injection and preparation of the solutions for injection were not reported. It is not possible to determine if the route of exposure was suited to the test substance.
Domain 4: Test Animals			
Metric 13:	Test Animal Characteristics	Medium	Male Fischer 344 rats were used. Starting bodyweight and age was not reported.
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Rats were maintained at a temperature of 21-23C, on a 12 hour light-dark cycle and were given free access to food and water. Humidity was not reported.

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Study Citation:	Valentovic, M. A., Ball, J. G., Anestis, D., Madan, E. (1993). Modification of P450 activity and its effect on 1,2-dichlorobenzene toxicity in Fischer 344 rats. Toxicology 79(3):169-180.
Health Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Nutritional/Metabolic: Body weight decreased after treatment; food consumption and water intake
Duration:	Acute (less than or equal to 24 hr) Rats treated with a single injection of 1,2-DCB
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	5248928

Domain	Metric	Rating	Comments
	Metric 15: Number of Animals per Group	Low	The numbers per group varied and the actual numbers that were in each group were not reported. The authors reported that each group had a minimum of four animals, but actual numbers were not reported and apparently varied.
Domain 5: Outcome Assessment			
	Metric 16: Outcome Assessment Methodology	High	The outcome assessment methodology addressed the intended outcome(s) of interest. Animals were weighed 24-hours after exposure.
	Metric 17: Consistency of Outcome Assessment	High	Details of the outcome assessment protocol were reported and outcomes were assessed consistently across study groups. Study authors state that "Food consumption, water intake, body weight, and urine output were measured for 24 h after 1,2-DCB or vehicle injection."
	Metric 18: Sampling Adequacy	High	Reported information indicates the study used adequate sampling for the outcome of interest.
	Metric 19: Blinding of Assessors	N/A	Blinding of assessor is not needed for this study
	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	Low	Study authors report that food and water consumption were measured, however, study authors do not state if there were any differences between treatment groups.
	Metric 22: Health Outcomes Unrelated to Exposure	High	This was an acute study. Although there was no reporting of infections or any other health outcome unrelated to exposure, there were no deaths in the control or other signs of sickness. The negative controls appeared to be healthy based on body weight and blood chemistry at the time of sacrifice.
	Metric 23: Data Presentation and Analysis	High	Statistical methods were described and were adequate for the dataset.
	Metric 24: Reporting of Data	Medium	Body weight was reported as mean +/- SEM with an n> 4/group. Food consumption and water intake were measured, however, results were not presented quantitatively, or described qualitatively.

Additional Comments: The major limitations of this study is the lack of reporting of exposure details. Although the authors reported that the rats were injected with 2 mmol/kg or 3 mmol/kg 1,2 DCD or corn oil as a control, the details of the site of injection and preparation of the solutions were not reported. The numbers per treatment group varied (reported as at least 4 animals/group) and the actual numbers that were in each group were not reported. The study does contain mechanistic evidence for the mechanism of liver and renal toxicity produced in the rats by 1,2 DCB exposure. After pre-treatment with inducers of cytochrome P450 the renal toxicity and hepatic toxicity of 1,2 DCA was enhanced. The cytochrome P450 inhibitor pretreatment decreased renal toxicity after treatment.

Overall Quality Determination

Medium

Study Citation:	Valentovic, M. A., Ball, J. G., Anestis, D., Madan, E. (1993). Modification of P450 activity and its effect on 1,2-dichlorobenzene toxicity in Fischer 344 rats. Toxicology 79(3):169-180.			
Health Outcome(s):	Renal/Kidney			
Reported Health Effect(s):	Renal/Kidney: Increased alanine amino-transferase activity in a dose-dependent manner; decreased renal cortical slice accumulation of p-aminohippurate (PAH) 24 h after injection of highest dose; increase in blood urea nitrogen in a dose-dependent manner; increase in urine output after injection of highest dose; kidney weight was measured but no change was reported between control and treatment without pretreating with a Cytochrome P450 enzyme inducer			
Duration:	Acute (less than or equal to 24 hr) Rats treated with a single injection of 1,2-DCB			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	5248928			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	The test substance was identified as 1,2-dichlorobenzene. No CASRN or structure were provided.	
	Metric 2: Test Substance Source	Low	The source of the test substance was not reported, and the identity was not analytically verified by the performing laboratory.	
	Metric 3: Test Substance Purity	Low	Purity and grade of the test substance were not reported.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	Appropriate negative controls were included.	
	Metric 5: Positive Controls	N/A	A positive control is not needed for this study.	
	Metric 6: Randomized Allocation of Animals	Medium	The study reported that the animals were randomly distributed into study groups.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Low	Information on the preparation of test substances or storage conditions were not reported.	
	Metric 8: Consistency of Exposure Administration	Low	The amount of corn oil used for the control was not reported. It is not possible to compare amounts of vehicle to amount of test substance administered.	
	Metric 9: Reporting of Doses/Concentrations	High	Doses were reported as vehicle (corn oil), 2 or 3 mmol/kg of 1,2-DCB (2 ml/kg).	
	Metric 10: Exposure Frequency and Duration	High	The exposure frequency and duration were appropriate for an acute study.	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	Medium	Two dose groups were included (2 and 3 mmol/kg 1,2-DCB). Study authors did not justify dose selection. Effects on rat body weight, and evidence of liver and kidney toxicity were observed at both dose levels, therefore the lowest dose was not low enough to identify a NOAEL.	
	Metric 12: Exposure Route and Method	Low	Although the authors reported that the rats were injected with 2 mmol/kg or 3 mmol/kg 1,2 DCA or corn oil as the control, the details of the site of injection and preparation of the solutions for injection were not reported. It is not possible to determine if the route of exposure was suited to the test substance.	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	Medium	Male Fischer 344 rats were used. Starting bodyweight and age was not reported.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Medium	Rats were maintained at a temperature of 21-23C, on a 12 hour light-dark cycle and were given free access to food and water. Humidity was not reported.	
	Metric 15: Number of Animals per Group	Low	The numbers per group varied and the actual numbers that were in each group were not reported. The authors reported that each group had a minimum of four animals, but actual numbers were not reported and apparently varied.	
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Study Citation:	Valentovic, M. A., Ball, J. G., Anestis, D., Madan, E. (1993). Modification of P450 activity and its effect on 1,2-dichlorobenzene toxicity in Fischer 344 rats. Toxicology 79(3):169-180.			
Health Outcome(s):	Renal/Kidney			
Reported Health Effect(s):	Renal/Kidney: Increased alanine amino-transferase activity in a dose-dependent manner; decreased renal cortical slice accumulation of p-aminohippurate (PAH) 24 h after injection of highest dose; increase in blood urea nitrogen in a dose-dependent manner; increase in urine output after injection of highest dose; kidney weight was measured but no change was reported between control and treatment without pretreating with a Cytochrome P450 enzyme inducer			
Duration:	Acute (less than or equal to 24 hr) Rats treated with a single injection of 1,2-DCB			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	5248928			
Domain	Metric	Rating	Comments	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	High	The outcome assessment methodology addressed the intended outcome(s) of interest.	
	Metric 17: Consistency of Outcome Assessment	Low	Details regarding the execution of the study protocol for outcome assessment were limited.	
	Metric 18: Sampling Adequacy	High	Reported information indicates the study used adequate sampling for the outcome of interest.	
	Metric 19: Blinding of Assessors	N/A	Blinding of assessor is not needed for this study	
	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	Low	Study authors report that food and water consumption were measured, however, study authors do not state if there were any differences between treatment groups.	
	Metric 22: Health Outcomes Unrelated to Exposure	High	This was an acute study. Although there was no reporting of infections or any other health outcome unrelated to exposure, there were no deaths in the control or other signs of sickness. The negative controls appeared to be healthy based on body weight and blood chemistry at the time of sacrifice.	
	Metric 23: Data Presentation and Analysis	High	Statistical methods were described and were adequate for the dataset.	
	Metric 24: Reporting of Data	High	Relative kidney weight, urine output, BUN, was reported as mean +/- SEM.	
Additional Comments:	The major limitations of this study is the lack of reporting of exposure details. Although the authors reported that the rats were injected with 2 mmol/kg or 3 mmol/kg 1,2 DCA or corn oil as a control, the details of the site of injection and preparation of the solutions were not reported. The numbers per treatment group varied, and the actual numbers that were in each group were not reported. The study does contain mechanistic evidence for the mechanism of liver and renal toxicity produced in the rats by 1,2 DCA exposure. After pre-treatment with inducers of cytochrome P450 the renal toxicity and hepatic toxicity of 1,2 DCA was enhanced. The cytochrome P450 inhibitor pretreatment decreased renal toxicity after treatment.			

Overall Quality Determination**Medium**

Study Citation:	Valentovic, M. A., Ball, J. G., Anestis, D., Madan, E. (1993). Modification of P450 activity and its effect on 1,2-dichlorobenzene toxicity in Fischer 344 rats. Toxicology 79(3):169-180.			
Health Outcome(s):	Hepatic/Liver			
Reported Health Effect(s):	Hepatic/Liver: An increase in alanine-amino transferase activity in a dose-dependent manner; changes to liver morphology; liver weight was measured but no change was reported between control and treatment groups without pretreating with a Cytochrome P450 enzyme inducer			
Duration:	Acute (less than or equal to 24 hr) Rats treated with a single injection of 1,2-DCB			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	5248928			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
Metric 1:	Test Substance Identity	High	The test substance was identified as 1,2-dichlorobenzene. No CASRN or structure were provided.	
Metric 2:	Test Substance Source	Low	The source of the test substance was not reported, and the identity was not analytically verified by the performing laboratory.	
Metric 3:	Test Substance Purity	Low	Purity and grade of the test substance were not reported.	
Domain 2: Test Design				
Metric 4:	Negative and Vehicle Controls	High	Appropriate negative controls were included.	
Metric 5:	Positive Controls	N/A	A positive control is not needed for this study.	
Metric 6:	Randomized Allocation of Animals	Medium	The study reported that the animals were randomly distributed into study groups.	
Domain 3: Exposure Characterization				
Metric 7:	Preparation and Storage of Test Substance	Low	Information on the preparation of test substances or storage conditions were not reported.	
Metric 8:	Consistency of Exposure Administration	Low	The amount of corn oil used for the control was not reported. It is not possible to compare amounts of vehicle to amount of test substance administered.	
Metric 9:	Reporting of Doses/Concentrations	High	Doses were reported as vehicle (corn oil), 2 or 3 mmol/kg of 1,2-DCB (2 ml/kg).	
Metric 10:	Exposure Frequency and Duration	High	The exposure frequency and duration were appropriate for an acute study.	
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	Two dose groups were included (2 and 3 mmol/kg 1,2-DCB). Study authors did not justify dose selection. Effects on rat body weight, and evidence of liver and kidney toxicity were observed at both dose levels, therefore the lowest dose was not low enough to identify a NOAEL.	
Metric 12:	Exposure Route and Method	Uninformative	Although the authors reported that the rats were injected with 2 mmol/kg or 3 mmol/kg 1,2 DCA or corn oil as the control, the details of the site of injection and preparation of the solutions for injection were not reported. It is not possible to determine if the route of exposure was suited to the test substance since liver metabolism and toxicity were evaluated.	
Domain 4: Test Animals				
Metric 13:	Test Animal Characteristics	Medium	Male Fischer 344 rats were used. Starting bodyweight and age was not reported.	
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Rats were maintained at a temperature of 21-23C, on a 12 hour light-dark cycle and were given free access to food and water. Humidity was not reported.	
Metric 15:	Number of Animals per Group	Low	The numbers per group varied and the actual numbers that were in each group were not reported. The authors reported that each group had a minimum of four animals, but actual numbers were not reported and apparently varied.	

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Study Citation:	Valentovic, M. A., Ball, J. G., Anestis, D., Madan, E. (1993). Modification of P450 activity and its effect on 1,2-dichlorobenzene toxicity in Fischer 344 rats. Toxicology 79(3):169-180.			
Health Outcome(s):	Hepatic/Liver			
Reported Health Effect(s):	Hepatic/Liver: An increase in alanine-amino transferase activity in a dose-dependent manner; changes to liver morphology; liver weight was measured but no change was reported between control and treatment groups without pretreating with a Cytochrome P450 enzyme inducer			
Duration:	Acute (less than or equal to 24 hr) Rats treated with a single injection of 1,2-DCB			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	5248928			
Domain	Metric	Rating	Comments	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	High	The outcome assessment methodology addressed the intended outcome(s) of interest.	
	Metric 17: Consistency of Outcome Assessment	Low	Details regarding the execution of the study protocol for outcome assessment were not reported.	
	Metric 18: Sampling Adequacy	High	Reported information indicates the study used adequate sampling for the outcome of interest.	
	Metric 19: Blinding of Assessors	N/A	Blinding of assessor is not needed for this study	
	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	Low	Study authors report that food and water consumption were measured, however, study authors do not state if there were any differences between treatment groups.	
	Metric 22: Health Outcomes Unrelated to Exposure	High	This was an acute study. Although there was no reporting of infections or any other health outcome unrelated to exposure, there were no deaths in the control or other signs of sickness. The negative controls appeared to be healthy based on body weight and blood chemistry at the time of sacrifice.	
	Metric 23: Data Presentation and Analysis	High	Statistical methods were described and were adequate for the dataset.	
	Metric 24: Reporting of Data	High	Data for exposure-related findings were presented for all outcomes by exposure group.	
Additional Comments:	The major limitations of this study is the lack of reporting of exposure details. Although the authors reported that the rats were injected with 2 mmol/kg or 3 mmol/kg 1,2 DCA or corn oil as a control, the details of the site of injection and preparation of the solutions were not reported. The numbers per treatment group varied, and the actual numbers that were in each group were not reported. The study does contain mechanistic evidence for the mechanism of liver and renal toxicity produced in the rats by 1,2 DCA exposure. After pre-treatment with inducers of cytochrome P450 the renal toxicity and hepatic toxicity of 1,2 DCA was enhanced. The cytochrome P450 inhibitor pretreatment decreased renal toxicity after treatment.			

Overall Quality Determination**Uninformative**

Study Citation:	Yang, K. H., Peterson, R. E., Fujimoto, J. M. (1979). Increased bile duct-pancreatic fluid flow in benzene and halogenated benzene-treated rats. Toxicology and Applied Pharmacology 47(3):505-514.			
Health Outcome(s):	Hepatic/Liver			
Reported Health Effect(s):	Hepatic/Liver: Bile flow and SGPT (ALT) activity			
Duration:	Acute (less than or equal to 24 hr) Single i.p injection			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	1994030			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
Metric 1:	Test Substance Identity	High	Test substance was identified as 1,4-dichlorobenzene.	
Metric 2:	Test Substance Source	Low	The source of the test substance was not reported. The batch/lot number were not reported.	
Metric 3:	Test Substance Purity	Medium	Test substance was reported to be reagent grade, no other information on purity is provided.	
Domain 2: Test Design				
Metric 4:	Negative and Vehicle Controls	High	A concurrent negative control was run (vehicle).	
Metric 5:	Positive Controls	N/A	A positive control was not required for this study type.	
Metric 6:	Randomized Allocation of Animals	Low	Study does not state how animals were allocated.	
Domain 3: Exposure Characterization				
Metric 7:	Preparation and Storage of Test Substance	Medium	Test substance preparation and storage were not adequately described, but the details that are unlikely to have a substantial impact on results since this is a single dose study.	
Metric 8:	Consistency of Exposure	High	Test substance was delivered consistently across study groups.	
Metric 9:	Administration Reporting of Doses/Concentrations	Medium	Only nominal concentrations were reported.	
Metric 10:	Exposure Frequency and Duration	High	The exposure frequency and duration were appropriate.	
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Low	Only one dose was tested, it would be helpful to have a range of responses.	
Metric 12:	Exposure Route and Method	High	The exposure route and method were appropriate.	
Domain 4: Test Animals				
Metric 13:	Test Animal Characteristics	Medium	Age and source of animals were not reported.	
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were not adequately reported. The only information provided is that after treatment rats were fasted with water available ad libitum.	
Metric 15:	Number of Animals per Group	Low	The number of animals/group was not reported.	
Domain 5: Outcome Assessment				
Metric 16:	Outcome Assessment Methodology	High	Outcome assessment methodology was appropriate for intended outcomes of interest.	
Metric 17:	Consistency of Outcome Assessment	High	Outcomes were assessed consistently across study groups.	
Metric 18:	Sampling Adequacy	High	Table 2 legend reports n= four or more animals.	

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Study Citation:	Yang, K. H., Peterson, R. E., Fujimoto, J. M. (1979). Increased bile duct-pancreatic fluid flow in benzene and halogenated benzene-treated rats. Toxicology and Applied Pharmacology 47(3):505-514.			
Health Outcome(s):	Hepatic/Liver			
Reported Health Effect(s):	Hepatic/Liver: Bile flow and SGPT (ALT) activity			
Duration:	Acute (less than or equal to 24 hr) Single i.p injection			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	1994030			
Domain	Metric		Rating	Comments
	Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary.
	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	Although the study did not report all information to determine confounding, reported information did not identify 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 in animal attrition or health outcomes unrelated to exposure.
	Metric 23:	Data Presentation and Analysis	High	Statistical analysis was appropriate.
	Metric 24:	Reporting of Data	High	Hepatic outcomes were fully reported.
Additional Comments: None				
Overall Quality Determination			High	

Study Citation:	Yang, K. H., Peterson, R. E., Fujimoto, J. M. (1979). Increased bile duct-pancreatic fluid flow in benzene and halogenated benzene-treated rats. Toxicology and Applied Pharmacology 47(3):505-514.			
Health Outcome(s):	Gastrointestinal			
Reported Health Effect(s):	Gastrointestinal: Bile duct-pancreatic fluid (BDPF) flow, BDPF protein concentration and BDPF chloride concentration			
Duration:	Acute (less than or equal to 24 hr) Single i.p injection			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	1994030			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	Test substance was identified as 1,4-dichlorobenzene.	
	Metric 2: Test Substance Source	Low	The source of the test substance was not reported. The batch/lot number were not reported.	
	Metric 3: Test Substance Purity	Medium	Test substance was reported to be reagent grade, no other information on purity is provided.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	A concurrent negative control was run (vehicle).	
	Metric 5: Positive Controls	N/A	A positive control was not required for this study type.	
	Metric 6: Randomized Allocation of Animals	Low	Study does not state how animals were allocated.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Medium	Test substance preparation and storage were not adequately described, but the details that are unlikely to have a substantial impact on results since this is a single dose study.	
	Metric 8: Consistency of Exposure Administration	High	Test substance was delivered consistently across study groups.	
	Metric 9: Reporting of Doses/Concentrations	Medium	Only nominal concentrations were reported.	
	Metric 10: Exposure Frequency and Duration	High	The exposure frequency and duration were appropriate.	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	Low	Only one dose was tested, it would be helpful to have a range of responses.	
	Metric 12: Exposure Route and Method	High	The exposure route and method were appropriate.	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	Medium	Age and source of animals were not reported.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were not adequately reported. The only information provided is that after treatment rats were fasted with water available ad libitum.	
	Metric 15: Number of Animals per Group	Low	The number of animals/group was not reported.	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	High	Outcome assessment methodology was appropriate for intended outcomes of interest.	
	Metric 17: Consistency of Outcome Assessment	High	Outcomes were assessed consistently across study groups.	
	Metric 18: Sampling Adequacy	High	Table 2 legend reports n= four or more animals.	
	Metric 19: Blinding of Assessors	N/A	Blinding was not necessary.	
	Metric 20: Negative Control Response	High	The negative control response was appropriate.	

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Study Citation:	Yang, K. H., Peterson, R. E., Fujimoto, J. M. (1979). Increased bile duct-pancreatic fluid flow in benzene and halogenated benzene-treated rats. Toxicology and Applied Pharmacology 47(3):505-514.
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	Gastrointestinal: Bile duct-pancreatic fluid (BDPF) flow, BDPF protein concentration and BDPF chloride concentration
Duration:	Acute (less than or equal to 24 hr) Single i.p injection
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	1994030

Domain	Metric	Rating	Comments
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 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	Statistical analysis was appropriate.
	Metric 24: Reporting of Data	Medium	Most data were reported (sodium and potassium concentration in BDPF were not reported).

Additional Comments: None

Overall Quality Determination**High**

Study Citation:	Ariyoshi, T., Ideguchi, K., Iwasaki, K., Arakaki, M. (1975). Relationship between chemical structure and activity. II. Influences of isomers in dichlorobenzene, trichlorobenzene, and tetrachlorobenzene on the activities of drug-metabolizing enzymes. Chemical and Pharmaceutical Bulletin 23(4):824-830.			
Health Outcome(s):	Nutritional/Metabolic			
Reported Health Effect(s):	Nutritional/Metabolic: Body weight			
Duration:	Short-term (>1-30 days) Short term- 3 days			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	4930792			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	Test substance was identified as o-dichlorobenzene.	
	Metric 2: Test Substance Source	High	The source of the test substance was Nakarai Chemicals Co. Ltd., Kyoto, Japan	
	Metric 3: Test Substance Purity	Low	Purity and/or grade of test substance were not reported.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	The negative control group was appropriate (vehicle control).	
	Metric 5: Positive Controls	N/A	Not applicable for this study.	
	Metric 6: Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Low	Minimal details were provided regarding test substance preparation (only that it was suspended in 2% tragacanth gum solution). Storage conditions are not reported. Given the volatility of the test substance, the lack of reporting these details may affect the results.	
	Metric 8: Consistency of Exposure	High	Exposure was consistent across study groups. Gavage volume was reasonable (5ml/kg).	
	Metric 9: Administration	High	The doses studied were reported without ambiguity (0 and 250 mg/kg/day).	
	Metric 10: Reporting of Doses/Concentrations	High	The exposure frequency and duration were reported and appropriate for the study design.	
	Metric 11: Exposure Frequency and Duration	High	The exposure frequency and duration were reported and appropriate for the study design.	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	Medium	Only one concentration was studied which was based on a previous study by the same author (Part I. Ariyoshi et al., Chem Pharm Bull (Tokyo), 23, 817; 1975). The aim of the study was not to establish a dose-response but to compare responses of different isomers/chemicals at the same dose.	
	Metric 12: Exposure Route and Method	High	The exposure route and method were appropriate.	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	Low	The species, strain, sex, age and starting body weight were reported. The source of the animals was not reported.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were not reported; therefore, it cannot be determined whether differences occurred between control and exposed populations.	
	Metric 15: Number of Animals per Group	Medium	The number of animals per study group was not reported in the methods; however, the sample sizes indicate there were at least 6 animals per group, which is appropriate for the outcomes of interest.	
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Study Citation:	Ariyoshi, T., Ideguchi, K., Iwasaki, K., Arakaki, M. (1975). Relationship between chemical structure and activity. II. Influences of isomers in dichlorobenzene, trichlorobenzene, and tetrachlorobenzene on the activities of drug-metabolizing enzymes. Chemical and Pharmaceutical Bulletin 23(4):824-830.
Health Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Nutritional/Metabolic: Body weight
Duration:	Short-term (>1-30 days) Short term- 3 days
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	4930792

Domain	Metric	Rating	Comments
Domain 5: Outcome Assessment			
	Metric 16: Outcome Assessment Methodology	High	The outcome assessment methodology addressed the intended outcomes of interest.
	Metric 17: Consistency of Outcome Assessment	High	Outcomes were assessed consistently across study groups.
	Metric 18: Sampling Adequacy	High	Sampling was adequate (n=6).
	Metric 19: Blinding of Assessors	N/A	Blinding was not necessary for outcomes of interest.
	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	No differences in body weights were seen between the groups. The study did not report any other 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	Statistical analysis was performed but not adequately described.
	Metric 24: Reporting of Data	High	Body weight data were adequately reported.

Additional Comments: None

Overall Quality Determination**High**

Study Citation:	Ariyoshi, T., Ideguchi, K., Iwasaki, K., Arakaki, M. (1975). Relationship between chemical structure and activity. II. Influences of isomers in dichlorobenzene, trichlorobenzene, and tetrachlorobenzene on the activities of drug-metabolizing enzymes. Chemical and Pharmaceutical Bulletin 23(4):824-830.			
Health Outcome(s):	Hepatic/Liver			
Reported Health Effect(s):	Hepatic/Liver: Liver weight, hepatic enzyme content and activities			
Duration:	Short-term (>1-30 days) Short term- 3 days			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	4930792			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	Test substance was identified as o-dichlorobenzene.	
	Metric 2: Test Substance Source	High	The source of the test substance was Nakarai Chemicals Co. Ltd., Kyoto, Japan	
	Metric 3: Test Substance Purity	Low	Purity and/or grade of test substance were not reported.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	The negative control group was appropriate (vehicle control).	
	Metric 5: Positive Controls	N/A	Not applicable for this study.	
	Metric 6: Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Low	Minimal details were provided regarding test substance preparation (only that it was suspended in 2% tragacanth gum solution). Storage conditions are not reported. Given the volatility of the test substance, the lack of reporting these details may affect the results.	
	Metric 8: Consistency of Exposure	High	Exposure was consistent across study groups. Gavage volume was reasonable (5ml/kg).	
	Metric 9: Administration	High	The doses studied were reported without ambiguity (0 and 250 mg/kg/day).	
	Metric 10: Reporting of Doses/Concentrations	High	The exposure frequency and duration were reported and appropriate for the study design.	
	Metric 11: Exposure Frequency and Duration	High	The exposure frequency and duration were reported and appropriate for the study design.	
	Metric 12: Number of Exposure Groups and Dose/Concentration Spacing	Medium	Only one concentration was studied which was based on a previous study by the same author (Part I. Ariyoshi et al., Chem Pharm Bull (Tokyo), 23, 817; 1975). The aim of the study was not to establish a dose-response but to compare responses of different isomers/chemicals at the same dose.	
	Metric 13: Exposure Route and Method	High	The exposure route and method were appropriate.	
Domain 4: Test Animals				
	Metric 14: Test Animal Characteristics	Low	The species, strain, sex, age and starting body weight were reported. The source of the animals was not reported.	
	Metric 15: Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were not reported; therefore, it cannot be determined whether differences occurred between control and exposed populations.	
	Metric 16: Number of Animals per Group	Medium	The number of animals per study group was not reported in the methods; however, the sample sizes indicate there were at least 6 animals per group, which is appropriate for the outcomes of interest.	
Domain 5: Outcome Assessment				

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Study Citation:	Ariyoshi, T., Ideguchi, K., Iwasaki, K., Arakaki, M. (1975). Relationship between chemical structure and activity. II. Influences of isomers in dichlorobenzene, trichlorobenzene, and tetrachlorobenzene on the activities of drug-metabolizing enzymes. Chemical and Pharmaceutical Bulletin 23(4):824-830.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	Hepatic/Liver: Liver weight, hepatic enzyme content and activities
Duration:	Short-term (>1-30 days) Short term- 3 days
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	4930792

Domain	Metric	Rating	Comments
	Metric 16: Outcome Assessment Methodology	High	The outcome assessment methodology addressed the intended outcomes of interest.
	Metric 17: Consistency of Outcome Assessment	Medium	Outcomes were assessed consistently across study groups. Details on assessment of enzyme activities and protein levels were cited in previous papers.
	Metric 18: Sampling Adequacy	High	Sampling was adequate. (n=6 for most outcomes; phospholipid values were mean of 3 groups of 2 rats).
	Metric 19: Blinding of Assessors	N/A	Blinding was not necessary for outcomes of interest.
	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	No differences in body weights were seen between the groups. The study did not report any other 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	Statistical analysis was performed but not adequately described.
	Metric 24: Reporting of Data	Medium	Absolute liver weights were not reported; however, this is unlikely to substantially impact results.

Additional Comments: None

Overall Quality Determination**Medium**

Study Citation:	Brondeau, M. T., Bonnet, P., Guenier, J. P., De, C. J. (1983). Short-term inhalation test for evaluating industrial hepatotoxicants in rats. Toxicology Letters 19(1-2):139-146.			
Health Outcome(s):	Hepatic/Liver (Serum enzyme activity for liver damage biomarkers: SDH, GLDH, GOT, and GPT.)			
Reported Health Effect(s):	Hepatic/Liver (Serum enzyme activity for liver damage biomarkers: SDH, GLDH, GOT, and GPT.): Serum enzyme activities (units per ml (U/ml), or nmol per min per ml) of liver hepatotoxicity biomarkers ALT (GPT), AST (GOT), glutamate dehydrogenase (GLDH) and sorbitol dehydrogenase (SHD).			
Duration:	Short-term (>1-30 days) Short-term- 6 hour for 2 or 4 days			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	200247			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	Test substance was identified in nomenclature as o-dichlorobenzene; no CASRN.	
	Metric 2: Test Substance Source	Low	The source of the test substance was Merck. Batch/lot numbers were not provided.Covers the lack of test substance identity in Metric 1 that did not report CASRN or chemical structure without double counting quality metrics.	
	Metric 3: Test Substance Purity	High	The purity of the test substance was reported as >99.0%.	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	Negative controls were exposed to clean filtered air.	
	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 if/how animals were allocated.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Low	Preparation and storage are adequately described given the volatility of the test substance.	
	Metric 8: Consistency of Exposure Administration	Medium	Details of exposure were limited; however, this is unlikely to substantially impact results.	
	Metric 9: Reporting of Doses/Concentrations	Medium	Target concentrations were not reported. Chemical concentration levels are means of 3-12 samples or more with continuous monitoring, with a coefficient of variation of < 13%.	
	Metric 10: Exposure Frequency and Duration	High	Exposure frequency and duration were reported and appropriate. 6 hour exposure (2 or 4 days).	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	Low	Only one dose group studied, based off of the lowest level of exposure that elicited significant difference (in 4 biochemical parameters, serum enzyme activity for biomarkers of liver damage) after 4 hour exposure.	
	Metric 12: Exposure Route and Method	Low	Dynamic whole body inhalation chambers were used with adjustable air flows of air (10-12 m3/hr).Unknown distribution of test substance in the whole body inhalation chamber, since not reported, despite describing sampling methods. Uncertainty in parameters related to using the whole body inhalation chamber, like the number of air changes (minimum of 10/hr being required), and weather the cages were big enough for the rats and unknown how the rats were caged, possibly with more than one rat per cage.	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	Medium	Age of rats and individual body weights at study initiation were not reported.	

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Study Citation:	Brondeau, M. T., Bonnet, P., Guenier, J. P., De, C. J. (1983). Short-term inhalation test for evaluating industrial hepatotoxicants in rats. Toxicology Letters 19(1-2):139-146.
Health Outcome(s):	Hepatic/Liver (Serum enzyme activity for liver damage biomarkers: SDH, GLDH, GOT, and GPT.)
Reported Health Effect(s):	Hepatic/Liver (Serum enzyme activity for liver damage biomarkers: SDH, GLDH, GOT, and GPT.): Serum enzyme activities (units per ml (U/ml), or nmol per min per ml) of liver hepatotoxicity biomarkers ALT (GPT), AST (GOT), glutamate dehydrogenase (GLDH) and sorbitol dehydrogenase (SHD).
Duration:	Short-term (>1-30 days) Short-term- 6 hour for 2 or 4 days
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	200247

Domain	Metric	Rating	Comments
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Low	No husbandry conditions were not reported, except that food and water were not available during exposure
	Metric 15: Number of Animals per Group	Low	The number of animals treated per group was not reported/uncertain.
Domain 5: Outcome Assessment			
	Metric 16: Outcome Assessment Methodology	Low	Histology and organ weight was not assessed (only serum chemistry).
	Metric 17: Consistency of Outcome Assessment	Low	Details regarding outcome assessment were limited. This is especially uncertain given the only measurements made were serum chemistry with no contextualization from body weights, liver weight, liver histology. The study authors did report that "The choice of seric parameters and sampling time was the result of preliminary experiments conducted to point out the best experimental conditions and not reported here." However, there was no reference or information provided on those parameters, which leaves uncertainty in outcome assessment consistency.
	Metric 18: Sampling Adequacy	Low	Number of samples were variable with no accounting for how many samples comprised a specific dose or duration. Authors stating, "Exposure concentrations are the mean of 3-12 samples, or more when continuous monitoring, with a coefficient of variation of < 13% (Figure 1)." Uncertainty and only 3 samples seem insufficient.
	Metric 19: Blinding of Assessors	N/A	Blinding was not necessary in this study.
	Metric 20: Negative Control Response	Low	The biological response of the negative control responses were not shown. Data are presented as test/control means values. Can not determine if response was appropriate. The study used a manufacturer kit to measure serum enzyme activity for liver damage biomarkers. The authors stated, "...diagnostic kits purchased from Boehringer Mannheim, France," and "...Quality controls were systematically performed (Precinorm E and S, Boehringer)."
Domain 6: Confounding / Variable Control			
	Metric 21: Confounding Variables in Test Design and Procedures	Low	Study did not report all information to determine confounding, reported information did not identify differences. o-DCB is a respiratory irritant and toxicant, without respiration rate information nor other individual animal information, e.g., body weights, food and water consumption, a low confidence level is most appropriate. (NJ DEH) https://www.nj.gov/health/eoh/rtkweb/documents/fs/0642.pdf (ATSDR) https://wwwn.cdc.gov/TSP/MMG/MMGDetails.aspx?mmgid=1208&toxid=126 (Thermo Fisher) https://www.fishersci.com/store/msds?partNumber=AC396961000&productDescription=1%2C2-DICHLOROBENZENE&vendorId=VN00032119&countryCode=US&language=en
	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 performed (Student's t-test).

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Study Citation:	Brondeau, M. T., Bonnet, P., Guenier, J. P., De, C. J. (1983). Short-term inhalation test for evaluating industrial hepatotoxicants in rats. Toxicology Letters 19(1-2):139-146.
Health Outcome(s):	Hepatic/Liver (Serum enzyme activity for liver damage biomarkers: SDH, GLDH, GOT, and GPT.)
Reported Health Effect(s):	Hepatic/Liver (Serum enzyme activity for liver damage biomarkers: SDH, GLDH, GOT, and GPT.): Serum enzyme activities (units per ml (U/ml), or nmol per min per ml) of liver hepatotoxicity biomarkers ALT (GPT), AST (GOT), glutamate dehydrogenase (GLDH) and sorbitol dehydrogenase (SHD).
Duration:	Short-term (>1-30 days) Short-term- 6 hour for 2 or 4 days
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	200247

Domain	Metric	Rating	Comments
	Metric 24: Reporting of Data	High	Exposure related to stated outcomes of interest were not completely reported for this duration. Controls were only presented in a ratio with treated (Figure 1).

Additional Comments: This study only evaluated male Sprague-Dawley rats. The two chemicals under active evaluation by EPA, that were evaluated in this study, are 1,2-dichloroethane and o-dichlorobenzene. A major limitation of this study was that both of these test substances are known respiratory irritants and this study did not measure respiration rate of animals to determine if that influenced the serum enzyme activity biomarkers for liver damage. The diagnostic value of the 4 serum biomarkers for liver damage was unclear, especially given there was no concurrent liver weights or liver histology/cytology. the serum enzyme biomarkers for liver damage, GOT and GPT seemed to be the least diagnostic of the 4 serum enzymes measured. There was no individual animal data reported, e.g., initial body weights, weight changes over the course of the study nor food and water consumption.

Overall Quality Determination

Medium

Study Citation:	Charbonneau, M., Strasser, J., Jr, Lock, E. A., Turner, M. J., Jr, Swenberg, J. A. (1989). Involvement of reversible binding to "alpha"2u-globulin in 1,4-dichlorobenzene-induced nephrotoxicity. Toxicology and Applied Pharmacology 99(1):122-132.			
Health Outcome(s):	Renal/Kidney			
Reported Health Effect(s):	Renal/Kidney: Kidney weight and/or histology (protein droplet formation)Increased chemical content measured within tissue homogenates relative to kidney weight and via globulin binding with chemicals, and/or histology (protein droplet formation)			
Duration:	Short-term (>1-30 days) 7 days - o-DCB			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	68063			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1:	Test Substance Identity	High	The test substance was definitively identified as 1,2-dichlorobenzene.
	Metric 2:	Test Substance Source	High	The source of the test substance was specified (i.e., purchased from a commercial source).
	Metric 3:	Test Substance Purity	High	The purity of the test substance was reported (i.e., 99%); observed effects would be due to the test substance itself.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	Negative controls were treated with corn oil (as indicated in Table 6) via gavage for 7 days (5 mL/kg).
	Metric 5:	Positive Controls	Low	The use of positive controls was not applicable to the study type.The use of 2,2,4-trimethylpentane (TMP, a component of unleaded gasoline) was shown in previous experiments by the same group to cause an increase in the metrics used in this study (ADME measures; excreted test chemical (urine) and alpha 2u globulin binding radiological assay).My rating for this is low since the only indication that this was a positive control was from the same lab. More information for the use of TMP in this was should have been provided for higher confidence.
	Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups.
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and Storage of Test Substance	Medium	Little information was provided with respect to test substance preparation and/or storage conditions; however, based on the route of exposure (gavage) and study duration (7 days), these omissions are unlikely to have an impact on the study results. Based on the website for the commercial source from which 1,2-DCB was purchased, the test substance is stable under recommended storage conditions.SCOPEs documents state that this chemical is miscible in most organic solvents, and PubChem indicate high lipid solubility
	Metric 8:	Consistency of Exposure Administration	Medium	Details of exposure administration were limited; however, missing information is unlikely to have a substantial impact on the results.
	Metric 9:	Reporting of Doses/Concentrations	High	The study indicated dosing volumes (mmol/kg) and the equivalent doses in mg/kg.
	Metric 10:	Exposure Frequency and Duration	High	The study duration was adequate to evaluate the outcomes of interest, and in line with studies evaluating the same types of effects for other test substances (as per information included in the introduction).
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Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Renal/Kidney: Kidney weight and/or histology (protein droplet formation)Increased chemical content measured within tissue homogenates relative to kidney weight and via globulin binding with chemicals, and/or histology (protein droplet formation)
Duration:	Short-term (>1-30 days) 7 days - o-DCB
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	68063

Domain	Metric	Rating	Comments
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	The study authors indicated that the doses used corresponded to the high doses used in cancer bioassays of 1,2-DCB and 1,4-DCB. The doses used in the study were adequate to detect effects on the outcomes of interest.
	Metric 12: Exposure Route and Method	High	The exposure route and method (i.e., gavage dosing) was well-suited to the test substance; this route/method was used in studies of other chemicals that evaluated similar effects and in cancer bioassays for 1,2-DCB.

Domain 4: Test Animals

Metric 13:	Test Animal Characteristics	Medium	The species/strain of rats used was specified, was the same as that used in the NTP cancer bioassay for 1,2-DCB, and was obtained from a commercial source. Details regarding the animals were sparse (only defined as "sexually mature" and a range of starting body weights reported).
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Little to no information was reported on husbandry conditions (other than temp was 21C and there was an artificial 12 hour light/dark cycle); there is no reason to believe that husbandry conditions differed among treatment groups.
Metric 15:	Number of Animals per Group	Medium	Three males per group were used in the 7-day study; however, this number appeared to be sufficient in most cases to detect statistically significant effects on the outcomes of interest.

Domain 5: Outcome Assessment

Metric 16:	Outcome Assessment Methodology	High	The study evaluated protein droplet formation histologically, and renal cell proliferation was quantitated by measuring [3H]TdR incorporation. The endpoints evaluated in the acute study complemented those evaluated in this study (7 days) to identify alpha 2u globulin-related kidney effects.
Metric 17:	Consistency of Outcome Assessment	High	The methodological details provided suggested that outcomes were consistently assessed across treatment groups.
Metric 18:	Sampling Adequacy	Medium	Data were recorded for all rats utilized in the experiments. Note: that scoring of protein droplets was based one section of kidney per animal.
Metric 19:	Blinding of Assessors	High	The histology evaluations were considered targeted, as the chemical of interest was specifically being evaluated as to its ability to bind a2u globulin and protein droplet formation in the kidney. The study authors reported that histology evaluations were performed without knowledge of treatment group, and severity data were based on mean scores for three analysts.
Metric 20:	Negative Control Response	Medium	A relatively low but detectable level of protein droplet formation was observed in male negative control animals (severity = 1.0, which fell into category of occasional droplet formation).

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Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	68063

Domain	Metric	Rating	Comments
Domain 6: Confounding / Variable Control			
Metric 21:	Confounding Variables in Test Design and Procedures	Medium	The study did not identify or report differences in study groups that would have confounded the study results.
Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information to support/dismiss differences among groups with respect to health outcomes unrelated to treatment.
Metric 23:	Data Presentation and Analysis	High	Statistical methods were adequately described.
Metric 24:	Reporting of Data	High	Data were reported quantitatively for males with respect to the severity of protein droplet formation and renal cell proliferation.

Additional Comments: None

Overall Quality Determination**High**

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Health Outcome(s):	Hepatic/Liver (2. Rabbits: animals exposed to 500 ppm exhibited lower absolute and relative liver weights than control animals, however these were not statistically significant but reflect maternal toxicity due to consistency of effects.); Reproductive/Developmental (Rabbit: A single litter among the rabbits exposed to 500 ppm was totally resorbed at the time of necropsy on day 19 of gestation. No significant reproductive effects following exposure to 200, 400 or 500 ppm of chemical.); Reproductive/Developmental (Rats: Embryo lethality was observed in the 500 ppm exposure group exhibiting the most severe signs of maternal toxicity. No statistically significant effects on reproductive parameters were observed at any exposure level.); Nutritional/Metabolic (1. Rats: Pregnant rats exposed to 500 ppm gained significantly less weight and total body weight; overall animals in this groups lost weight. Pregnant rats exposed to 400 ppm of ODCB gained significantly less weight on days 6 through 7 of gestation. and the overall body weight gain was lower than controls, though this difference was not statistically significant. Food consumption among rats exposed to 400 and 500 ppm of ODCB was significantly decreased during days 6 through 8, 9 through 11, and 12 through 14 of gestation when compared to controls. There were no differences in water 2. Pregnant rabbits exposed to 500pm had body weight loss during day 6-18 of gestation that was not statistically significant. At 200pm, pregnant rabbits demonstrated statistically significant loss of body weight on days 9-11 of gestation.); Renal/Kidney (Rats: Increased relative kidney weights were observed among rats exposed to 400 ppm of ODCB); Gastrointestinal (Two rats exposed to 500 ppm exhibited nonspecific manifestation of toxicity including gastric ulcers or mucosal roughening, decreased abdominal adipose tissue and decreased ingesta in the gastrointestinal tract.); Hepatic/Liver (1. Rats: organ-to-body weight ratios for liver were significantly increased in pregnant rats exposed to 400 ppm and 500 ppm when compared to control values. pregnant rats exposed to 500 ppm of ODCB exhibited slight to moderate hepatic enlargement or slight paleness of the liver. Among rats exposed to 400 PPII of ODCB, 4 of 10 bred rats exhibited slight to moderate enlargement of the liver); Nutritional/Metabolic (1. Rats: Pregnant rats exposed to 500 ppm gained significantly less weight and total body weight; overall animals in this groups lost weight. Pregnant rats exposed to 400 ppm of ODCB gained significantly less weight on days 6 through 7 of gestation. and the overall body weight gain was lower than controls, though this difference was not statistically significant. Food consumption among rats exposed to 400 and 500 ppm of ODCB was significantly decreased during days 6 through 8, 9 through 11, and 12 through 14 of gestation when compared to controls. There were no differences in water consumption observed among rats exposed to ODC. 2. Pregnant rabbits exposed to 500pm had body weight loss during day 6-18 of gestation that was not statistically significant. At 200pm, pregnant rabbits demonstrated statistically significant loss of body weight on days 9-11 of gestation.); Renal/Kidney (Rabbits: Results were not discussed; however, data in Table 6 indicated no differences in absolute and relative kidney weights between controls and treated animals); Skin/Connective Tissue (1. Rats: All rats exposed to 500 ppm of ODCB exhibited gross lesions attributable to exposure. No gross lesions were observed among rats exposed to 200 ppm of o-DCB.);
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Health Outcome(s):	Hepatic/Liver (2. Rabbits: animals exposed to 500 ppm exhibited lower absolute and relative liver weights than control animals, however these were not statistically significant but reflect maternal toxicity due to consistency of effects.); Reproductive/Developmental (Rabbit: A single litter among the rabbits exposed to 500 ppm was totally resorbed at the time of necropsy on day 19 of gestation. No significant reproductive effects following exposure to 200, 400 or 500 ppm of chemical.); Reproductive/Developmental (Rats: Embryo lethality was observed in the 500 ppm exposure group exhibiting the most severe signs of maternal toxicity. No statistically significant effects on reproductive parameters were observed at any exposure level.); Nutritional/Metabolic (1. Rats: Pregnant rats exposed to 500 ppm gained significantly less weight and total body weight; overall animals in this groups lost weight. Pregnant rats exposed to 400 ppm of ODCB gained significantly less weight on days 6 through 7 of gestation. and the overall body weight gain was lower than controls, though this difference was not statistically significant. Food consumption among rats exposed to 400 and 500 ppm of ODCB was significantly decreased during days 6 through 8, 9 through 11, and 12 through 14 of gestation when compared to controls. There were no differences in water 2. Pregnant rabbits exposed to 500pm had body weight loss during day 6-18 of gestation that was not statistically significant. At 200pm, pregnant rabbits demonstrated statistically significant loss of body weight on days 9-11 of gestation.); Renal/Kidney (Rats: Increased relative kidney weights were observed among rats exposed to 400 ppm of ODCB); Gastrointestinal (Two rats exposed to 500 ppm exhibited nonspecific manifestation of toxicity including gastric ulcers or mucosal roughening, decreased abdominal adipose tissue and decreased ingesta in the gastrointestinal tract.); Hepatic/Liver (1. Rats: organ-to-body weight ratios for liver were significantly increased in pregnant rats exposed to 400 ppm and 500 ppm when compared to control values. pregnant rats exposed to 500 ppm of ODCB exhibited slight to moderate hepatic enlargement or slight paleness of the liver. Among rats exposed to 400 PPII of ODCB, 4 of 10 bred rats exhibited slight to moderate enlargement of the liver); Nutritional/Metabolic (1. Rats: Pregnant rats exposed to 500 ppm gained significantly less weight and total body weight; overall animals in this groups lost weight. Pregnant rats exposed to 400 ppm of ODCB gained significantly less weight on days 6 through 7 of gestation. and the overall body weight gain was lower than controls, though this difference was not statistically significant. Food consumption among rats exposed to 400 and 500 ppm of ODCB was significantly decreased during days 6 through 8, 9 through 11, and 12 through 14 of gestation when compared to controls. There were no differences in water consumption observed among rats exposed to ODC. 2. Pregnant rabbits exposed to 500pm had body weight loss during day 6-18 of gestation that was not statistically significant. At 200pm, pregnant rabbits demonstrated statistically significant loss of body weight on days 9-11 of gestation.); Renal/Kidney (Rabbits: Results were not discussed; however, data in Table 6 indicated no differences in absolute and relative kidney weights between controls and treated animals); Skin/Connective Tissue (1. Rats: All rats exposed to 500 ppm of ODCB exhibited gross lesions attributable to exposure. No gross lesions were observed among rats exposed to 200 ppm of o-DCB.);
Reported Health Effect(s):	Hepatic/Liver (2. Rabbits: animals exposed to 500 ppm exhibited lower absolute and relative liver weights than control animals, however these were not statistically significant but reflect maternal toxicity due to consistency of effects.): enlarged liver or liver discoloration (paleness), increased organ-to-body weight ratios for liver, absolute and relative liver weights; Reproductive/Developmental (Rabbit: A single litter among the rabbits exposed to 500 ppm was totally resorbed at the time of necropsy on day 19 of gestation. No significant reproductive effects following exposure to 200, 400 or 500 ppm of chemical.); Embryotoxicity, fetal resorption; Reproductive/Developmental (Rats: Embryo lethality was observed in the 500 ppm exposure group exhibiting the most severe signs of maternal toxicity. No statistically significant effects on reproductive parameters were observed at any exposure level.); Embryotoxicity, fetal resorption; Nutritional/Metabolic (1. Rats: Pregnant rats exposed to 500 ppm gained significantly less weight and total body weight; overall animals in this groups lost weight. Pregnant rats exposed to 400 ppm of ODCB gained significantly less weight on days 6 through 7 of gestation. and the overall body weight gain was lower than controls, though this difference was not statistically significant. Food consumption among rats exposed to 400 and 500 ppm of ODCB was significantly decreased during days 6 through 8, 9 through 11, and 12 through 14 of gestation when compared to controls. There were no differences in water 2. Pregnant rabbits exposed to 500pm had body weight loss during day 6-18 of gestation that was not statistically significant. At 200pm, pregnant rabbits demonstrated statistically significant loss of body weight on days 9-11 of gestation.); loss of body weight, decrease in absolute and relative organ weights; changes in food and water consumption; Renal/Kidney (Rats: Increased relative kidney weights were observed among rats exposed to 400 ppm of ODCB): absolute and relative kidney weight; Gastrointestinal (Two rats exposed to 500 ppm exhibited nonspecific manifestation of toxicity including gastric ulcers or mucosal roughening, decreased abdominal adipose tissue and decreased ingesta in the gastrointestinal tract.): manifestation of toxicity including gastric ulcers or mucosal roughening, decreased abdominal adipose tissue and decreased fngesta inthe gastrointestinal tract at high dose in rats; Hepatic/Liver (1. Rats: organ-to-body weight ratios for liver were significantly increased in pregnant rats exposed to 400 ppm and 500 ppm when compared to control values. pregnant rats exposed to 500 ppm of ODCB exhibited slight to moderate hepatic enlargement or slight paleness of the liver. Among rats exposed to 400 PPII of ODCB, 4 of 10 bred rats exhibited slight to moderate enlargement of the liver): enlarged liver or liver discoloration (paleness), increased organ-to-body weight ratios for liver, absolute and relative liver weights; Nutritional/Metabolic (1. Rats: Pregnant rats exposed to 500 ppm gained significantly less weight and total body weight; overall animals in this groups lost weight. Pregnant rats exposed to 400 ppm of ODCB gained significantly less weight on days 6 through 7 of gestation. and the overall body weight gain was lower than controls, though this difference was not statistically significant. Food consumption among rats exposed to 400 and 500 ppm of ODCB was significantly decreased during days 6 through 8, 9

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Study Citation:	Dow Chemical, (1981). Initial submission: Orthodichlorobenzene: Inhalation teratology probe study in rats and rabbits (final report) with cover letter dated 102591. :Epa/Ots #88-92000044.
Health Outcome(s):	Hepatic/Liver (2. Rabbits: animals exposed to 500 ppm exhibited lower absolute and relative liver weights than control animals, however these were not statistically significant but reflect maternal toxicity due to consistency of effects.); Reproductive/Developmental (Rabbit: A single litter among the rabbits exposed to 500 ppm was totally resorbed at the time of necropsy on day 19 of gestation. No significant reproductive effects following exposure to 200, 400 or 500 ppm of chemical.); Reproductive/Developmental (Rats: Embryo lethality was observed in the 500 ppm exposure group exhibiting the most severe signs of maternal toxicity. No statistically significant effects on reproductive parameters were observed at any exposure level.); Nutritional/Metabolic (1. Rats: Pregnant rats exposed to 500 ppm gained significantly less weight and total body weight; overall animals in this groups lost weight. Pregnant rats exposed to 400 ppm of ODCB gained significantly less weight on days 6 through 7 of gestation. and the overall body weight gain was lower than controls, though this difference was not statistically significant. Food consumption among rats exposed to 400 and 500 ppm of ODCB was significantly decreased during days 6 through 8, 9 through 11, and 12 through 14 of gestation when compared to controls. There were no differences in water 2. Pregnant rabbits exposed to 500pm had body weight loss during day 6-18 of gestation that was not statistically significant. At 200pm, pregnant rabbits demonstrated statistically significant loss of body weight on days 9-11 of gestation.); Renal/Kidney (Rats: Increased relative kidney weights were observed among rats exposed to 400 ppm of ODCB); Gastrointestinal (Two rats exposed to 500 ppm exhibited nonspecific manifestation of toxicity including gastric ulcers or mucosal roughening, decreased abdominal adipose tissue and decreased ingesta in the gastrointestinal tract.); Hepatic/Liver (1. Rats: organ-to-body weight ratios for liver were significantly increased in pregnant rats exposed to 400 ppm and 500 ppm when compared to control values. pregnant rats exposed to 500 ppm of ODCB exhibited slight to moderate hepatic enlargement or slight paleness of the liver. Among rats exposed to 400 PPII of ODCB, 4 of 10 bred rats exhibited slight to moderate enlargement of the liver); Nutritional/Metabolic (1. Rats: Pregnant rats exposed to 500 ppm gained significantly less weight and total body weight; overall animals in this groups lost weight. Pregnant rats exposed to 400 ppm of ODCB gained significantly less weight on days 6 through 7 of gestation. and the overall body weight gain was lower than controls, though this difference was not statistically significant. Food consumption among rats exposed to 400 and 500 ppm of ODCB was significantly decreased during days 6 through 8, 9 through 11, and 12 through 14 of gestation when compared to controls. There were no differences in water consumption observed among rats exposed to ODC. 2. Pregnant rabbits exposed to 500pm had body weight loss during day 6-18 of gestation that was not statistically significant. At 200pm, pregnant rabbits demonstrated statistically significant loss of body weight on days 9-11 of gestation.); Renal/Kidney (Rabbits: Results were not discussed; however, data in Table 6 indicated no differences in absolute and relative kidney weights between controls and treated animals); Skin/Connective Tissue (1. Rats: All rats exposed to 500 ppm of ODCB exhibited gross lesions attributable to exposure. No gross lesions were observed among rats exposed to 200 ppm of o-DCB.);
Reported Health Effect(s):	Hepatic/Liver (2. Rabbits: animals exposed to 500 ppm exhibited lower absolute and relative liver weights than control animals, however these were not statistically significant but reflect maternal toxicity due to consistency of effects.): enlarged liver or liver discoloration (paleness), increased organ-to-body weight ratios for liver, absolute and relative liver weights; Reproductive/Developmental (Rabbit: A single litter among the rabbits exposed to 500 ppm was totally resorbed at the time of necropsy on day 19 of gestation. No significant reproductive effects following exposure to 200, 400 or 500 ppm of chemical.); Embryotoxicity, fetal resorption; Reproductive/Developmental (Rats: Embryo lethality was observed in the 500 ppm exposure group exhibiting the most severe signs of maternal toxicity. No statistically significant effects on reproductive parameters were observed at any exposure level.); Embryotoxicity, fetal resorption; Nutritional/Metabolic (1. Rats: Pregnant rats exposed to 500 ppm gained significantly less weight and total body weight; overall animals in this groups lost weight. Pregnant rats exposed to 400 ppm of ODCB gained significantly less weight on days 6 through 7 of gestation. and the overall body weight gain was lower than controls, though this difference was not statistically significant. Food consumption among rats exposed to 400 and 500 ppm of ODCB was significantly decreased during days 6 through 8, 9 through 11, and 12 through 14 of gestation when compared to controls. There were no differences in water 2. Pregnant rabbits exposed to 500pm had body weight loss during day 6-18 of gestation that was not statistically significant. At 200pm, pregnant rabbits demonstrated statistically significant loss of body weight on days 9-11 of gestation.); loss of body weight, decrease in absolute and relative organ weights; changes in food and water consumption; Renal/Kidney (Rats: Increased relative kidney weights were observed among rats exposed to 400 ppm of ODCB): absolute and relative kidney weight; Gastrointestinal (Two rats exposed to 500 ppm exhibited nonspecific manifestation of toxicity including gastric ulcers or mucosal roughening, decreased abdominal adipose tissue and decreased ingesta in the gastrointestinal tract.): manifestation of toxicity including gastric ulcers or mucosal roughening, decreased abdominal adipose tissue and decreased ingesta in the gastrointestinal tract at high dose in rats; Hepatic/Liver (1. Rats: organ-to-body weight ratios for liver were significantly increased in pregnant rats exposed to 400 ppm and 500 ppm when compared to control values. pregnant rats exposed to 500 ppm of ODCB exhibited slight to moderate hepatic enlargement or slight paleness of the liver. Among rats exposed to 400 PPII of ODCB, 4 of 10 bred rats exhibited slight to moderate enlargement of the liver): enlarged liver or liver discoloration (paleness), increased organ-to-body weight ratios for liver, absolute and relative liver weights; Nutritional/Metabolic (1. Rats: Pregnant rats exposed to 500 ppm gained significantly less weight and total body weight; overall animals in this groups lost weight. Pregnant rats exposed to 400 ppm of ODCB gained significantly less weight on days 6 through 7 of gestation. and the overall body weight gain was lower than controls, though this difference was not statistically significant. Food consumption among rats exposed to 400 and 500 ppm of ODCB was significantly decreased during days 6 through 8, 9

Study Citation:	Haas,, R.a. (1979). o-Dichlorobenzene myelotoxicity & cytogenetic study in rats. :Order this.		
Health Outcome(s):	Nutritional/Metabolic; Renal/Kidney; Immune/Hematological; Hepatic/Liver;		
Reported Health Effect(s):	Nutritional/Metabolic: Body weight; Renal/Kidney: Kidney relative and absolute tissue weights.; Immune/Hematological: Packed cell volume, red cell count, hemoglobin, white cell count, white cell differential. Thymus and spleen absolute and relative tissue weights.; Hepatic/Liver: Liver absolute and relative tissue weights.;		
Duration:	Short-term (>1-30 days) 16 days		
Chemical:	o-Dichlorobenzene- Parent compound		
HERO ID:	5279907		
Domain	Metric	Rating	Comments
Domain 1: Test Substance			
	Metric 1: Test Substance Identity	High	All Outcomes: Test substance was identified by nomenclature, and CAS number (95-50-1) was listed.
	Metric 2: Test Substance Source	High	All Outcomes: 1,2-DCB was purchased from Aldrich Chemical Co. (Lot No. 040387).
	Metric 3: Test Substance Purity	Medium	All Outcomes: Purity of test substance reported as 98%. Impurities not listed, study results were not likely to be substantially impacted by the impurities.
Domain 2: Test Design			
	Metric 4: Negative and Vehicle Controls	High	All Outcomes: Negative control group was identified as olive oil administered subcutaneously at a volume of 2.0 ml/kg/day.
	Metric 5: Positive Controls	Medium	All Outcomes: A positive control was used (benzene) and a positive response was observed.
	Metric 6: Randomized Allocation of Animals	Medium	All Outcomes: The study reported that animals were randomly allocated into study groups.
Domain 3: Exposure Characterization			
	Metric 7: Preparation and Storage of Test Substance	Medium	All Outcomes: The study characterizes the test substance preparation. Dosing solutions were freshly prepared daily except on the weekends. No weekend storage information listed.
	Metric 8: Consistency of Exposure Administration	High	All Outcomes: Details of exposure administration were reported and exposures were administered consistently across study groups. Animals were subcutaneously injected once a day in the morning (volume of 2.0 ml/kg/day); up to 16 consecutive days. Positive control benzene administered subcutaneously at a volume of 2.0 ml/kg; up to 16 consecutive days.
	Metric 9: Reporting of Doses/Concentrations	High	All Outcomes: Administered doses were reported without ambiguity: 1.0, 0.2, 0.04 g/kg/day.
	Metric 10: Exposure Frequency and Duration	High	All Outcomes: The exposure frequency and duration of exposure were reported and appropriate for this study type and evaluated outcomes (once a day for up to 16 days).
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Study Citation:	Haas,, R.a. (1979). o-Dichlorobenzene myelotoxicity & cytogenetic study in rats. :Order this.
Health Outcome(s):	Nutritional/Metabolic; Renal/Kidney; Immune/Hematological; Hepatic/Liver;
Reported Health Effect(s):	Nutritional/Metabolic: Body weight; Renal/Kidney: Kidney relative and absolute tissue weights.; Immune/Hematological: Packed cell volume, red cell count, hemoglobin, white cell count, white cell differential. Thymus and spleen absolute and relative tissue weights.; Hepatic/Liver: Liver absolute and relative tissue weights.;
Duration:	Short-term (>1-30 days) 16 days
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	5279907

Domain	Metric	Rating	Comments
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	Medium	Nutritional/Metabolic: The number of exposure groups and spacing of exposure levels were adequate to show results relevant to body weight.; Renal/Kidney: The number of exposure groups and spacing of exposure levels were adequate to show results relevant to kidney weight.; Immune/Hematological: The number of exposure groups and spacing of exposure levels were adequate to show results relevant to liver weight.; Hepatic/Liver: The number of exposure groups and spacing of exposure levels were adequate to show results relevant to liver weight.
	Metric 12: Exposure Route and Method	High	All Outcomes: The exposure route (subcutaneous injection) and method were appropriate and justified in the protocol.
Domain 4: Test Animals			
	Metric 13: Test Animal Characteristics	Medium	All Outcomes: The test animal species, strain, sex, and starting body weight were reported, and the test animal was obtained from Charles River Lab. Age not specified. The test species and strain were an appropriate animal model for the evaluation.
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Medium	All Outcomes: Temperature (22 ± 1 °C), humidity (40-60%), light- dark cycle (12hrs), diet and water availability (ad libitum), housing (groups of 6 in cages) listed in the protocol. Groups listed for sacrifice at day 8 to day 16 were moved to individual cages because of poor health and to prevent cannibalization. This difference is considered minor and are unlikely to have a substantial impact on results.
	Metric 15: Number of Animals per Group	Medium	All Outcomes: 30 animals per dosing group, 6 animals per dose were sacrificed at different intervals after a number of days after treatment.
Domain 5: Outcome Assessment			
	Metric 16: Outcome Assessment Methodology	High	All Outcomes: The outcome assessment methodology addressed the intended outcomes of interest and the assessment methodology was sensitive and appropriate for the outcomes of interest.
	Metric 17: Consistency of Outcome Assessment	High	All Outcomes: Details of the outcome assessment protocol were reported and outcomes were assessed consistently across study groups.
	Metric 18: Sampling Adequacy	High	All Outcomes: All exposed animals were sampled adequately.
	Metric 19: Blinding of Assessors	N/A	Nutritional/Metabolic: Blinding is not required to assess quantitative results such as body weight.; Renal/Kidney: Blinding is not required to assess quantitative results such as kidney weight.; Immune/Hematological: Blinding is not required to assess quantitative results.; Hepatic/Liver: Blinding is not required to assess quantitative results such as liver weight.
	Metric 20: Negative Control Response	High	All Outcomes: The biological responses of the negative control group were adequate.
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Study Citation:	Haas,, R.a. (1979). o-Dichlorobenzene myelotoxicity & cytogenetic study in rats. :Order this.
Health Outcome(s):	Nutritional/Metabolic; Renal/Kidney; Immune/Hematological; Hepatic/Liver;
Reported Health Effect(s):	Nutritional/Metabolic: Body weight; Renal/Kidney: Kidney relative and absolute tissue weights.; Immune/Hematological: Packed cell volume, red cell count, hemoglobin, white cell count, white cell differential. Thymus and spleen absolute and relative tissue weights.; Hepatic/Liver: Liver absolute and relative tissue weights.;
Duration:	Short-term (>1-30 days) 16 days
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	5279907

Domain	Metric	Rating	Comments
Domain 6: Confounding / Variable Control			
Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: Reported information did not identify differences in confounding factors.
Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: Details regarding animal attrition and health outcomes unrelated to exposure were reported for each study group. There were only minor differences among study groups.
Metric 23:	Data Presentation and Analysis	High	All Outcomes: Statistical significance was determined for outcome.
Metric 24:	Reporting of Data	High	Nutritional/Metabolic: Data for exposure-related findings were presented for body weight by exposure group.; Renal/Kidney: Data for exposure-related findings were presented for kidney weight by exposure group.; Immune/Hematological: Data for exposure-related findings were presented for all outcomes by exposure group.; Hepatic/Liver: Data for exposure-related findings were presented for liver weight by exposure group.

Additional Comments: None

Overall Quality Determination**High**

Study Citation:	Haas,, R.a. (1979). o-Dichlorobenzene myelotoxicity & cytogenetic study in rats. :Order this.			
Health Outcome(s):	Mortality			
Reported Health Effect(s):	Mortality: Mortality			
Duration:	Short-term (>1-30 days) 16 days			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	5279907			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1:	Test Substance Identity	High	Test substance was identified by nomenclature, and CAS number (95-50-1) was listed. 1,2-DCB was purchased from Aldrich Chemical Co. (Lot No. 040387). Purity of test substance reported as 98%. Impurities not listed, study results were not likely to be substantially impacted by the impurities.
	Metric 2:	Test Substance Source	High	
	Metric 3:	Test Substance Purity	Medium	
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	Negative control group was identified as olive oil administered subcutaneously at a volume of 2.0 ml/kg/day.
	Metric 5:	Positive Controls	Medium	A positive control was used (benzene) and a positive response was observed.
	Metric 6:	Randomized Allocation of Animals	Medium	The study reported that animals were randomly allocated into study groups.
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and Storage of Test Substance	Medium	The study characterizes the test substance preparation. Dosing solutions were freshly prepared daily except on the weekends. No weekend storage information listed. Details of exposure administration were reported and exposures were administered consistently across study groups. Animals were subcutaneously injected once a day in the morning (volume of 2.0 ml/kg/day); up to 16 consecutive days. Positive control benzene administered subcutaneously at a volume of 2.0 ml/kg; up to 16 consecutive days.
	Metric 8:	Consistency of Exposure Administration	High	
	Metric 9:	Reporting of Doses/Concentrations	High	Administered doses were reported without ambiguity: 1.0, 0.2, 0.04 g/kg/day.
	Metric 10:	Exposure Frequency and Duration	High	The exposure frequency and duration of exposure were reported and appropriate for this study type and evaluated outcomes (once a day for up to 16 days).
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	The number of exposure groups and spacing of exposure levels were adequate to show results of mortality.
	Metric 12:	Exposure Route and Method	High	The exposure route (subcutaneous injection) and method were appropriate for a volatile substance and justified in the protocol.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Medium	The test animal species, strain, sex, and starting body weight were reported, and the test animal was obtained from Charles River Lab. Age not specified. The test species and strain were an appropriate animal model for the evaluation.

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Study Citation:	Haas,, R.a. (1979). o-Dichlorobenzene myelotoxicity & cytogenetic study in rats. :Order this.			
Health Outcome(s):	Mortality			
Reported Health Effect(s):	Mortality: Mortality			
Duration:	Short-term (>1-30 days) 16 days			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	5279907			
Domain		Metric	Rating	Comments
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	Temperature (22 ± 1 °C), humidity (40-60%), light- dark cycle (12hrs), diet and water availability (ad libitum), housing (groups of 6 in cages) listed in the protocol. Groups listed for sacrifice at day 8 to day 16 were moved to individual cages because of poor health and to prevent cannibalization. This difference is considered minor and are unlikely to have a substantial impact on results.
	Metric 15:	Number of Animals per Group	Medium	30 animals per dosing group, 6 animals per dose were sacrificed at different intervals after a number of days after treatment.
Domain 5: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	High	The outcome assessment methodology addressed the intended outcomes 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	All exposed animals were sampled adequately.
	Metric 19:	Blinding of Assessors	N/A	Blinding of assessors is not necessary for measuring mortality.
	Metric 20:	Negative Control Response	High	The biological responses of the negative control group were adequate with low incidence of outcomes of interest in the study (moribund/premature death in one rat on day 4).
Domain 6: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Reported information did not identify differences in confounding factors.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	Details regarding animal attrition and health outcomes unrelated to exposure were reported for each study group. There were only minor differences among study groups.
	Metric 23:	Data Presentation and Analysis	Uninformative	Statistical significance was not determined for outcome.
	Metric 24:	Reporting of Data	High	Data for exposure-related findings were presented for mortality by exposure group.
Additional Comments:	None			

Overall Quality Determination**Uninformative**

Study Citation:	Haas,, R.a. (1979). o-Dichlorobenzene myelotoxicity & cytogenetic study in rats. :Order this.			
Health Outcome(s):	Clinical signs (Clinical signs)			
Reported Health Effect(s):	Clinical signs (Clinical signs): Skin irritation at injection site, diarrhea, opacity of the eye, reddish-brown stains, dirty appearance/loss of fur/ruffled fur, gross injuries, moribund/premature death.			
Duration:	Short-term (>1-30 days) 16 days			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	5279907			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1:	Test Substance Identity	High	Test substance was identified by nomenclature, and CAS number (95-50-1) was listed.
	Metric 2:	Test Substance Source	High	1,2-DCB was purchased from Aldrich Chemical Co. (Lot No. 040387).
	Metric 3:	Test Substance Purity	Medium	Purity of test substance reported as 98%. Impurities not listed, study results were not likely to be substantially impacted by the impurities.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	Negative control group was identified as olive oil administered subcutaneously at a volume of 2.0 ml/kg/day.
	Metric 5:	Positive Controls	Medium	A positive control was used (benzene) and a positive response was observed.
	Metric 6:	Randomized Allocation of Animals	Medium	The study reported that animals were randomly allocated into study groups.
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and Storage of Test Substance	Medium	The study characterizes the test substance preparation. Dosing solutions were freshly prepared daily except on the weekends. No weekend storage information listed.
	Metric 8:	Consistency of Exposure Administration	High	Details of exposure administration were reported and exposures were administered consistently across study groups. Animals were subcutaneously injected once a day in the morning (volume of 2.0 ml/kg/day); up to 16 consecutive days. Positive control benzene administered subcutaneously at a volume of 2.0 ml/kg; up to 16 consecutive days.
	Metric 9:	Reporting of Doses/Concentrations	High	Administered doses were reported without ambiguity: 1.0, 0.2, 0.04 g/kg/day.
	Metric 10:	Exposure Frequency and Duration	High	The exposure frequency and duration of exposure were reported and appropriate for this study type and evaluated outcomes (once a day for up to 16 days).
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	The number of exposure groups and spacing of exposure levels were adequate to show results relevant to clinical signs.
	Metric 12:	Exposure Route and Method	High	The exposure route (subcutaneous injection) and method were appropriate and justified in the protocol.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Medium	The test animal species, strain, sex, and starting body weight were reported, and the test animal was obtained from Charles River Lab. Age not specified. The test species and strain were an appropriate animal model for the evaluation.

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Study Citation:	Haas,, R.a. (1979). o-Dichlorobenzene myelotoxicity & cytogenetic study in rats. :Order this.
Health Outcome(s):	Clinical signs (Clinical signs)
Reported Health Effect(s):	Clinical signs (Clinical signs): Skin irritation at injection site, diarrhea, opacity of the eye, reddish-brown stains, dirty appearance/loss of fur/ruffled fur, gross injuries, moribund/premature death.
Duration:	Short-term (>1-30 days) 16 days
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	5279907

Domain	Metric	Rating	Comments
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Medium	Temperature (22 ± 1 °C), humidity (40-60%), light- dark cycle (12hrs), diet and water availability (ad libitum), housing (groups of 6 in cages) listed in the protocol. Groups listed for sacrifice at day 8 to day 16 were moved to individual cages because of poor health and to prevent cannibalization. This difference is considered minor and are unlikely to have a substantial impact on results.
	Metric 15: Number of Animals per Group	Medium	30 animals per dosing group, 6 animals per dose were sacrificed at different intervals after a number of days after treatment.
Domain 5: Outcome Assessment			
	Metric 16: Outcome Assessment Methodology	High	The outcome assessment methodology addressed the intended outcomes of interest and the assessment methodology was sensitive and appropriate for the outcomes 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	All exposed animals were sampled adequately.
	Metric 19: Blinding of Assessors	Low	The study did not report whether assessors were blinded to treatment group for clinical observations, and this deficiency is likely to have a substantial impact on results.
	Metric 20: Negative Control Response	High	The biological responses of the negative control group were adequate with low incidence of outcomes of interest in the study (skin irritation in one rat on day 16, moribund/premature death in one rat on day 4).
Domain 6: Confounding / Variable Control			
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	Reported information did not identify differences in confounding factors.
	Metric 22: Health Outcomes Unrelated to Exposure	Medium	Details regarding animal attrition and health outcomes unrelated to exposure were reported for each study group. There were only minor differences among study groups.
	Metric 23: Data Presentation and Analysis	N/A	Statistical significance was not determined or necessary for outcome.
	Metric 24: Reporting of Data	High	Data for exposure-related findings were presented for all outcomes by exposure group.

Additional Comments: None

Overall Quality Determination**High**

Study Citation:	Kulkarni, S. G., Duong, H., Gomila, R., Mehendale, H. M. (1996). Strain differences in tissue repair response to 1,2-dichlorobenzene. Archives of Toxicology 70(11):714-723.			
Health Outcome(s):	Hepatic/Liver			
Reported Health Effect(s):	Hepatic/Liver: Male rats only.Liver injury including altered ALT and AST levels. Also, significantly higher depletion of hepatic glycogen observed in F344 rats following administration of 0.2 and 0.6 ml o-DCB/kg occurred without significant changes in plasma glucose and is consistent with highly stimulated tissue repair seen in F344 rats at the corresponding doses.Depletion of estimated glycogen (/g of liver) with no corresponding change in estimated plasma glucose levels. F344 had greater glycogen depletion, consistent with greater rate of stimulated tissue repair documented in this strain.Centrilobular hepatocellular necrosis observed with histopathology and including macrophage infiltration (H&E only); F344 >>> S-D rats. Some recovery was seen at 96hrs in surviving mice, to a lesser extent in F344 strain.Low-dose effects observed at the lowest dose tested, 0.2ml/kg o-DCB.The highest dose tested was reported to be approx. 25% lethal, at 1.2mL DCB/kg.Cell cycle phases (IHC liver; PCNA staining) and S-phase synthesis (H-thymidine incorporation) were measured to determine whether strain-specific differences in liver injury and repair were the result of cell division and stimulated liver tissue repair. Fold changes were not sufficiently reported and/or in the discussion section of the paper, especially for the plasma enzymes measured, ALT and SDM.			
Duration:	Short-term (>1-30 days) 14 days			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	5254311			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance	Metric 1: Test Substance Identity	Medium	No CASRN.	
	Metric 2: Test Substance Source	Low	No source reported. No test substance section under 'Materials and methods.' No other mention of test substance characterization.	
	Metric 3: Test Substance Purity	Low	Purity of test substance was not reported. No mention of test substance was in 'Materials and methods.'	
Domain 2: Test Design	Metric 4: Negative and Vehicle Controls	N/A	Acute, LD50 determination does not require vehicle control. The figure legends mentioned corn oil controls, but there was no other indication a vehicle control was performed nor factored into data presentation, e.g. fold-changes over control, etc.	
	Metric 5: Positive Controls	Uninformative	No positive controls were needed for LD50 determination. However, the mechanistic data such as serum enzymes and IHC performed should have had positive controls and did not.	
	Metric 6: Randomized Allocation of Animals	Low	No reports of randomization of animals.	
Domain 3: Exposure Characterization	Metric 7: Preparation and Storage of Test Substance	Low	No information on the test substance or its preparation were reported. No test substance section under 'Materials and methods.'	
	Metric 8: Consistency of Exposure Administration	Medium	Consistency of exposure timing over the course of the study was not reported, specifically when liver, blood samples and necropsy were sampled and performed.	
	Metric 9: Reporting of Doses/Concentrations	High	Was not clear what the study authors based the dose selection/ range on.	
	Metric 10: Exposure Frequency and Duration	High	Missing Comment	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	Missing Comment	
	Metric 12: Exposure Route and Method	High	Missing Comment	

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Study Citation:	Kulkarni, S. G., Duong, H., Gomila, R., Mehendale, H. M. (1996). Strain differences in tissue repair response to 1,2-dichlorobenzene. Archives of Toxicology 70(11):714-723.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	Hepatic/Liver: Male rats only. Liver injury including altered ALT and AST levels. Also, significantly higher depletion of hepatic glycogen observed in F344 rats following administration of 0.2 and 0.6 ml o-DCB/kg occurred without significant changes in plasma glucose and is consistent with highly stimulated tissue repair seen in F344 rats at the corresponding doses. Depletion of estimated glycogen (g of liver) with no corresponding change in estimated plasma glucose levels. F344 had greater glycogen depletion, consistent with greater rate of stimulated tissue repair documented in this strain. Centrilobular hepatocellular necrosis observed with histopathology and including macrophage infiltration (H&E only); F344 >>> S-D rats. Some recovery was seen at 96hrs in surviving mice, to a lesser extent in F344 strain. Low-dose effects observed at the lowest dose tested, 0.2ml/kg o-DCB. The highest dose tested was reported to be approx. 25% lethal, at 1.2mL DCB/kg. Cell cycle phases (IHC liver; PCNA staining) and S-phase synthesis (H-thymidine incorporation) were measured to determine whether strain-specific differences in liver injury and repair were the result of cell division and stimulated liver tissue repair. Fold changes were not sufficiently reported and/or in the discussion section of the paper, especially for the plasma enzymes measured, ALT and SDM.
Duration:	Short-term (>1-30 days) 14 days
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	5254311

Domain	Metric	Rating	Comments
Domain 4: Test Animals			
	Metric 13: Test Animal Characteristics	High	Missing Comment
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	High	Missing Comment
	Metric 15: Number of Animals per Group	Low	Only 4 animals per group, it could be more, but it is still sufficient for statistical analysis.
Domain 5: Outcome Assessment			
	Metric 16: Outcome Assessment Methodology	High	Missing Comment
	Metric 17: Consistency of Outcome Assessment	High	Missing Comment
	Metric 18: Sampling Adequacy	High	Missing Comment
	Metric 19: Blinding of Assessors	N/A	Blinding of assessors was not necessary for this study.
	Metric 20: Negative Control Response	Low	The biological response of the negative control groups were not reported. Only known that they were given same amount of corn oil as the other treatment groups.
Domain 6: Confounding / Variable Control			
	Metric 21: Confounding Variables in Test Design and Procedures	High	Missing Comment
	Metric 22: Health Outcomes Unrelated to Exposure	High	Missing Comment
	Metric 23: Data Presentation and Analysis	High	Missing Comment
	Metric 24: Reporting of Data	Medium	I put medium only because there were no reports of control group effects.
Additional Comments: None			

Overall Quality Determination**High**

Study Citation:	Lehman-Mckeeman, L. D., Caudill, D. (1999). Development of an in vitro competitive binding assay to predict α 2u-globulin nephropathy. In Vitro & Molecular Toxicology 12(2):83-95.			
Health Outcome(s):	Renal/Kidney			
Reported Health Effect(s):	Renal/Kidney: Histopathology of the kidney, kidney weights (organ weight data not reported)			
Duration:	Short-term (>1-30 days) 3-days			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	654546			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
Metric 1:	Test Substance Identity	High	The test substance was identified as 1,2-dichlorobenzene, CASRN 95-50-1. The form (e.g., liquid vs. solid) was not specified, but the chemical was dissolved in a corn oil vehicle.	
Metric 2:	Test Substance Source	High	The test chemical was purchased from Aldrich Chemical Co. The catalog/lot or batch number was not provided. The chemical was not analytically verified by the performing laboratory but would have been certified/verified by the commercial source.	
Metric 3:	Test Substance Purity	Medium	The test substance purity was not explicitly reported. The study text indicated that “reagents were of the highest purity”; however, this statement was likely referring to other reagents used in in vitro assays. The commercial source sells multiple options for this chemical (anhydrous, or in a solution containing methanol, or 1% acetone). The purity of solids was $\geq 99\%$.	
Domain 2: Test Design				
Metric 4:	Negative and Vehicle Controls	High	Concurrent negative controls were administered corn oil along (5 mL/kg).	
Metric 5:	Positive Controls	N/A	A positive control was not included and likely not necessary in the study; however, several chemicals were tested, including one known to induce nephropathy at the concentrations used.	
Metric 6:	Randomized Allocation of Animals	Low	The method of animal allocation into study groups was not reported.	
Domain 3: Exposure Characterization				
Metric 7:	Preparation and Storage of Test Substance	Low	Minimal details of the test substance preparation were provided. The test substance was dissolved in a corn oil vehicle. No information on frequency of preparation or storage was reported for a volatile chemical. Given the lack of information in stability or solubility of the test substance in this study, and the known physical/chemical properties of the test substance, this could have a significant impact on the study results, even in a short-term study.	
Metric 8:	Consistency of Exposure Administration	Medium	The study text indicated that “All chemicals were dissolved or diluted in corn oil which was also dosed to control animals (5 mL/kg).” It was assumed that the gavage volume reported was consistent across groups, although there is some uncertainty based on the working in the text.	
Metric 9:	Reporting of Doses/Concentrations	Low	The dose was reported as 1mmol/kg, which is presumed to be a nominal dose. Measured/analytical doses were not reported. The chemical has low solubility, so proper mixing/heterogeneity would be important to assure accurate dosing. This information regarding preparation was not provided. Animal body weights were not reported.	

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Study Citation:	Lehman-Mckeeman, L. D., Caudill, D. (1999). Development of an in vitro competitive binding assay to predict α2u-globulin nephropathy. In Vitro & Molecular Toxicology 12(2):83-95.			
Health Outcome(s):	Renal/Kidney			
Reported Health Effect(s):	Renal/Kidney: Histopathology of the kidney, kidney weights (organ weight data not reported)			
Duration:	Short-term (>1-30 days) 3-days			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	654546			
Domain	Metric	Rating	Comments	
	Metric 10:	Exposure Frequency and Duration	High	The exposure frequency and duration were reported (daily for 3 days) and was appropriate for the purposes of the study
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The study used a single dose, which precludes the ability to evaluate a dose-response. However, the purpose of the study was to determine whether the proposed in vitro assays could accurately assess the ability of a chemical to cause alpha2U-globulin nephropathy. The in vivo portion of the study was simply used as a yes or no comparator and was not intended to evaluate a dose-response.
	Metric 12:	Exposure Route and Method	High	Animals were dosed via gavage, which is an appropriate route of exposure for the test chemical.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Medium	The test animal species (rat), strain (Fisher 344), sex (both sexes), age, and source were reported, and these animals were an appropriate model for the outcomes of interest. Animal starting body weights were not reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	Limited animal husbandry conditions were reported. It was noted that animals were housed in humidity and temperature-controlled rooms (values not specified). Animals were allowed free access to food and water. The number of animals per cage was not reported. Insufficient information is provided to determine whether there were any differences between the control and treatment groups.
	Metric 15:	Number of Animals per Group	Medium	The number of animals per group (4/sex/group) was appropriate/adequate for the purposes of the study.
Domain 5: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	High	The study was focused on evaluating a specific outcome (alpha2U-globulin nephropathy), and therefore histopathology and kidney weights were the only endpoints evaluated. These were sensitive and appropriate for the purposes of the study.
	Metric 17:	Consistency of Outcome Assessment	High	Details regarding the timing of sacrifice, and limited details on the tissue fixation process and histopathological scoring system used were provided and appear to be consistent across groups.
	Metric 18:	Sampling Adequacy	High	All animals used in the study were assessed for the outcomes of interest.
	Metric 19:	Blinding of Assessors	N/A	Although blinding is generally not required/recommended for initial histopathology, because this is a specialized study that is attempting to assess/validate in vitro assays by comparing results to in vivo, histopathological examination of the kidneys was performed without knowledge of the treatment group. Blinding seems appropriate for histopathology in this case. Other endpoints (organ weights) are not subjective in nature.

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Study Citation:	Lehman-Mckeeman, L. D., Caudill, D. (1999). Development of an in vitro competitive binding assay to predict α 2u-globulin nephropathy. In Vitro & Molecular Toxicology 12(2):83-95.			
Health Outcome(s):	Renal/Kidney			
Reported Health Effect(s):	Renal/Kidney: Histopathology of the kidney, kidney weights (organ weight data not reported)			
Duration:	Short-term (>1-30 days) 3-days			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	654546			
Domain	Metric	Rating	Comments	
	Metric 20:	Negative Control Response	Medium	The histopathology score for the control male rats was provided and as expected, no protein droplets were observed in female controls. Results for kidney weight measurements were not reported so it cannot be determined whether the weights of the negative controls were appropriate.
Domain 6: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	The study did not report information needed to determine confounding (e.g., animal body weights, food and water intake).
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	Based on the number of animals sampled, no deaths were observed. There was no other information provided to suggest that there were differences among groups in animal attrition or health outcomes unrelated to exposure.
	Metric 23:	Data Presentation and Analysis	High	The statistical method was clearly reported and appropriate for the dataset.
	Metric 24:	Reporting of Data	Medium	Data were reported for some, but not all endpoints for this outcome. Kidney weight data were not reported. Quantitative hyaline droplet scores for males were presented as means $\pm$ SE. Individual animal scores were not provided.

Additional Comments: The study included sever in vitro assays. These data were not evaluated.

Overall Quality Determination

Medium

Study Citation:	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.			
Health Outcome(s):	Mortality; Nutritional/Metabolic; Nutritional/Metabolic;			
Reported Health Effect(s):	Mortality: Death; Nutritional/Metabolic: Body weight; Nutritional/Metabolic: Body weight;			
Duration:	Short-term (>1-30 days) 14 days Rat			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	1944492			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
Metric 1:	Test Substance Identity	High	Mortality: Test substance was identified by nomenclature, CAS number, and structure; Nutritional/Metabolic: Test substance was identified by nomenclature, CAS number, and structure; Nutritional/Metabolic: test substance was identified by nomenclature, CAS number, and structure	
Metric 2:	Test Substance Source	High	Mortality: Test substance was obtained from a commercial source: " ICC solvent Chemical Company (New York, NY) Lot number SC61377 and analytically verified.; Nutritional/Metabolic: Test substance was obtained from a commercial source: "ICC solvent Chemical Company (New York, NY) Lot number SC61377 and analytically verified.; Nutritional/Metabolic: Test substance was obtained from a commercial source: " ICC solvent Chemical Company (New York, NY) Lot number SC61377 and analytically verified.	
Metric 3:	Test Substance Purity	High	Mortality: Test substance was >99% purity verified analytically. impurities were reported "Acidic components (assumed to be hydrochloric acid) were found to be present at a concentration of 10.8 ppm. one impurity with an area that was approximately 0.7% of the major peak area; this impurity, identified as 1 ,4-dichlorobenzene"; Nutritional/Metabolic: Test substance was >99% purity verified analytically. Impurities were reported "Acidic components (assumed to be hydrochloric acid) were found to be present at a concentration of 10.8 ppm. one impurity with an area that was approximately 0.7% of the major peak area; this impurity, identified as 1 ,4-dichlorobenzene"; Nutritional/Metabolic: Test substance was >99% purity verified analytically. Impurities were reported "Acidic components (assumed to be hydrochloric acid) were found to be present at a concentration of 10.8 ppm. One impurity with an area that was approximately 0.7% of the major peak area; this impurity, identified as 1 ,4-dichlorobenzene"	
Domain 2: Test Design				
Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Concurrently treated vehicle control was used and appropriate for the study	
Metric 5:	Positive Controls	N/A	All Outcomes: Not necessary for the study type	
Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: The study reported the random allocation of animals into groups	
Domain 3: Exposure Characterization				
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Study Citation:	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.			
Health Outcome(s):	Mortality; Nutritional/Metabolic; Nutritional/Metabolic;			
Reported Health Effect(s):	Mortality: Death; Nutritional/Metabolic: Body weight; Nutritional/Metabolic: Body weight;			
Duration:	Short-term (>1-30 days) 14 days Rat			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	1944492			
Domain	Metric	Rating	Comments	
	Metric 7: Preparation and Storage of Test Substance	High	Mortality: Dose preparation and storage were reported "adding a weighed amount of 1 ,2-dichlorobenzene to the appropriate volume of corn oil and mixing for 15 minutes" then doses solutions were prepared by dilution. The mixture was stable at room temp for 7 days and solutions were stored no longer than 14 days at 4 degrees C; Nutritional/Metabolic: Dose preparation and storage were reported "adding a weighed amount of 1 ,2-dichlorobenzene to the appropriate volume of corn oil and mixing for 15 minutes" then doses solutions were prepared by dilution. The mixture was stable at room temp for 7 days and solutions were stored no longer than 14days at 4 degrees C; Nutritional/Metabolic: Dose preparation and storage were reported "adding a weighed amount of 1 ,2-dichlorobenzene to the appropriate volume of corn oil and mixing for 15 minutes" then doses solutions were prepared by dilution. The mixture was stable at room temp for 7 days and solutions were stored no longer than 14 days at 4 degrees C	
	Metric 8: Consistency of Exposure Administration	High	Mortality: Details of exposure administration were reported and consistent. gavage volume was not excessive 5ml/kg.; Nutritional/Metabolic: Details of exposure administration were reported and consistent. gavage volume was not excessive 5ml/kg.; Nutritional/Metabolic: Details of exposure administration were reported and consistent, gavage volume was not excessive 5ml/kg.	
	Metric 9: Reporting of Doses/Concentrations	High	All Outcomes: Doses were reported clearly	
	Metric 10: Exposure Frequency and Duration	High	All Outcomes: Exposure frequency (daily) and duration (14d) were appropriate for the study type	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	Mortality: Number of exposure groups was adequate and consisted of 5 treated groups and a control. spacing was sufficient to encompass a full range of response; Nutritional/Metabolic: Number of exposure groups was adequate and consisted of 5 treated groups and a control. Spacing was sufficient to encompass a full range of response.; Nutritional/Metabolic: Number of exposure groups was adequate and consisted of 5 treated groups and a control. Spacing was sufficient to encompass a full range of response	
	Metric 12: Exposure Route and Method	High	All Outcomes: Exposure route and method were suited to the test substance; gavage is appropriate	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	High	All Outcomes: Species, strain, sex, and age were all reported in table 1. Initial body weight was reported in the results	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: All husbandry conditions were reported in table 1: temperature, humidity, light- dark cycle, diet, water availability and were adequate and consistent across all groups	
	Metric 15: Number of Animals per Group	Medium	All Outcomes: The number of animals per group was reported and appropriate for the study type: 5/group for short term	
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Study Citation:	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.
Health Outcome(s):	Mortality; Nutritional/Metabolic; Nutritional/Metabolic;
Reported Health Effect(s):	Mortality: Death; Nutritional/Metabolic: Body weight; Nutritional/Metabolic: Body weight;
Duration:	Short-term (>1-30 days) 14 days Rat
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	1944492

Domain	Metric	Rating	Comments
Domain 5: Outcome Assessment			
	Metric 16: Outcome Assessment Methodology	High	Mortality: Outcome assessment was sensitive and appropriate for the outcome; Nutritional/Metabolic: Outcome assessment was sensitive and appropriate for the outcome of interest; Nutritional/Metabolic: Outcome assessment was sensitive and appropriate for the outcome of interest
	Metric 17: Consistency of Outcome Assessment	High	All Outcomes: Outcome was assessed consistently across groups
	Metric 18: Sampling Adequacy	High	Mortality: Sampling was adequate for the outcome of interest.; Nutritional/Metabolic: Sampling was from each animal; Nutritional/Metabolic: Sampling was from each animal
	Metric 19: Blinding of Assessors	N/A	All Outcomes: Blinding was not necessary for the study type
	Metric 20: Negative Control Response	High	Mortality: Control group responded adequately: all survived; Nutritional/Metabolic: Control group responded adequately: gained body weight; Nutritional/Metabolic: Control group responded adequately: gained body weight
Domain 6: Confounding / Variable Control			
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	All Outcomes: Reported information did not identify differences in confounding factors
	Metric 22: Health Outcomes Unrelated to Exposure	Medium	All Outcomes: No information was reported to either support or dismiss differences unrelated to exposure
	Metric 23: Data Presentation and Analysis	High	All Outcomes: Statistical methods were reported and appropriate for the data
	Metric 24: Reporting of Data	High	All Outcomes: Data were reported for all outcomes by group and sex
Additional Comments: None			

Overall Quality Determination**High**

Study Citation:	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.			
Health Outcome(s):	Nutritional/Metabolic			
Reported Health Effect(s):	Nutritional/Metabolic: Body weight			
Duration:	Short-term (>1-30 days) 14 days Mouse: high dose			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	1944492			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	Test substance was identified by nomenclature, CAS number, and structure	
	Metric 2: Test Substance Source	High	Test substance was obtained from a commercial source: " ICC solvent Chemical Company (New York, NY) Lot number SC61377 and analytically verified.	
	Metric 3: Test Substance Purity	High	Test substance was >99% purity verified analytically. Impurities were reported "Acidic components (assumed to be hydrochloric acid) were found to be present at a concentration of 10.8 ppm. One impurity with an area that was approximately 0.7% of the major peak area; this impurity, identified as 1 ,4-dichlorobenzene"	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	Concurrently treated vehicle control was used and appropriate for the study	
	Metric 5: Positive Controls	N/A	Not necessary for the study type	
	Metric 6: Randomized Allocation of Animals	Medium	The study reported the random allocation of animals into groups	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	High	Dose preparation and storage were reported "adding a weighed amount of 1 ,2-dichlorobenzene to the appropriate volume of corn oil and mixing for 15 minutes" then doses solutions were prepared by dilution. The mixture was stable at room temp for 7 days and solutions were stored no longer than 14 days at 4 degrees C	
	Metric 8: Consistency of Exposure Administration	High	Details of exposure administration were reported and consistent, gavage volume was not excessive 5ml/kg.	
	Metric 9: Reporting of Doses/Concentrations	High	Doses were reported clearly	
	Metric 10: Exposure Frequency and Duration	High	Exposure frequency (daily) and duration (14d) were appropriate for the study type	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	Number of exposure groups was adequate and consisted of 5 treated groups and a control. Spacing was sufficient to encompass a full range of response	
	Metric 12: Exposure Route and Method	High	Exposure route and method were suited to the test substance: gavage is appropriate	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	High	Species, strain, sex, and age were all reported in table 1. Initial body weight was reported in the results	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were reported in table 1: temperature, humidity, light- dark cycle, diet, water availability and were adequate and consistent across all groups	
	Metric 15: Number of Animals per Group	Medium	The number of animals per group was reported and appropriate for the study type: 5/group for short term	
Domain 5: Outcome Assessment				

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Study Citation:	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.			
Health Outcome(s):	Nutritional/Metabolic			
Reported Health Effect(s):	Nutritional/Metabolic: Body weight			
Duration:	Short-term (>1-30 days) 14 days Mouse: high dose			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	1944492			
Domain	Metric	Rating	Comments	
	Metric 16:	Outcome Assessment Methodology	High	Outcome assessment was sensitive and appropriate for the outcome of interest
	Metric 17:	Consistency of Outcome Assessment	High	Outcome was assessed consistently across groups
	Metric 18:	Sampling Adequacy	High	Sampling was from each animal
	Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary for the study type
	Metric 20:	Negative Control Response	High	Control group responded adequately: gained body weight
Domain 6: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Reported information did not identify differences in confounding factors
	Metric 22:	Health Outcomes Unrelated to Exposure	Uninformative	Complete mortality at all but the lowest dose prevented thorough evaluation of body weight
	Metric 23:	Data Presentation and Analysis	High	Statistical methods were reported and appropriate for the data
	Metric 24:	Reporting of Data	High	Data were reported for all outcomes by group and sex
Additional Comments:	None			

Overall Quality Determination**Uninformative**

Study Citation:	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.			
Health Outcome(s):	Hepatic/Liver			
Reported Health Effect(s):	Hepatic/Liver: Liver weight, histopathology, vlinical chemistry (Mice & rats: ALP, GGT, and glutamic pyruvic transaminase; Rats only: bilirubin, cholesterol, triglycerides, BUN, glucose, total protein)			
Duration:	Short-term (>1-30 days) 14 days Mouse			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	1944492			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	test substance was identified by nomenclature, CAS number, and structure	
	Metric 2: Test Substance Source	High	Test substance was obtained from a commercial source: " ICC solvent Chemical Company (New York, NY) Lot number SC61377 and analytically verified.	
	Metric 3: Test Substance Purity	High	Test substance was >99% purity verified analytically. Impurities were reported "Acidic components (assumed to be hydrochloric acid) were found to be present at a concentration of 10.8 ppm. One impurity with an area that was approximately 0.7% of the major peak area; this impurity, identified as 1 ,4-dichlorobenzene"	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	Concurrently treated vehicle control was used and appropriate for the study	
	Metric 5: Positive Controls	N/A	Not necessary for the study type	
	Metric 6: Randomized Allocation of Animals	Medium	The study reported the random allocation of animals into groups	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	High	Dose preparation and storage were reported "adding a weighed amount of 1 ,2-dichlorobenzene to the appropriate volume of corn oil and mixing for 15 minutes" then doses solutions were prepared by dilution. The mixture was stable at room temp for 7 days and solutions were stored no longer than 14 days at 4 degrees C	
	Metric 8: Consistency of Exposure Administration	High	Details of exposure administration were reported and consistent, gavage volume was not excessive 5ml/kg.	
	Metric 9: Reporting of Doses/Concentrations	High	Doses were reported clearly	
	Metric 10: Exposure Frequency and Duration	High	Exposure frequency (daily) and duration (14d) were appropriate for the study type	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	Number of exposure groups was adequate and consisted of 5 treated groups and a control. Spacing was sufficient to encompass a full range of response	
	Metric 12: Exposure Route and Method	High	Exposure route and method were suited to the test substance: gavage is appropriate	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	High	Species, strain, sex, and age were all reported in table 1. Initial body weight was reported in the results	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were reported in table 1: temperature, humidity, light- dark cycle, diet, water availability and were adequate and consistent across all groups	
	Metric 15: Number of Animals per Group	Medium	The number of animals per group was reported and appropriate for the study type: 5/group for short term	
Domain 5: Outcome Assessment				
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Study Citation:	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	Hepatic/Liver: Liver weight, histopathology, vlinical chemistry (Mice & rats: ALP, GGT, and glutamic pyruvic transaminase; Rats only: bilirubin, cholesterol, triglycerides, BUN, glucose, total protein)
Duration:	Short-term (>1-30 days) 14 days Mouse
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	1944492

Domain	Metric	Rating	Comments
	Metric 16: Outcome Assessment Methodology	Medium	Outcome assessment was limited to liver histopathology. Liver weight and clinical chemistry were not evaluated.
	Metric 17: Consistency of Outcome Assessment	High	Outcome was assessed consistently across groups
	Metric 18: Sampling Adequacy	Medium	Sampling was from 4 animals from the high dose group and controls
	Metric 19: Blinding of Assessors	N/A	Blinding was not necessary for the study type
	Metric 20: Negative Control Response	High	Control group responded adequately
Domain 6: Confounding / Variable Control			
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	Reported information did not identify differences in confounding factors
	Metric 22: Health Outcomes Unrelated to Exposure	Medium	No information was reported to either support or dismiss differences unrelated to exposure
	Metric 23: Data Presentation and Analysis	High	Statistical methods were reported and appropriate for the data
	Metric 24: Reporting of Data	High	Data were reported for all outcomes by group and sex

Additional Comments: None

Overall Quality Determination**High**

Study Citation:	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.
Health Outcome(s):	Mortality
Reported Health Effect(s):	Mortality: Death
Duration:	Short-term (>1-30 days) 14 days Mouse
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	1944492

Domain	Metric	Rating	Comments
Domain 1: Test Substance			
	Metric 1: Test Substance Identity	High	Test substance was identified by nomenclature, CAS number, and structure
	Metric 2: Test Substance Source	High	Test substance was obtained from a commercial source: " ICC solvent Chemical Company (New York, NY) Lot number SC61377 and analytically verified.
	Metric 3: Test Substance Purity	High	Test substance was >99% purity verified analytically. Impurities were reported "Acidic components (assumed to be hydrochloric acid) were found to be present at a concentration of 10.8 ppm. One impurity with an area that was approximately 0.7% of the major peak area; this impurity, identified as 1 ,4-dichlorobenzene"
Domain 2: Test Design			
	Metric 4: Negative and Vehicle Controls	High	Concurrently treated vehicle control was used and appropriate for the study
	Metric 5: Positive Controls	N/A	Not necessary for the study type
	Metric 6: Randomized Allocation of Animals	Medium	The study reported the random allocation of animals into groups
Domain 3: Exposure Characterization			
	Metric 7: Preparation and Storage of Test Substance	High	Dose preparation and storage were reported "adding a weighed amount of 1 ,2-dichlorobenzene to the appropriate volume of corn oil and mixing for 15 minutes" then doses solutions were prepared by dilution. The mixture was stable at room temp for 7 days and solutions were stored no longer than 14 days at 4 degrees C
	Metric 8: Consistency of Exposure Administration	High	Details of exposure administration were reported and consistent. Gavage volume was not excessive 5ml/kg.
	Metric 9: Reporting of Doses/Concentrations	High	Doses were reported clearly
	Metric 10: Exposure Frequency and Duration	High	Exposure frequency (daily) and duration (14d) were appropriate for the study type
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	Medium	Number of exposure groups was adequate and consisted of 5 treated groups and a control. It was unclear if the highest dose was high enough
	Metric 12: Exposure Route and Method	High	Exposure route and method were suited to the test substance: gavage is appropriate
Domain 4: Test Animals			
	Metric 13: Test Animal Characteristics	High	Species, strain, sex, and age were all reported in table 1. Initial body weight was reported in the results
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were reported in table 1: temperature, humidity, light- dark cycle, diet, water availability and were adequate and consistent across all groups
	Metric 15: Number of Animals per Group	Medium	The number of animals per group was reported and appropriate for the study type: 5/group for short term
Domain 5: Outcome Assessment			

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Study Citation:	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.
Health Outcome(s):	Mortality
Reported Health Effect(s):	Mortality: Death
Duration:	Short-term (>1-30 days) 14 days Mouse
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	1944492

Domain	Metric	Rating	Comments
	Metric 16: Outcome Assessment Methodology	High	Outcome assessment was sensitive and appropriate for the outcome of interest
	Metric 17: Consistency of Outcome Assessment	High	Outcome was assessed consistently across groups
	Metric 18: Sampling Adequacy	High	Sampling was adequate
	Metric 19: Blinding of Assessors	N/A	Blinding was not necessary for the study type
	Metric 20: Negative Control Response	High	Control group responded adequately: all survived

Domain 6: Confounding / Variable Control

	Metric 21: Confounding Variables in Test Design and Procedures	Medium	Reported information did not identify differences in confounding factors
	Metric 22: Health Outcomes Unrelated to Exposure	Medium	No information was reported to either support or dismiss differences unrelated to exposure
	Metric 23: Data Presentation and Analysis	High	Statistical methods were reported and appropriate for the data
	Metric 24: Reporting of Data	High	Data were reported for all outcomes by group and sex

Additional Comments: None

Overall Quality Determination**High**

Study Citation:	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.			
Health Outcome(s):	Mortality			
Reported Health Effect(s):	Mortality: Death			
Duration:	Short-term (>1-30 days) 14 days Mouse: high dose			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	1944492			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	Test substance was identified by nomenclature, CAS number, and structure	
	Metric 2: Test Substance Source	High	Test substance was obtained from a commercial source: "ICC solvent Chemical Company (New York, NY) Lot number SC61377 and analytically verified.	
	Metric 3: Test Substance Purity	High	Test substance was >99% purity verified analytically. Impurities were reported "Acidic components (assumed to be hydrochloric acid) were found to be present at a concentration of 10.8 ppm. one impurity with an area that was approximately 0.7% of the major peak area; this impurity, identified as 1 ,4-dichlorobenzene"	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	Concurrently treated vehicle control was used and appropriate for the study	
	Metric 5: Positive Controls	N/A	Not necessary for the study type	
	Metric 6: Randomized Allocation of Animals	Medium	The study reported the random allocation of animals into groups	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	High	Dose preparation and storage were reported "adding a weighed amount of 1 ,2-dichlorobenzene to the appropriate volume of corn oil and mixing for 15 minutes" then doses solutions were prepared by dilution. The mixture was stable at room temp for 7 days and solutions were stored no longer than 14days at 4 degrees C	
	Metric 8: Consistency of Exposure Administration	High	Details of exposure administration were reported and consistent. gavage volume was not excessive 5ml/kg.	
	Metric 9: Reporting of Doses/Concentrations	High	Doses were reported clearly	
	Metric 10: Exposure Frequency and Duration	High	Exposure frequency (daily) and duration (14d) were appropriate for the study type	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	Uninformative	Number of exposure groups was adequate and consisted of 5 treated groups and a control. Dose spacing resulted in excessive mortality at all doses	
	Metric 12: Exposure Route and Method	High	Exposure route and method were suited to the test substance: gavage is appropriate	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	High	Species, strain, sex, and age were all reported in table 1. Initial body weight was reported in the results	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were reported in table 1: temperature, humidity, light- dark cycle, diet, water availability and were adequate and consistent across all groups	
	Metric 15: Number of Animals per Group	Medium	The number of animals per group was reported and appropriate for the study type: 5/group for short term	
Domain 5: Outcome Assessment				

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Study Citation:	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.			
Health Outcome(s):	Mortality			
Reported Health Effect(s):	Mortality: Death			
Duration:	Short-term (>1-30 days) 14 days Mouse: high dose			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	1944492			
Domain	Metric	Rating	Comments	
	Metric 16: Outcome Assessment Methodology	High	Outcome assessment was sensitive and appropriate for the outcome	
	Metric 17: Consistency of Outcome Assessment	High	Outcome was assessed consistently across groups	
	Metric 18: Sampling Adequacy	High	Sampling was adequate.	
	Metric 19: Blinding of Assessors	N/A	Blinding was not necessary for the study type	
	Metric 20: Negative Control Response	Low	There was one death in the male control group	
Domain 6: Confounding / Variable Control				
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	Reported information did not identify differences in confounding factors	
	Metric 22: Health Outcomes Unrelated to Exposure	Medium	No information was reported to either support or dismiss differences unrelated to exposure	
	Metric 23: Data Presentation and Analysis	High	Statistical methods were reported and appropriate for the data	
	Metric 24: Reporting of Data	High	Data were reported for all outcomes by group and sex	
Additional Comments:	None			

Overall Quality Determination**Uninformative**

Study Citation:	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.		
Health Outcome(s):	Hepatic/Liver		
Reported Health Effect(s):	Hepatic/Liver: Liver weight, histopathology, vlinical chemistry (Mice & rats: ALP, GGT, and glutamic pyruvic transaminase; Rats only: bilirubin, cholesterol, triglycerides, BUN, glucose, total protein)		
Duration:	Short-term (>1-30 days) 14 days Mouse: high dose		
Chemical:	o-Dichlorobenzene- Parent compound		
HERO ID:	1944492		
Domain	Metric	Rating	Comments
Domain 1: Test Substance			
	Metric 1: Test Substance Identity	High	test substance was identified by nomenclature, CAS number, and structure
	Metric 2: Test Substance Source	High	Test substance was obtained from a commercial source: " ICC solvent Chemical Company (New York, NY) Lot number SC61377 and analytically verified.
	Metric 3: Test Substance Purity	High	test substance was >99% purity verified analytically. impurities were reported "Acidic components (assumed to be hydrochloric acid) were found to be present at a concentration of 10.8 ppm. one impurity with an area that was approximately 0.7% of the major peak area; this impurity, identified as 1 ,4-dichlorobenzene"
Domain 2: Test Design			
	Metric 4: Negative and Vehicle Controls	High	Concurrently treated vehicle control was used and appropriate for the study
	Metric 5: Positive Controls	N/A	not necessary for the study type
	Metric 6: Randomized Allocation of Animals	Medium	the study reported the random allocation of animals into groups
Domain 3: Exposure Characterization			
	Metric 7: Preparation and Storage of Test Substance	High	dose preparation and storage were reported "adding a weighed amount of 1 ,2-dichlorobenzene to the appropriate volume of corn oil and mixing for 15 minutes" then doses solutions were prepared by dilution. The mixture was stable at room temp for 7 days and solutions were stored no longer than 14days at 4 degrees C
	Metric 8: Consistency of Exposure Administration	High	details of exposure administration were reported and consistent. gavage volume was not excessive 5ml/kg.
	Metric 9: Reporting of Doses/Concentrations	High	doses were reported clearly
	Metric 10: Exposure Frequency and Duration	High	exposure frequency (daily) and duration (14d) were appropriate for the study type
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	Uninformative	Number of exposure groups was adequate and consisted of 5 treated groups and a control. Dose spacing resulted in excessive mortality at all doses
	Metric 12: Exposure Route and Method	High	Exposure route and method were suited to the test substance: gavage is appropriate
Domain 4: Test Animals			
	Metric 13: Test Animal Characteristics	High	Species, strain, sex, and age were all reported in table 1. initial body weight was reported in the results
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were reported in table 1: temperature, humidity, light- dark cycle, diet, water availability and were adequate and consistent across all groups
	Metric 15: Number of Animals per Group	Medium	The number of animals per group was reported and appropriate for the study type: 5/group for short term
Domain 5: Outcome Assessment			

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Study Citation:	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.			
Health Outcome(s):	Hepatic/Liver			
Reported Health Effect(s):	Hepatic/Liver: Liver weight, histopathology, vlinical chemistry (Mice & rats: ALP, GGT, and glutamic pyruvic transaminase; Rats only: bilirubin, cholesterol, triglycerides, BUN, glucose, total protein)			
Duration:	Short-term (>1-30 days) 14 days Mouse: high dose			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	1944492			
Domain	Metric	Rating	Comments	
	Metric 16:	Outcome Assessment Methodology	High	Outcome assessment was sensitive and appropriate for the outcome it is unclear whether the timing of evaluation of hepatic histology was done consistently as only 2 dose groups were evaluated, male and females doses were different and the mortality in these dose groups occurred early and at different times samples were from only 3 animals, and few dose groups blinding was not necessary for the study type control group responded appropriately
	Metric 17:	Consistency of Outcome Assessment	Low	
	Metric 18:	Sampling Adequacy	Low	
	Metric 19:	Blinding of Assessors	N/A	
	Metric 20:	Negative Control Response	High	
Domain 6: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	reported information did not identify differences in confounding factors
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	No information was reported to either support or dismiss differences unrelated to exposure
	Metric 23:	Data Presentation and Analysis	High	Statistical methods were reported and appropriate for the data
	Metric 24:	Reporting of Data	High	Data were reported for all outcomes by group and sex

Additional Comments: None

Overall Quality Determination**Uninformative**

Study Citation:	Robinson, M., Bercz, J. P., Ringhand, H. P., Condie, L. W., Parnell, M. J. (1991). Ten- and ninety-day toxicity studies of 1,2-dichlorobenzene administered by oral gavage to Sprague-Dawley rats. Drug and Chemical Toxicology 14(1-2):83-112.			
Health Outcome(s):	Hepatic/Liver; Renal/Kidney; Reproductive/Developmental; Immune/Hematological; Cardiovascular; Neurological/Behavioral; Lung/Respiratory;			
Reported Health Effect(s):	Hepatic/Liver: Liver weights and liver-to-weight body ratios; microscopic hepatocellular changes.; Renal/Kidney: Urinalysis: Samples were analyzed for pH, glucose, protein, bilirubin, urobilinogen, and occult blood. Increased kidney weight and kidney-to-body weight ratio and increased BUN levels.; Reproductive/Developmental: Organ weights for testes/ovaries.; Immune/Hematological: Hematological parameters, consisting of hemoglobin (Hgb), hematocrit (Hct), red blood cell (RBC) count, white blood cell (WBC)count, and mean cell volume (MCV); organ weights for thymus and spleen.; Cardiovascular: Heart organ weight.; Neurological/Behavioral: Brain organ weight; Lung/Respiratory: Lung organ weight;			
Duration:	Short-term (>1-30 days) 10-day			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	5099073			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	All Outcomes: Chemical identified by nomenclature,	
	Metric 2: Test Substance Source	High	All Outcomes: 1,2-Dichlorobenzene (Lot AM/9202 PL) was obtained from Aldrich-Chemical Company (Milwaukee, WI).	
	Metric 3: Test Substance Purity	High	All Outcomes: specified as 99% pure by the vendor, was analyzed for purity by mass spectrometry prior to use in these studies. There were no impurities present	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	All Outcomes: Appropriate vehicle control (corn oil) used	
	Metric 5: Positive Controls	N/A	Hepatic/Liver: Missing Comment ; Renal/Kidney: Missing Comment ; Reproductive/Developmental: Missing Comment ; Immune/Hematological: Missing Comment ; Cardiovascular: Missing Comment ; Neurological/Behavioral: Missing Comment ; Lung/Respiratory: Missing Comment	
	Metric 6: Randomized Allocation of Animals	Medium	All Outcomes: animals randomly assigned to vehicle and treatment groups using a computer-generated table of random numbers.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Low	All Outcomes: Preparation and storage was not adequately described. The authors noted that dosing formulations were made using corn oil and administered by oral gavage with a 20-gauge intubating needle attached to a 1-mL disposable syringe. All doses of DCB were delivered at a constant volume of 1.0 mL/kg. Control animals received corn oil at the samevolume.	
	Metric 8: Consistency of Exposure Administration	High	All Outcomes: Details of exposure administration were reported and exposures were administered consistently across study groups.	
	Metric 9: Reporting of Doses/Concentrations	High	All Outcomes: All doses are reported	
	Metric 10: Exposure Frequency and Duration	High	All Outcomes: The exposure frequency and duration of exposure were reported and appropriate for this study type.	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: The number of exposure groups were adequate.	
	Metric 12: Exposure Route and Method	High	All Outcomes: The route and method of exposure were reported and were suited to the test substance.	

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Study Citation:	Robinson, M., Bercz, J. P., Ringhand, H. P., Condie, L. W., Parnell, M. J. (1991). Ten- and ninety-day toxicity studies of 1,2-dichlorobenzene administered by oral gavage to Sprague-Dawley rats. Drug and Chemical Toxicology 14(1-2):83-112.			
Health Outcome(s):	Hepatic/Liver; Renal/Kidney; Reproductive/Developmental; Immune/Hematological; Cardiovascular; Neurological/Behavioral; Lung/Respiratory;			
Reported Health Effect(s):	Hepatic/Liver: Liver weights and liver-to-weight body ratios; microscopic hepatocellular changes.; Renal/Kidney: Urinalysis: Samples were analyzed for pH, glucose, protein, bilirubin, urobilinogen, and occult blood. Increased kidney weight and kidney-to-body weight ratio and increased BUN levels.; Reproductive/Developmental: Organ weights for testes/ovaries.; Immune/Hematological: Hematological parameters, consisting of hemoglobin (Hgb), hematocrit (Hct), red blood cell (RBC) count, white blood cell (WBC)count, and mean cell volume (MCV); organ weights for thymus and spleen.; Cardiovascular: Heart organ weight.; Neurological/Behavioral: Brain organ weight; Lung/Respiratory: Lung organ weight;			
Duration:	Short-term (>1-30 days) 10-day			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	5099073			
Domain	Metric	Rating	Comments	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	High	All Outcomes: Age and starting body weight were not reported.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: All husbandry conditions were reported (e.g., temperature, humidity, light- dark cycle, diet, water availability) and were adequate.	
	Metric 15: Number of Animals per Group	Medium	All Outcomes: Appropriate number of animals used to observe toxicological effects	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	Medium	All Outcomes: Histopathological analyses were only conducted for controls and high dose animals.	
	Metric 17: Consistency of Outcome Assessment	Medium	All Outcomes: Details about timing of sampling collections were not provided	
	Metric 18: Sampling Adequacy	Medium	All Outcomes: Some treatment-related changes were observed at the high dose. A significant increase in the incidence of hepatocellular necrosis was seen in the 300 mg/kg group of males compared to controls; Males also displayed significant increases in ALT (300 mg/kg) and increased hepatocellular lesions	
	Metric 19: Blinding of Assessors	N/A	Hepatic/Liver: Missing Comment ; Renal/Kidney: Missing Comment ; Reproductive/Developmental: Missing Comment ; Immune/Hematological: Missing Comment ; Cardiovascular: Missing Comment ; Neurological/Behavioral: Missing Comment ; Lung/Respiratory: Missing Comment	
	Metric 20: Negative Control Response	High	All Outcomes: The biological responses of the negative control groups 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.	
	Metric 22: Health Outcomes Unrelated to Exposure	High	All Outcomes: No information suggesting 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: Appropriate statistical analyses were performed; data on males and females were analyzed separately	
	Metric 24: Reporting of Data	Low	All Outcomes: All outcomes and results were not presented	
Additional Comments:	None			

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Study Citation:	Robinson, M., Bercz, J. P., Ringhand, H. P., Condie, L. W., Parnell, M. J. (1991). Ten- and ninety-day toxicity studies of 1,2-dichlorobenzene administered by oral gavage to Sprague-Dawley rats. Drug and Chemical Toxicology 14(1-2):83-112.
Health Outcome(s):	Hepatic/Liver; Renal/Kidney; Reproductive/Developmental; Immune/Hematological; Cardiovascular; Neurological/Behavioral; Lung/Respiratory;
Reported Health Effect(s):	Hepatic/Liver: Liver weights and liver-to-weight body ratios; microscopic hepatocellular changes.; Renal/Kidney: Urinalysis: Samples were analyzed for pH, glucose, protein, bilirubin, urobilinogen, and occult blood. Increased kidney weight and kidney-to-body weight ratio and increased BUN levels.; Reproductive/Developmental: Organ weights for testes/ovaries.; Immune/Hematological: Hematological parameters, consisting of hemoglobin (Hgb), hematocrit (Hct), red blood cell (RBC) count, white blood cell (WBC)count, and mean cell volume (MCV); organ weights for thymus and spleen.; Cardiovascular: Heart organ weight.; Neurological/Behavioral: Brain organ weight; Lung/Respiratory: Lung organ weight;
Duration:	Short-term (>1-30 days) 10-day
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	5099073

Domain	Metric	Rating	Comments
Overall Quality Determination		High	

Study Citation:	Robinson, M., Bercz, J. P., Ringhand, H. P., Condie, L. W., Parnell, M. J. (1991). Ten- and ninety-day toxicity studies of 1,2-dichlorobenzene administered by oral gavage to Sprague-Dawley rats. Drug and Chemical Toxicology 14(1-2):83-112.			
Health Outcome(s):	Mortality; Nutritional/Metabolic;			
Reported Health Effect(s):	Mortality: Animals were checked twice daily. No deaths were observed.; Nutritional/Metabolic: Body weight changes and food and water consumption;			
Duration:	Short-term (>1-30 days) 10-day			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	5099073			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	All Outcomes: Chemical identified by nomenclature,	
	Metric 2: Test Substance Source	High	All Outcomes: 1,2-Dichlorobenzene (Lot AM/9202 PL) was obtained from Aldrich-Chemical Company (Milwaukee, WI).	
	Metric 3: Test Substance Purity	High	All Outcomes: specified as 99% pure by the vendor, was analyzed for purity by mass spectrometry prior to use in these studies. There were no impurities present	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	All Outcomes: Appropriate vehicle control (corn oil) used	
	Metric 5: Positive Controls	N/A	Mortality: Missing Comment ; Nutritional/Metabolic: Missing Comment	
	Metric 6: Randomized Allocation of Animals	Medium	All Outcomes: animals randomly assigned to vehicle and treatment groups using a computer-generated table of random numbers.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Low	All Outcomes: Preparation and storage was not adequately described. The authors noted that dosing formulations were made using corn oil and administered by oral gavage with a 20-gauge intubating needle attached to a 1-mL disposable syringe. All doses of DCB were delivered at a constant volume of 1.0 mL/kg. Control animals received corn oil at the same volume.	
	Metric 8: Consistency of Exposure Administration	High	All Outcomes: Details of exposure administration were reported and exposures were administered consistently across study groups.	
	Metric 9: Reporting of Doses/Concentrations	High	All Outcomes: All doses are reported	
	Metric 10: Exposure Frequency and Duration	High	All Outcomes: The exposure frequency and duration of exposure were reported and appropriate for this study type.	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: The number of exposure groups were adequate.	
	Metric 12: Exposure Route and Method	High	All Outcomes: The route and method of exposure were reported and were suited to the test substance.	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	Medium	All Outcomes: Age and starting body weight were not reported.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: All husbandry conditions were reported (e.g., temperature, humidity, light- dark cycle, diet, water availability) and were adequate.	
	Metric 15: Number of Animals per Group	Medium	All Outcomes: Appropriate number of animals used to observe toxicological effects	
Domain 5: Outcome Assessment				
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Study Citation:	Robinson, M., Bercz, J. P., Ringhand, H. P., Condie, L. W., Parnell, M. J. (1991). Ten- and ninety-day toxicity studies of 1,2-dichlorobenzene administered by oral gavage to Sprague-Dawley rats. Drug and Chemical Toxicology 14(1-2):83-112.
Health Outcome(s):	Mortality; Nutritional/Metabolic;
Reported Health Effect(s):	Mortality: Animals were checked twice daily. No deaths were observed.; Nutritional/Metabolic: Body weight changes and food and water consumption;
Duration:	Short-term (>1-30 days) 10-day
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	5099073

Domain	Metric	Rating	Comments
	Metric 16: Outcome Assessment Methodology	High	All Outcomes: The outcome assessment methodology addressed the intended outcome.
	Metric 17: Consistency of Outcome Assessment	Medium	All Outcomes: Details about timing of sampling collections were not provided
	Metric 18: Sampling Adequacy	High	All Outcomes: Reported information indicates the study used adequate sampling for the outcome.
	Metric 19: Blinding of Assessors	N/A	Mortality: Missing Comment ; Nutritional/Metabolic: Missing Comment
	Metric 20: Negative Control Response	High	All Outcomes: The biological responses of the negative control groups 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.
	Metric 22: Health Outcomes Unrelated to Exposure	High	All Outcomes: No information suggesting 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	All Outcomes: No statistical analyses needed as no mortality occurred
	Metric 24: Reporting of Data	High	All Outcomes: No mortality was reported.

Additional Comments: None

Overall Quality Determination**High**

Study Citation:	Zissu, D. (1995). Histopathological changes in the respiratory tract of mice exposed to ten families of airborne chemicals. Journal of Applied Toxicology 15(3):207-213.			
Health Outcome(s):	Mortality			
Reported Health Effect(s):	Mortality: Mortality			
Duration:	Short-term (>1-30 days) 14-day inhalation study			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	201742			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
Metric 1:	Test Substance Identity	High	The chemical is identified by name as 1,2-dichlorobenzene, which is o-dichlorobenzene. No CASRN is reported.	
Metric 2:	Test Substance Source	High	The test substance source is reported. No explicit analytical verification of the test substance identity was described, but test substance concentrations were measured during the exposure study so the identity may have been determined concurrently.	
Metric 3:	Test Substance Purity	High	The test substance was reported and is sufficiently high.	
Domain 2: Test Design				
Metric 4:	Negative and Vehicle Controls	High	An appropriate negative control of filtered air was used.	
Metric 5:	Positive Controls	N/A	A positive control was not required for the experiment’s design.	
Metric 6:	Randomized Allocation of Animals	Low	No method of randomization or any allocation methods were described by the authors.	
Domain 3: Exposure Characterization				
Metric 7:	Preparation and Storage of Test Substance	Low	Test substance preparation and generation of the vapors were described in adequate detail, but no information on test substance storage is described, which may be concerning due to the volatility of the test substance.	
Metric 8:	Consistency of Exposure Administration	High	The exposure administration appears to be consistent between groups.	
Metric 9:	Reporting of Doses/Concentrations	Medium	The target, nominal and analytical concentrations were reported, but the range of analytical concentrations varied by more than 10%.	
Metric 10:	Exposure Frequency and Duration	High	The exposure frequency and duration are reported and are appropriate for the study design.	
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	There are minor concerns regarding concentration spacing in that only 2 concentrations were used, which limits the study’s ability to determine dose-response.	
Metric 12:	Exposure Route and Method	Medium	A dynamic exposure chamber was used, but the authors do not report air changes/hour.	
Domain 4: Test Animals				
Metric 13:	Test Animal Characteristics	Medium	Test animal, species, sex, strain, starting body weight and source were reported. Starting age was not reported, but is unlikely to have a large impact on the results.	
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	The authors report temperature and day/night cycle for animal housing conditions, along with food and water availability but do not report humidity.	
Metric 15:	Number of Animals per Group	Medium	The number of animals per group is sufficient.	

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Study Citation:	Zissu, D. (1995). Histopathological changes in the respiratory tract of mice exposed to ten families of airborne chemicals. Journal of Applied Toxicology 15(3):207-213.			
Health Outcome(s):	Mortality			
Reported Health Effect(s):	Mortality: Mortality			
Duration:	Short-term (>1-30 days) 14-day inhalation study			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	201742			
Domain	Metric	Rating	Comments	
Domain 5: Outcome Assessment				
Metric 16:	Outcome Assessment Methodology	High	The outcome assessment methodology adequately assessed the outcomes of interest.	
Metric 17:	Consistency of Outcome Assessment	High	There do not appear to be any issues with the consistency of outcome assessments across groups.	
Metric 18:	Sampling Adequacy	High	All individual animals assessed for mortality.	
Metric 19:	Blinding of Assessors	High	Blinding was not reported but mortality is not subjective.	
Metric 20:	Negative Control Response	High	The authors report results from the negative control group and report that no effects were observed, so the negative control response was adequate.	
Domain 6: Confounding / Variable Control				
Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Not all information was reported to evaluate confounding. The authors did report that the chosen concentrations were taken from an earlier study in which an RD50 for decreased respiratory rate was taken, and the study concentrations were the RD50 and 0.3 X RD50. But the authors did not explicitly report if the respiratory rate was measured in this study, but they would have been aware of the chemical’s irritant properties.	
Metric 22:	Health Outcomes Unrelated to Exposure	High	The authors report clinical signs and mortality and did not indicate that any attrition had occurred.	
Metric 23:	Data Presentation and Analysis	Uninformative	Proper statistics were not reported. The total number of dead animals were presented but not compared to the starting number.	
Metric 24:	Reporting of Data	High	Author reported no mortality in exposed and control groups.	
Additional Comments:	Percentage dead not reported. The methods refer to an earlier publication, but the available data is not considered sufficient for statistical risk assessment purposes.			

Overall Quality Determination**Uninformative**

Study Citation:	Zissu, D. (1995). Histopathological changes in the respiratory tract of mice exposed to ten families of airborne chemicals. Journal of Applied Toxicology 15(3):207-213.			
Health Outcome(s):	Lung/Respiratory; Lung/Respiratory; Lung/Respiratory;			
Reported Health Effect(s):	Lung/Respiratory: Nasal turbinate histopathology, respiratory and olfactory epithelium lesions.; Lung/Respiratory: Nasal turbinate histopathology, respiratory and olfactory epithelium lesions.;			
Duration:	Short-term (>1-30 days) 4-day inhalation study			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	201742			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
Metric 1:	Test Substance Identity	High	All Outcomes: The chemical is identified by name as 1,2-dichlorobenzene, which is o-dichlorobenzene. No CASRN is reported.	
Metric 2:	Test Substance Source	High	All Outcomes: The test substance source is reported. No explicit analytical verification of the test substance identity was described, but test substance concentrations were measured during the exposure study so the identity may have been determined concurrently.	
Metric 3:	Test Substance Purity	High	All Outcomes: The test substance was reported and is sufficiently high.	
Domain 2: Test Design				
Metric 4:	Negative and Vehicle Controls	High	All Outcomes: An appropriate negative control of filtered air was used.	
Metric 5:	Positive Controls	N/A	All Outcomes: A positive control was not required for the experiment’s design.	
Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: No method of randomization or any allocation methods were described by the authors.	
Domain 3: Exposure Characterization				
Metric 7:	Preparation and Storage of Test Substance	Low	All Outcomes: Test substance preparation and generation of the vapors were described in adequate detail, but no information on test substance storage is described, which may be concerning due to the volatility of the test substance.	
Metric 8:	Consistency of Exposure Administration	High	All Outcomes: The exposure administration appears to be consistent between groups.	
Metric 9:	Reporting of Doses/Concentrations	Medium	All Outcomes: The target, nominal and analytical concentrations were reported, but the range of analytical concentrations varied by more than 10%.	
Metric 10:	Exposure Frequency and Duration	High	All Outcomes: The exposure frequency and duration are reported and are appropriate for the study design.	
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	All Outcomes: There are minor concerns regarding concentration spacing in that only 2 concentrations were used, which limits the study’s ability to determine dose-response.	
Metric 12:	Exposure Route and Method	Medium	All Outcomes: A dynamic exposure chamber was used, but the authors do not report air changes/hour.	
Domain 4: Test Animals				
Metric 13:	Test Animal Characteristics	Medium	All Outcomes: Test animal, species, sex, strain, starting body weight and source were reported. Starting age was not reported, but is unlikely to have a large impact on the results.	
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	All Outcomes: The authors report temperature and day/night cycle for animal housing conditions, along with food and water availability but do not report humidity.	
Metric 15:	Number of Animals per Group	Medium	All Outcomes: The number of animals per group is sufficient.	

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Study Citation:	Zissu, D. (1995). Histopathological changes in the respiratory tract of mice exposed to ten families of airborne chemicals. Journal of Applied Toxicology 15(3):207-213.
Health Outcome(s):	Lung/Respiratory; Lung/Respiratory; Lung/Respiratory;
Reported Health Effect(s):	Lung/Respiratory: Nasal turbinate histopathology, respiratory and olfactory epithelium lesions.; Lung/Respiratory: Nasal turbinate histopathology, respiratory and olfactory epithelium lesions.;
Duration:	Short-term (>1-30 days) 4-day inhalation study
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	201742

Domain	Metric	Rating	Comments
Domain 5: Outcome Assessment			
	Metric 16: Outcome Assessment Methodology	High	All Outcomes: The outcome assessment methodology adequately assessed the outcomes of interest.
	Metric 17: Consistency of Outcome Assessment	High	All Outcomes: There do not appear to be any issues with the consistency of outcome assessments across groups.
	Metric 18: Sampling Adequacy	Low	All Outcomes: Number of tissue slices surveyed was not reported.
	Metric 19: Blinding of Assessors	Medium	All Outcomes: Blinding was not reported but is not likely to have a large impact on the results given that the outcome was essentially screening level histopathology.
	Metric 20: Negative Control Response	High	All Outcomes: The authors report results from the negative control group and report that no effects were observed, so the negative control response was adequate.
Domain 6: Confounding / Variable Control			
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	All Outcomes: Not all information was reported to evaluate confounding. The authors did report that the chosen concentrations were taken from an earlier study in which an RD50 for decreased respiratory rate was taken, and the study concentrations were the RD50 and 0.3 X RD50. But the authors did not explicitly report if the respiratory rate was measured in this study, but they would have been aware of the chemical's irritant properties.
	Metric 22: Health Outcomes Unrelated to Exposure	High	All Outcomes: The authors report clinical signs and mortality and did not indicate that any attrition had occurred.
	Metric 23: Data Presentation and Analysis	N/A	All Outcomes: Statistical methods were not necessary as the study was focused on pathology findings.
	Metric 24: Reporting of Data	Low	All Outcomes: Only data were reported for pathology at the lowest concentration rather than the highest concentration. Severity scores are described, but are not presented with all concentrations used in the study.

Additional Comments: None

Overall Quality Determination**Medium**

Study Citation:	Battelle, (1978). Subchronic toxicity study - ortho-dichlorobenzene, Fischer 344 rats. 7820535:#40-7820535.			
Health Outcome(s):	Mortality; Immune/Hematological; Renal/Kidney; Lung/Respiratory; Gastrointestinal; Neurological/Behavioral; Reproductive/Developmental; Pancreas (Pancreas); Hepatic/Liver;			
Reported Health Effect(s):	Mortality: Death; Immune/Hematological: Spleen and thymus weight, histopathology hematology (hemoglobin, hematocrit, white blood cell count, red blood cell count, mean corpuscular volume, platelet count, reticulocyte count), globulin fractions; Renal/Kidney: Kidney weight and histopathology, urinalysis (pH, protein, glucose, ketones, bilirubin, occult blood, specific gravity, creatinine, uroporphyrins, coproporphyrins); Lung/Respiratory: Lung weight and histopathology; Gastrointestinal: Histopathology of salivary gland, esophagus, colon and cecum; Neurological/Behavioral: Brain weight, clinical signs (none reported), histopathology of spinal cord; Reproductive/Developmental: Testicle, ovary, uterus weight; Pancreas (Pancreas): Histopathology of pancreas; Hepatic/Liver: Liver weight and histopathology, Clinical chemistry (ALP, SGPT, gamma-glutamyl transpeptidase, bilirubin, cholesterol, triglycerides, BUN, glucose, total protein); Subchronic (>30-91 days) 13 weeks			
Duration:	Subchronic (>30-91 days) 13 weeks			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	5264231			
Domain		Metric	Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test Substance Identity	High	All Outcomes: Test substance identified as o-dichlorobenzene. The chemical structure was provided in appendix A.
	Metric 2:	Test Substance Source	High	Mortality: Test substance was purchased from Midwest Research Institute. Batch and Lot #s were provided in Appendix A.; Immune/Hematological: Test substance was purchased from Midwest Research Institute. Batch # was provided in Appendix A.; Renal/Kidney: Test substance was purchased from Midwest Research Institute. Batch # was provided in Appendix A.; Lung/Respiratory: Test substance was purchased from Midwest Research Institute. Batch # was provided in Appendix A.; Gastrointestinal: Test substance was purchased from Midwest Research Institute. Batch # was provided in Appendix A.; Neurological/Behavioral: Test substance was purchased from Midwest Research Institute. Batch # was provided in Appendix A.; Reproductive/Developmental: Test substance was purchased from Midwest Research Institute. Batch # was provided in Appendix A.; Pancreas (Pancreas): Test substance was purchased from Midwest Research Institute. Batch # was provided in Appendix A.; Hepatic/Liver: Test substance was purchased from Midwest Research Institute. Batch # was provided in Appendix A.
	Metric 3:	Test Substance Purity	High	All Outcomes: Purity reported as 99%. The Batch Chemical Data Record and analytical reports were provided in Appendix A.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: An appropriate control was included. Control animals received plain corn oil
	Metric 5:	Positive Controls	N/A	All Outcomes: No positive controls needed for this study.
	Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: The study reported that animals were randomly allocated into study groups.
Domain 3: Exposure Characterization				
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Study Citation:	Battelle, (1978). Subchronic toxicity study - ortho-dichlorobenzene, Fischer 344 rats. 7820535:#40-7820535.			
Health Outcome(s):	Mortality; Immune/Hematological; Renal/Kidney; Lung/Respiratory; Gastrointestinal; Neurological/Behavioral; Reproductive/Developmental; Pancreas (Pancreas); Hepatic/Liver;			
Reported Health Effect(s):	Mortality: Death; Immune/Hematological: Spleen and thymus weight, histopathology hematology (hemoglobin, hematocrit, white blood cell count, red blood cell count, mean corpuscular volume, platelet count, reticulocyte count), globulin fractions; Renal/Kidney: Kidney weight and histopathology, urinalysis (pH, protein, glucose, ketones, bilirubin, occult blood, specific gravity, creatinine, uroporphyrins, coproporphyrins); Lung/Respiratory: Lung weight and histopathology; Gastrointestinal: Histopathology of salivary gland, esophagus, colon and cecum; Neurological/Behavioral: Brain weight, clinical signs (none reported), histopathology of spinal cord; Reproductive/Developmental: Testicle, ovary, uterus weight; Pancreas (Pancreas): Histopathology of pancreas; Hepatic/Liver: Liver weight and histopathology, Clinical chemistry (ALP, SGPT, gamma-glutamyl transpeptidase, bilirubin, cholesterol, triglycerides, BUN, glucose, total protein);			
Duration:	Subchronic (>30-91 days) 13 weeks			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	5264231			
Domain		Metric	Rating	Comments
	Metric 7:	Preparation and Storage of Test Substance	High	All Outcomes: "The selected doses were prepared by placing a weighed portion of ortho-dichlorobenzene into a mixing graduated cylinder and adding corn oil to make up the proper volume for the highest selected dose of 500 ~g/kg. This mixture was stirred for 15 minutes. The remaining four doses were prepared by sequential dilutions of the stock (highest dose) solution." Mixtures were prepared fresh weekly. One analysis of dose concentrations was performed to confirm dose accuracy.
	Metric 8:	Consistency of Exposure Administration	High	Mortality: Test substance was administered via oral gavage. Gavage volume was not excessive (0.5 ml/100g of body weight).; Immune/Hematological: Test substance was administered via oral gavage. Gavage volume was not excessive (0.5 ml/100g of body weight).; Renal/Kidney: Test substance was administered via oral gavage. Gavage volume was not excessive (0.5 ml/100g of body weight).; Lung/Respiratory: Test substance was administered via oral gavage. Gavage volume was not excessive (0.5 ml/100g of body weight).; Gastrointestinal: Test substance was administered via oral gavage. Gavage volume was not excessive (0.5 ml/100g of body weight).; Neurological/Behavioral: Test substance was administered via oral gavage. Gavage volume was not excessive (0.5 ml/100g of body weight).; Reproductive/Developmental: Test substance was administered via oral gavage. Gavage volume was not excessive (0.5 ml/100g of body weight).; Pancreas (Pancreas): Test substance was administered via oral gavage. Gavage volume was not excessive (0.5 ml/100g of body weight).; Hepatic/Liver: Test substance was administered via oral gavage. Gavage volume was not excessive (0.5 ml/100g of body weight).
	Metric 9:	Reporting of Doses/Concentrations	High	All Outcomes: Doses were reported without ambiguity.
	Metric 10:	Exposure Frequency and Duration	Medium	All Outcomes: Animals were dosed 5 days per week. Current OECD TG 408 recommended dosing 7 days per week for a 90-day study. Justification is required for a lower frequency of dosing. Study author do not justify dosing animals for only 5 days per week.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: A control plus 5 treatment groups was included, which was sufficient to see a full range of responses.
	Metric 12:	Exposure Route and Method	High	All Outcomes: Oral gavage was appropriate for this study type.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	High	All Outcomes: Strain, species, sex, age and starting body weight were reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: All husbandry conditions were reported and were appropriate.

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Study Citation:	Battelle, (1978). Subchronic toxicity study - ortho-dichlorobenzene, Fischer 344 rats. 7820535:#40-7820535.			
Health Outcome(s):	Mortality; Immune/Hematological; Renal/Kidney; Lung/Respiratory; Gastrointestinal; Neurological/Behavioral; Reproductive/Developmental; Pancreas (Pancreas); Hepatic/Liver;			
Reported Health Effect(s):	Mortality: Death; Immune/Hematological: Spleen and thymus weight, histopathology hematology (hemoglobin, hematocrit, white blood cell count, red blood cell count, mean corpuscular volume, platelet count, reticulocyte count), globulin fractions; Renal/Kidney: Kidney weight and histopathology, urinalysis (pH, protein, glucose, ketones, bilirubin, occult blood, specific gravity, creatinine, uroporphyrins, coproporphyrins); Lung/Respiratory: Lung weight and histopathology; Gastrointestinal: Histopathology of salivary gland, esophagus, colon and cecum; Neurological/Behavioral: Brain weight, clinical signs (none reported), histopathology of spinal cord; Reproductive/Developmental: Testicle, ovary, uterus weight; Pancreas (Pancreas): Histopathology of pancreas; Hepatic/Liver: Liver weight and histopathology, Clinical chemistry (ALP, SGPT, gamma-glutamyl transpeptidase, bilirubin, cholesterol, triglycerides, BUN, glucose, total protein); Subchronic (>30-91 days) 13 weeks			
Duration:	Subchronic (>30-91 days) 13 weeks			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	5264231			
Domain	Metric	Rating	Comments	
	Metric 15: Number of Animals per Group	Medium	All Outcomes: 10 rats per sex were included in each treatment group, which is appropriate for subchronic studies.	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	High	All Outcomes: The outcome assessment methodology addressed the intended outcome(s) of interest AND the assessment methodology was sensitive and appropriate for the outcomes(s) of interest.	
	Metric 17: Consistency of Outcome Assessment	High	All Outcomes: 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: No need to blind assessors in this study.	
	Metric 20: Negative Control Response	High	All Outcomes: The biological responses of the negative control group(s) were adequate (e.g., no/low incidence of outcomes of interest in the study).	
Domain 6: Confounding / Variable Control				
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	All Outcomes: Food intake did not vary across treatment groups. Water intake was not recorded.	
	Metric 22: Health Outcomes Unrelated to Exposure	High	Mortality: Missing Comment ; Immune/Hematological: Missing Comment ; Renal/Kidney: Missing Comment ; Lung/Respiratory: Missing Comment ; Gastrointestinal: Missing Comment ; Neurological/Behavioral: Missing Comment ; Reproductive/Developmental: Missing Comment ; Pancreas (Pancreas): Missing Comment ; Hepatic/Liver: Missing Comment	
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Study Citation:	Battelle, (1978). Subchronic toxicity study - ortho-dichlorobenzene, Fischer 344 rats. 7820535:#40-7820535.
Health Outcome(s):	Mortality; Immune/Hematological; Renal/Kidney; Lung/Respiratory; Gastrointestinal; Neurological/Behavioral; Reproductive/Developmental; Pancreas (Pancreas); Hepatic/Liver;
Reported Health Effect(s):	Mortality: Death; Immune/Hematological: Spleen and thymus weight, histopathology hematology (hemoglobin, hematocrit, white blood cell count, red blood cell count, mean corpuscular volume, platelet count, reticulocyte count), globulin fractions; Renal/Kidney: Kidney weight and histopathology, urinalysis (pH, protein, glucose, ketones, bilirubin, occult blood, specific gravity, creatinine, uroporphyrins, coproporphyrins); Lung/Respiratory: Lung weight and histopathology; Gastrointestinal: Histopathology of salivary gland, esophagus, colon and cecum; Neurological/Behavioral: Brain weight, clinical signs (none reported), histopathology of spinal cord; Reproductive/Developmental: Testicle, ovary, uterus weight; Pancreas (Pancreas): Histopathology of pancreas; Hepatic/Liver: Liver weight and histopathology, Clinical chemistry (ALP, SGPT, gamma-glutamyl transpeptidase, bilirubin, cholesterol, triglycerides, BUN, glucose, total protein);
Duration:	Subchronic (>30-91 days) 13 weeks
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	5264231

Domain	Metric	Rating	Comments
Metric 23:	Data Presentation and Analysis	High	Mortality: Statistical analysis was not performed, however, Sufficient data were provided in Appendix C to conduct an independent statistical analysis.; Immune/Hematological: Statistical analysis was not performed, however, Sufficient data were provided to conduct an independent statistical analysis.; Renal/Kidney: Statistical analysis was not performed, however, Sufficient data were provided in Appendix C to conduct an independent statistical analysis.; Lung/Respiratory: Statistical analysis was not performed, however, sufficient data were provided to conduct an independent statistical analysis.; Gastrointestinal: Statistical analysis was not performed, however, Sufficient data were provided to conduct an independent statistical analysis.; Neurological/Behavioral: Statistical analysis was not performed, however, Sufficient data were provided to conduct an independent statistical analysis.; Reproductive/Developmental: Statistical analysis was not performed, however, Sufficient data were provided to conduct an independent statistical analysis.; Pancreas (Pancreas): Statistical analysis was not performed, however, Sufficient data were provided to conduct an independent statistical analysis.; Hepatic/Liver: Statistical analysis was not performed, however, Sufficient data were provided to conduct an independent statistical analysis.

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Study Citation:	Battelle, (1978). Subchronic toxicity study - ortho-dichlorobenzene, Fischer 344 rats. 7820535:#40-7820535.
Health Outcome(s):	Mortality; Immune/Hematological; Renal/Kidney; Lung/Respiratory; Gastrointestinal; Neurological/Behavioral; Reproductive/Developmental; Pancreas (Pancreas); Hepatic/Liver;
Reported Health Effect(s):	Mortality: Death; Immune/Hematological: Spleen and thymus weight, histopathology hematology (hemoglobin, hematocrit, white blood cell count, red blood cell count, mean corpuscular volume, platelet count, reticulocyte count), globulin fractions; Renal/Kidney: Kidney weight and histopathology, urinalysis (pH, protein, glucose, ketones, bilirubin, occult blood, specific gravity, creatinine, uroporphyrins, coproporphyrins); Lung/Respiratory: Lung weight and histopathology; Gastrointestinal: Histopathology of salivary gland, esophagus, colon and cecum; Neurological/Behavioral: Brain weight, clinical signs (none reported), histopathology of spinal cord; Reproductive/Developmental: Testicle, ovary, uterus weight; Pancreas (Pancreas): Histopathology of pancreas; Hepatic/Liver: Liver weight and histopathology, Clinical chemistry (ALP, SGPT, gamma-glutamyl transpeptidase, bilirubin, cholesterol, triglycerides, BUN, glucose, total protein);
Duration:	Subchronic (>30-91 days) 13 weeks
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	5264231

Domain	Metric	Rating	Comments
Metric 24:	Reporting of Data	High	Mortality: All survival data was sufficiently reported in Appendix C.; Immune/Hematological: Organ weight and hematology data is reported as mean, SD and sample size.; Renal/Kidney: Data for exposure-related findings were presented for all outcomes by exposure group and sex (if applicable) with quantal and/or continuous presentation and description of severity scores if applicable.; Lung/Respiratory: Data for exposure-related findings were presented for all outcomes by exposure group and sex (if applicable) with quantal and/or continuous presentation and description of severity scores if applicable. Negative findings were reported qualitatively or quantitatively.; Gastrointestinal: Data for exposure-related findings were presented for all outcomes by exposure group and sex (if applicable) with quantal and/or continuous presentation and description of severity scores if applicable. Negative findings were reported qualitatively or quantitatively.; Neurological/Behavioral: Data for exposure-related findings were presented for all outcomes by exposure group and sex (if applicable) with quantal and/or continuous presentation and description of severity scores if applicable. Negative findings were reported qualitatively or quantitatively.; Reproductive/Developmental: Data for exposure-related findings were presented for all outcomes by exposure group and sex (if applicable) with quantal and/or continuous presentation and description of severity scores if applicable. Negative findings were reported qualitatively or quantitatively.; Pancreas (Pancreas): Data for exposure-related findings were presented for all outcomes by exposure group and sex (if applicable) with quantal and/or continuous presentation and description of severity scores if applicable. Negative findings were reported qualitatively or quantitatively.; Hepatic/Liver: Data for exposure-related findings were presented for all outcomes by exposure group and sex (if applicable) with quantal and/or continuous presentation and description of severity scores if applicable. Negative findings were reported qualitatively or quantitatively.

Additional Comments: None

Overall Quality Determination**High**

Study Citation:	Battelle, (1978). Subchronic toxicity study - ortho-dichlorobenzene, Fischer 344 rats. 7820535:#40-7820535.			
Health Outcome(s):	Nutritional/Metabolic			
Reported Health Effect(s):	Nutritional/Metabolic: Body weight, food consumption			
Duration:	Subchronic (>30-91 days) 13 weeks			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	5264231			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1:	Test Substance Identity	High	Test substance identified as o-dichlorobenzene. The chemical structure was provided in appendix A.
	Metric 2:	Test Substance Source	High	Test substance was purchased from Midwest Research Institute. Batch # was provided in Appendix A.
	Metric 3:	Test Substance Purity	High	Purity reported as 99%. The Batch Chemical Data Record and analytical reports were provided in Appendix A.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	An appropriate control was included. Control animals received plain corn oil
	Metric 5:	Positive Controls	N/A	No positive controls needed for this study.
	Metric 6:	Randomized Allocation of Animals	Medium	The study reported that animals were randomly allocated into study groups.
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and Storage of Test Substance	High	”The selected doses were prepared by placing a weighed portion of ortho-dichlorobenzene into a mixing graduated cylinder and adding corn oil to make up the proper volume for the highest selected dose of 500 ~g/kg. This mixture was stirred for 15 minutes. The remaining four doses were prepared by sequential dilutions of the stock (highest dose) solution.” Mixtures were prepared fresh weekly. One analysis of dose concentrations was performed to confirm dose accuracy.
	Metric 8:	Consistency of Exposure Administration	High	Test substance was administered via oral gavage. Gavage volume was not excessive (0.5 ml/100g of body weight).
	Metric 9:	Reporting of Doses/Concentrations	High	Doses were reported without ambiguity.
	Metric 10:	Exposure Frequency and Duration	Medium	Animals were dosed 5 days per week. Current OECD TG 408 recommended dosing 7 days per week for a 90-day study. Justification is required for a lower frequency of dosing. Study author do not justify dosing animals for only 5 days per week.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	A control plus 5 treatment groups was included, which was sufficient to see a full range of responses.
	Metric 12:	Exposure Route and Method	High	Oral gavage was appropriate for this study type.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	High	Strain, species, sex, age and starting body weight were reported.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were reported and were appropriate.
	Metric 15:	Number of Animals per Group	Medium	10 rats per sex were included in each treatment group, which is appropriate for sub-chronic studies.

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Study Citation:	Battelle, (1978). Subchronic toxicity study - ortho-dichlorobenzene, Fischer 344 rats. 7820535:#40-7820535.		
Health Outcome(s):	Nutritional/Metabolic		
Reported Health Effect(s):	Nutritional/Metabolic: Body weight, food consumption		
Duration:	Subchronic (>30-91 days) 13 weeks		
Chemical:	o-Dichlorobenzene- Parent compound		
HERO ID:	5264231		
Domain	Metric	Rating	Comments
Domain 5: Outcome Assessment			
Metric 16:	Outcome Assessment Methodology	High	The outcome assessment methodology addressed the intended outcome(s) of interest AND the assessment methodology was sensitive and appropriate for the outcomes(s) 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	No need to blind assessors in this study.
Metric 20:	Negative Control Response	High	The biological responses of the negative control group(s) were adequate (e.g., no/low incidence of outcomes of interest in the study).
Domain 6: Confounding / Variable Control			
Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Food intake did not vary across treatment groups. Water intake was not recorded.
Metric 22:	Health Outcomes Unrelated to Exposure	High	Missing Comment
Metric 23:	Data Presentation and Analysis	Uninformative	Statistical analysis was not performed on food consumption of body weight data. Food consumption and body weight data was reported as the weekly average. No measure of variance was provided prohibiting an independent statistical analysis
Metric 24:	Reporting of Data	Low	Average weekly food consumption and body weight were reported without measures of variability.
Additional Comments: None			

Overall Quality Determination**Uninformative**

Study Citation:	Battelle, (1978). Subchronic toxicity study - ortho-dichlorobenzene, Fischer 344 rats. 7820535:#40-7820535.			
Health Outcome(s):	Cardiovascular			
Reported Health Effect(s):	Cardiovascular: Heart weight and histopathology			
Duration:	Subchronic (>30-91 days) 13 weeks			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	5264231			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
Metric 1:	Test Substance Identity	High	Test substance identified as o-dichlorobenzene. The chemical structure was provided in appendix A.	
Metric 2:	Test Substance Source	High	Test substance was purchased from Midwest Research Institute. Batch # was provided in Appendix A.	
Metric 3:	Test Substance Purity	High	Purity reported as 99%. The Batch Chemical Data Record and analytical reports were provided in Appendix A.	
Domain 2: Test Design				
Metric 4:	Negative and Vehicle Controls	High	An appropriate control was included. Control animals received plain corn oil	
Metric 5:	Positive Controls	N/A	No positive controls needed for this study.	
Metric 6:	Randomized Allocation of Animals	Missing Conf	The study reported that animals were randomly allocated into study groups.	
Domain 3: Exposure Characterization				
Metric 7:	Preparation and Storage of Test Substance	High	”The selected doses were prepared by placing a weighed portion of ortho-dichlorobenzene into a mixing graduated cylinder and adding corn oil to make up the proper volume for the highest selected dose of 500 ~g/kg. This mixture was stirred for 15 minutes. The remaining four doses were prepared by sequential dilutions of the stock (highest dose) solution.” Mixtures were prepared fresh weekly. One analysis of dose concentrations was performed to confirm dose accuracy.	
Metric 8:	Consistency of Exposure Administration	High	Test substance was administered via oral gavage. Gavage volume was not excessive (0.5 ml/100g of body weight).	
Metric 9:	Reporting of Doses/Concentrations	High	Doses were reported without ambiguity.	
Metric 10:	Exposure Frequency and Duration	Medium	Animals were dosed 5 days per week. Current OECD TG 408 recommended dosing 7 days per week for a 90-day study. Justification is required for a lower frequency of dosing. Study author do not justify dosing animals for only 5 days per week.	
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	A control plus 5 treatment groups was included, which was sufficient to see a full range of responses.	
Metric 12:	Exposure Route and Method	High	Oral gavage was appropriate for this study type.	
Domain 4: Test Animals				
Metric 13:	Test Animal Characteristics	High	Strain, species, sex, age and starting body weight were reported.	
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were reported and were appropriate.	
Metric 15:	Number of Animals per Group	Medium	10 rats per sex were included in each treatment group, which is appropriate for sub-chronic studies.	

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Study Citation:	Battelle, (1978). Subchronic toxicity study - ortho-dichlorobenzene, Fischer 344 rats. 7820535:#40-7820535.		
Health Outcome(s):	Cardiovascular		
Reported Health Effect(s):	Cardiovascular: Heart weight and histopathology		
Duration:	Subchronic (>30-91 days) 13 weeks		
Chemical:	o-Dichlorobenzene- Parent compound		
HERO ID:	5264231		
Domain	Metric	Rating	Comments
Domain 5: Outcome Assessment			
Metric 16:	Outcome Assessment Methodology	High	The outcome assessment methodology addressed the intended outcome(s) of interest AND the assessment methodology was sensitive and appropriate for the outcomes(s) 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	No need to blind assessors in this study.
Metric 20:	Negative Control Response	High	The biological responses of the negative control group(s) were adequate (e.g., no/low incidence of outcomes of interest in the study).
Domain 6: Confounding / Variable Control			
Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Food intake did not vary across treatment groups. Water intake was not recorded.
Metric 22:	Health Outcomes Unrelated to Exposure	High	Missing Comment
Metric 23:	Data Presentation and Analysis	High	Statistical analysis was not performed, however, Sufficient data were provided to conduct an independent statistical analysis.
Metric 24:	Reporting of Data	High	Data for exposure-related findings were presented for all outcomes by exposure group and sex (if applicable) with quantal and/or continuous presentation and description of severity scores if applicable. Negative findings were reported qualitatively or quantitatively.
Additional Comments: None			
Overall Quality Determination		High	

Study Citation:	Battelle, (1978). Subchronic toxicity study - ortho-dichlorobenzene, B6C3F1 mice.		
Health Outcome(s):	Clinical signs		
Reported Health Effect(s):	Clinical signs: Clinical signs of toxicity		
Duration:	Subchronic (>30-91 days) 13 weeks		
Chemical:	o-Dichlorobenzene- Parent compound		
HERO ID:	5278656		
Domain	Metric	Rating	Comments
Domain 1: Test Substance			
Metric 1:	Test Substance Identity	High	The test substance was identified as ortho-dichlorobenzene. Chemical structure and molecular formula were provided.
Metric 2:	Test Substance Source	High	The source of the test substance was reported (manufactured by Solvent Chemical Company, ICC Industries and obtained by Midwest Research Institute). The batch/lot number was identified (01/SC61377), and the chemical identity was verified by the source.
Metric 3:	Test Substance Purity	High	Purity of the test substance was reported as 99% (label grade).
Domain 2: Test Design			
Metric 4:	Negative and Vehicle Controls	High	Study authors reported using an appropriate, concurrent negative control group (i.e., the control group was administered plain corn oil via gavage at the same volume as treatment groups).
Metric 5:	Positive Controls	N/A	Not necessary for this study type.
Metric 6:	Randomized Allocation of Animals	Medium	Animals were randomized to test groups by tables of random numbers; 60 mice/sex were randomly distributed to 12 cages (5 animals/cage), then the 12 cages were randomly assigned to the 5 dose groups and control group.
Domain 3: Exposure Characterization			
Metric 7:	Preparation and Storage of Test Substance	High	Test substance preparation was described. "Prepared by placing a weighed portion of ortho-dichlorobenzene into a mixing graduated cylinder and adding corn oil to make up the proper volume for the highest dose of 500 mg/kg. this mixture was stirred for 15 minutes. The remaining 4 doses were prepared by sequential dilutions of the stock..." Stability and homogeneity analysis was conducted. Storage conditions were specified.
Metric 8:	Consistency of Exposure Administration	High	Details of exposure administration were reported and exposures were administered consistently across study groups in a scientifically sound manner (gavage volume of 0.01 ml/2 g bw); 5 days/week for 13 weeks
Metric 9:	Reporting of Doses/Concentrations	High	Administered doses were reported without ambiguity: 30, 60, 125, 250, and 500 mg/kg. One analysis for dose concentration accuracy was performed; results were within +/- 10% of desired concentration.
Metric 10:	Exposure Frequency and Duration	High	The exposure frequency and duration of exposure were reported and appropriate for this study type and evaluated outcomes (5 days/week, 13 weeks)
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The number of exposure groups and dose spacing were justified by study authors; dose selections for this study were based on clinical toxicity and pathological findings observed in a previous repeated dose study (unspecified); suggested doses based on "death patterns, 1st repeat dose, and histopathology results, both repeat dose studies". The selected range sufficiently covered the full range of responses.
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Study Citation:	Battelle, (1978). Subchronic toxicity study - ortho-dichlorobenzene, B6C3F1 mice.			
Health Outcome(s):	Clinical signs			
Reported Health Effect(s):	Clinical signs: Clinical signs of toxicity			
Duration:	Subchronic (>30-91 days) 13 weeks			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	5278656			
Domain	Metric	Rating	Comments	
	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 (date of birth), and starting body weight were reported, and the test animal was obtained from a commercial source. The test species and strain were an appropriate animal model for the evaluation of the outcomes of interest.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were reported (e.g., temperature, humidity, light- dark cycle, diet, water availability) and were adequate and the same for control and exposed populations.
	Metric 15:	Number of Animals per Group	Medium	The number of animals per study group was reported (i.e., 10/sex/group) and were appropriate for the study type.
Domain 5: Outcome Assessment	Metric 16:	Outcome Assessment Methodology	High	The outcome assessment methodology addressed the intended outcome of interest; animals were observed twice daily for mortality and clinical signs of toxicity. Observations were separated by at least 6 hours.
	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
	Metric 19:	Blinding of Assessors	N/A	Not necessary for this study type or outcome.
	Metric 20:	Negative Control Response	High	The biological responses of the negative control group were adequate. No clinical signs of toxicity were noted in the control group.
Domain 6: Confounding / Variable Control	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	The study reported body weight and food consumption changes. There were no differences in food consumption greater than 10% compared to controls. There were body weight changes (>10%) at the higher doses. Water intake was not reported.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	2 mice of each sex were necropsied before random assignment to be tested for disease and none was found. There was no additional 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	Statistics were not performed; however, statistical analysis was not necessary. Incidence of clinical signs were noted in text.
	Metric 24:	Reporting of Data	Low	Data for exposure-related findings were not shown for each study group, but results were described in the text
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Study Citation:	Battelle, (1978). Subchronic toxicity study - ortho-dichlorobenzene, B6C3F1 mice.		
Health	Clinical signs		
Outcome(s):			
Reported Health	Clinical signs: Clinical signs of toxicity		
Effect(s):			
Duration:	Subchronic (>30-91 days) 13 weeks		
Chemical:	o-Dichlorobenzene- Parent compound		
HERO ID:	5278656		
Domain	Metric	Rating	Comments
Additional Comments:	None		
Overall Quality Determination		High	

Study Citation:	Battelle, (1978). Subchronic toxicity study - ortho-dichlorobenzene, B6C3F1 mice.		
Health Outcome(s):	Mortality		
Reported Health Effect(s):	Mortality: survival		
Duration:	Subchronic (>30-91 days) 13 weeks		
Chemical:	o-Dichlorobenzene- Parent compound		
HERO ID:	5278656		
Domain	Metric	Rating	Comments
Domain 1: Test Substance			
Metric 1:	Test Substance Identity	High	The test substance was identified as ortho-dichlorobenzene. Chemical structure and molecular formula were provided.
Metric 2:	Test Substance Source	High	The source of the test substance was reported (manufactured by Solvent Chemical Company, ICC Industries and obtained by Midwest Research Institute). The batch/lot number was identified (01/SC61377), and the chemical identity was verified by the source.
Metric 3:	Test Substance Purity	High	Purity of the test substance was reported as 99% (label grade).
Domain 2: Test Design			
Metric 4:	Negative and Vehicle Controls	High	Study authors reported using an appropriate, concurrent negative control group (i.e., the control group was administered plain corn oil via gavage at the same volume as treatment groups).
Metric 5:	Positive Controls	N/A	Not necessary for this study type.
Metric 6:	Randomized Allocation of Animals	Medium	Animals were randomized to test groups by tables of random numbers; 60 mice/sex were randomly distributed to 12 cages (5 animals/cage), then the 12 cages were randomly assigned to the 5 dose groups and control group.
Domain 3: Exposure Characterization			
Metric 7:	Preparation and Storage of Test Substance	High	Test substance preparation was described. "Prepared by placing a weighed portion of ortho-dichlorobenzene into a mixing graduated cylinder and adding corn oil to make up the proper volume for the highest dose of 500 mg/kg. this mixutre was stirred for 15 minutes. The remaining 4 doses were prepared by sequential dilutions of the stock..." Stability and homogeniety analysis was conducted. Storage conditions were specified.
Metric 8:	Consistency of Exposure Administration	High	Details of exposure administration were reported and exposures were administered consistently across study groups in a scientifically sound manner (gavage volume of 0.01 ml/2 g bw); 5 days/week for 13 weeks
Metric 9:	Reporting of Doses/Concentrations	High	Administered doses were reported without ambiguity: 30, 60,125, 250, and 500 mg/kg
Metric 10:	Exposure Frequency and Duration	High	The exposure frequency and duration of exposure were reported and appropriate for this study type and evaluated outcomes (5 days/week, 13 weeks)
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The number of exposure groups and dose spacing were justified by study authors; dose selections for this study were based on clinical toxicity and pathological findings observed in a previous repeated dose study (unspecified); suggested doses based on "death patterns, 1st repeat dose, and histopathology results, both repeat dose studies". The selected range sufficiently covered the full range of responses.
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			
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Study Citation:	Battelle, (1978). Subchronic toxicity study - ortho-dichlorobenzene, B6C3F1 mice.			
Health Outcome(s):	Mortality			
Reported Health Effect(s):	Mortality: survival			
Duration:	Subchronic (>30-91 days) 13 weeks			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	5278656			
Domain	Metric	Rating	Comments	
	Metric 13: Test Animal Characteristics	High	The test animal species, strain, sex, age (date of birth), and starting body weight were reported, and the test animal was obtained from a commercial source. The test species and strain were an appropriate animal model for the evaluation of the outcomes of interest.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were reported (e.g., temperature, humidity, light- dark cycle, diet, water availability) and were adequate and the same for control and exposed populations.	
	Metric 15: Number of Animals per Group	Medium	The number of animals per study group was reported (i.e., 10/sex/group) and were appropriate for the study type.	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	High	The outcome assessment methodology addressed the intended outcome of interest; animals were observed twice daily for mortality and clinical signs of toxicity.	
	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	
	Metric 19: Blinding of Assessors	N/A	Not necessary for this study type or outcome.	
	Metric 20: Negative Control Response	High	The biological responses of the negative control group were adequate. No mortality was observed in control animals of either sex.	
Domain 6: Confounding / Variable Control				
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	The study reported body weight and food consumption changes. There were no differences in food consumption > 10% compared to controls. There were body weight changes at the higher doses.	
	Metric 22: Health Outcomes Unrelated to Exposure	Medium	2 mice of each sex were necropsied before random assignment to be tested for disease. There was no additional 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 were not performed; however, sufficient data were provided to conduct an independent statistical analysis.	
	Metric 24: Reporting of Data	High	Data for exposure related findings were presented for all outcomes by control and exposure groups and by sex.	
Additional Comments:	None			

Overall Quality Determination**High**

Study Citation:	Battelle, (1978). Subchronic toxicity study - ortho-dichlorobenzene, B6C3F1 mice.		
Health Outcome(s):	Nutritional/Metabolic		
Reported Health Effect(s):	Nutritional/Metabolic: body weight, body weight gain, food consumption		
Duration:	Subchronic (>30-91 days) 13 weeks		
Chemical:	o-Dichlorobenzene- Parent compound		
HERO ID:	5278656		
Domain	Metric	Rating	Comments
Domain 1: Test Substance			
Metric 1:	Test Substance Identity	High	The test substance was identified as ortho-dichlorobenzene. Chemical structure and molecular formula were provided.
Metric 2:	Test Substance Source	High	The source of the test substance was reported (manufactured by Solvent Chemical Company, ICC Industries and obtained by Midwest Research Institute). The batch/lot number was identified (01/SC61377), and the chemical identity was verified by the source.
Metric 3:	Test Substance Purity	High	Purity of the test substance was reported as 99% (label grade).
Domain 2: Test Design			
Metric 4:	Negative and Vehicle Controls	High	Study authors reported using an appropriate, concurrent negative control group (i.e., the control group was administered plain corn oil via gavage at the same volume as treatment groups).
Metric 5:	Positive Controls	N/A	Not necessary for this study type.
Metric 6:	Randomized Allocation of Animals	Medium	Animals were randomized to test groups by tables of random numbers; 60 mice/sex were randomly distributed to 12 cages (5 animals/cage), then the 12 cages were randomly assigned to the 5 dose groups and control group.
Domain 3: Exposure Characterization			
Metric 7:	Preparation and Storage of Test Substance	High	Test substance preparation was described. "Prepared by placing a weighed portion of ortho-dichlorobenzene into a mixing graduated cylinder and adding corn oil to make up the proper volume for the highest dose of 500 mg/kg. this mixutre was stirred for 15 minutes. The remaining 4 doses were prepared by sequential dilutions of the stock..." Stability and homogeniety analysis was conducted. Storage conditions were specified.
Metric 8:	Consistency of Exposure Administration	High	Details of exposure administration were reported and exposures were administered consistently across study groups in a scientifically sound manner (gavage volume of 0.01 ml/2 g bw); 5 days/week for 13 weeks
Metric 9:	Reporting of Doses/Concentrations	High	Administered doses were reported without ambiguity: 30, 60,125, 250, and 500 mg/kg. One analysis for dose concentration accuracy was performed; results were within +/- 10% of desired concentration.
Metric 10:	Exposure Frequency and Duration	High	The exposure frequency and duration of exposure were reported and appropriate for this study type and evaluated outcomes (5 days/week, 13 weeks)
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The number of exposure groups and dose spacing were justified by study authors; dose selections for this study were based on clinical toxicity and pathological findings observed in a previous repeated dose study (unspecified); suggested doses based on "death patterns, 1st repeat dose, and histopathology results, both repeat dose studies". The selected range sufficiently covered the full range of responses.
Metric 12:	Exposure Route and Method	High	The route (oral) and method (gavage) of exposure were reported and were suited to the test substance

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Study Citation:	Battelle, (1978). Subchronic toxicity study - ortho-dichlorobenzene, B6C3F1 mice.			
Health Outcome(s):	Nutritional/Metabolic			
Reported Health Effect(s):	Nutritional/Metabolic: body weight, body weight gain, food consumption			
Duration:	Subchronic (>30-91 days) 13 weeks			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	5278656			
Domain	Metric	Rating	Comments	
Domain 4: Test Animals				
Metric 13:	Test Animal Characteristics	High	The test animal species, strain, sex, age (date of birth), and starting body weight were reported, and the test animal was obtained from a commercial source. The test species and strain were an appropriate animal model for the evaluation of the outcomes of interest.	
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were reported (e.g., temperature, humidity, light- dark cycle, diet, water availability) and were adequate and the same for control and exposed populations.	
Metric 15:	Number of Animals per Group	Medium	The number of animals per study group was reported (i.e., 10/sex/group) and were appropriate for the study type.	
Domain 5: Outcome Assessment				
Metric 16:	Outcome Assessment Methodology	High	The outcome assessment methodology addressed the intended outcome of interest; individual animal weight and food consumption (per cage) were recorded weekly.	
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	
Metric 19:	Blinding of Assessors	N/A	Not necessary for this study type or outcome.	
Metric 20:	Negative Control Response	High	The biological responses of the negative control group were adequate.	
Domain 6: Confounding / Variable Control				
Metric 21:	Confounding Variables in Test Design and Procedures	Medium	The study reported body weight and food consumption changes. There were no differences in food consumption greater than 10% compared to controls. There were body weight changes (>10%) at the higher doses. Water intake was not reported.	
Metric 22:	Health Outcomes Unrelated to Exposure	Medium	2 mice of each sex were necropsied before random assignment to be tested for disease and none was found. There was no additional 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 described; however, there are sufficient data to conduct statistical analysis on mean food consumption and body weight.	
Metric 24:	Reporting of Data	Medium	Continuous data for mean body weight and food intake through out the study was presented without measures of variability. Starting and final body weight data (and percent weight gain) were provided for individual animals by sex and treatment group, which is sufficient to allow for variability to be calculated. Data is not sufficiently reported to allow for measures of variability to be calculated for food intake, however, this is unlikely to have a substantial impact on results.	
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Study Citation:	Battelle, (1978). Subchronic toxicity study - ortho-dichlorobenzene, B6C3F1 mice.		
Health	Nutritional/Metabolic		
Outcome(s):			
Reported Health Effect(s):	Nutritional/Metabolic: body weight, body weight gain, food consumption		
Duration:	Subchronic (>30-91 days) 13 weeks		
Chemical:	o-Dichlorobenzene- Parent compound		
HERO ID:	5278656		
Domain	Metric	Rating	Comments
Additional Comments:	None		
Overall Quality Determination		High	

Study Citation:	Battelle, (1978). Subchronic toxicity study - ortho-dichlorobenzene, B6C3F1 mice.		
Health Outcome(s):	Renal/Kidney		
Reported Health Effect(s):	Renal/Kidney: urinalysis (pH, protein, glucose, ketones, bilirubin, occult blood, specific gravity, urinary creatinine), kidney weight		
Duration:	Subchronic (>30-91 days) 13 weeks		
Chemical:	o-Dichlorobenzene- Parent compound		
HERO ID:	5278656		
Domain	Metric	Rating	Comments
Domain 1: Test Substance			
Metric 1:	Test Substance Identity	High	The test substance was identified as ortho-dichlorobenzene. Chemical structure and molecular formula were provided.
Metric 2:	Test Substance Source	High	The source of the test substance was reported (manufactured by Solvent Chemical Company, ICC Industries and obtained by Midwest Research Institute). The batch/lot number was identified (01/SC61377), and the chemical identity was verified by the source.
Metric 3:	Test Substance Purity	High	Purity of the test substance was reported as 99% (label grade).
Domain 2: Test Design			
Metric 4:	Negative and Vehicle Controls	High	Study authors reported using an appropriate, concurrent negative control group (i.e., the control group was administered plain corn oil via gavage at the same volume as treatment groups).
Metric 5:	Positive Controls	N/A	Not necessary for this study type.
Metric 6:	Randomized Allocation of Animals	Medium	Animals were randomized to test groups by tables of random numbers; 60 mice/sex were randomly distributed to 12 cages (5 animals/cage), then the 12 cages were randomly assigned to the 5 dose groups and control group.
Domain 3: Exposure Characterization			
Metric 7:	Preparation and Storage of Test Substance	High	Test substance preparation was described. "Prepared by placing a weighed portion of ortho-dichlorobenzene into a mixing graduated cylinder and adding corn oil to make up the proper volume for the highest dose of 500 mg/kg. this mixutre was stirred for 15 minutes. The remaining 4 doses were prepared by sequential dilutions of the stock..." Stability and homogeniety analysis was conducted. Storage conditions were specified.
Metric 8:	Consistency of Exposure Administration	High	Details of exposure administration were reported and exposures were administered consistently across study groups in a scientifically sound manner (gavage volume of 0.01 ml/2 g bw); 5 days/week for 13 weeks
Metric 9:	Reporting of Doses/Concentrations	High	Administered doses were reported without ambiguity: 30, 60,125, 250, and 500 mg/kg. One analysis for dose concentration accuracy was performed; results were within +/- 10% of desired concentration.
Metric 10:	Exposure Frequency and Duration	High	The exposure frequency and duration of exposure were reported and appropriate for this study type and evaluated outcomes (5 days/week, 13 weeks)
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The number of exposure groups and dose spacing were justified by study authors; dose selections for this study were based on clinical toxicity and pathological findings observed in a previous repeated dose study (unspecified); suggested doses based on "death patterns, 1st repeat dose, and histopathology results, both repeat dose studies". The selected range sufficiently covered the full range of responses.
Metric 12:	Exposure Route and Method	High	The route (oral) and method (gavage) of exposure were reported and were suited to the test substance

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Study Citation:	Battelle, (1978). Subchronic toxicity study - ortho-dichlorobenzene, B6C3F1 mice.		
Health Outcome(s):	Renal/Kidney		
Reported Health Effect(s):	Renal/Kidney: urinalysis (pH, protein, glucose, ketones, bilirubin, occult blood, specific gravity, urinary creatinine), kidney weight		
Duration:	Subchronic (>30-91 days) 13 weeks		
Chemical:	o-Dichlorobenzene- Parent compound		
HERO ID:	5278656		
Domain	Metric	Rating	Comments
Domain 4: Test Animals			
Metric 13:	Test Animal Characteristics	High	The test animal species, strain, sex, age (date of birth), and starting body weight were reported, and the test animal was obtained from a commercial source. The test species and strain were an appropriate animal model for the evaluation of the outcomes of interest.
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were reported (e.g., temperature, humidity, light- dark cycle, diet, water availability) and were adequate and the same for control and exposed populations.
Metric 15:	Number of Animals per Group	Medium	The number of animals per study group was reported (i.e., 10/sex/group) and were appropriate for the study type.
Domain 5: Outcome Assessment			
Metric 16:	Outcome Assessment Methodology	Low	The outcome assessment methodology partially addressed the intended outcome of interest; surviving mice were terminated on day 91 with full necropsy, organ weights, and tissue collection. Mice who died early also underwent full necropsy and included measurement of organ weights. Study authors state that microscopic examinations were performed on all tissues from the control and high dose groups, however, the kidney is not listed in the pathology results tables, so there is uncertainty as to whether or not microscopic examinations were conducted. Urinalysis, including porphyrin analysis, was conducted in the highest surviving dose and control group during the week before sacrifice. No further methodology information was provided. The assessment methodology for conducting histopathology and urine analysis was not clearly reported; however the methodology for porphyrin analysis was adequately described.
Metric 17:	Consistency of Outcome Assessment	Low	Details of the outcome assessment protocol for most outcomes were reported and most outcomes were assessed consistently across study groups. Urinalysis was conducted only in control animals and in the "highest surviving" dose during the week before sacrifice. It is unclear if this analysis occurred concurrently among the groups or on different days/times. There was incomplete reporting of details of outcome assessment protocol execution, including methodology for conducting histopathology and urine analysis.
Metric 18:	Sampling Adequacy	High	Reported information indicates the study used adequate sampling for the outcome
Metric 19:	Blinding of Assessors	N/A	Not necessary for this study type or outcome.
Metric 20:	Negative Control Response	High	The biological responses of the negative control group were adequate.
Domain 6: Confounding / Variable Control			
Metric 21:	Confounding Variables in Test Design and Procedures	Medium	The study reported body weight and food consumption changes. There were no differences in food consumption greater than 10% compared to controls. There were body weight changes (>10%) at the higher doses. Water intake was not reported.

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Study Citation:	Battelle, (1978). Subchronic toxicity study - ortho-dichlorobenzene, B6C3F1 mice.			
Health Outcome(s):	Renal/Kidney			
Reported Health Effect(s):	Renal/Kidney: urinalysis (pH, protein, glucose, ketones, bilirubin, occult blood, specific gravity, urinary creatinine), kidney weight			
Duration:	Subchronic (>30-91 days) 13 weeks			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	5278656			
Domain	Metric	Rating	Comments	
	Metric 22: Health Outcomes Unrelated to Exposure	Medium	2 mice of each sex were necropsied before random assignment to be tested for disease and none was found. There was no additional 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	Statistical analysis was not conducted; however, there are sufficient data to conduct statistical analysis on results for kidney weight. Results from urinalysis were not reported and therefore, independent statistics could not be performed on that outcome.	
	Metric 24: Reporting of Data	Low	Mean kidney weight (+/-SD) data was adequately reported by sex and exposure group. Urinalysis results were partially described in text, however, data for exposure related findings were not adequately presented. Study authors state that all tissues from animals in the control and high dose group were microscopically examined, however, findings for the kidney are not described in text or summarized in the available data tables.	
Additional Comments: None				
Overall Quality Determination		High		

Study Citation:	Battelle, (1978). Subchronic toxicity study - ortho-dichlorobenzene, B6C3F1 mice.		
Health Outcome(s):	Lung/Respiratory; Cardiovascular; Reproductive/Developmental; Musculoskeletal;		
Reported Health Effect(s):	Lung/Respiratory: lung weight, histopathology; Cardiovascular: heart weight, histopathology; Reproductive/Developmental: testicle weight (males), ovary and uterus weight (female), histopathology; Musculoskeletal: histopathology on skeletal muscle;		
Duration:	Subchronic (>30-91 days) 13 weeks		
Chemical:	o-Dichlorobenzene- Parent compound		
HERO ID:	5278656		
Domain	Metric	Rating	Comments
Domain 1: Test Substance			
Metric 1:	Test Substance Identity	High	All Outcomes: The test substance was identified as ortho-dichlorobenzene. Chemical structure and molecular formula were provided.
Metric 2:	Test Substance Source	High	All Outcomes: The source of the test substance was reported (manufactured by Solvent Chemical Company, ICC Industries and obtained by Midwest Research Institute). The batch/lot number was identified (01/SC61377), and the chemical identity was verified by the source.
Metric 3:	Test Substance Purity	High	All Outcomes: Purity of the test substance was reported as 99% (label grade).
Domain 2: Test Design			
Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Study authors reported using an appropriate, concurrent negative control group (i.e., the control group was administered plain corn oil via gavage at the same volume as treatment groups).
Metric 5:	Positive Controls	N/A	All Outcomes: Not necessary for this study type.
Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: Animals were randomized to test groups by tables of random numbers; 60 mice/sex were randomly distributed to 12 cages (5 animals/cage), then the 12 cages were randomly assigned to the 5 dose groups and control group.
Domain 3: Exposure Characterization			
Metric 7:	Preparation and Storage of Test Substance	High	All Outcomes: Test substance preparation was described. "Prepared by placing a weighed portion of ortho-dichlorobenzene into a mixing graduated cylinder and adding corn oil to make up the proper volume for the highest dose of 500 mg/kg. this mixutre was stirred for 15 minutes. The remaining 4 doses were prepared by sequential dilutions of the stock..." Stability and homogeniety analysis was conducted. Storage conditions were specified.
Metric 8:	Consistency of Exposure Administration	High	All Outcomes: Details of exposure administration were reported and exposures were administered consistently across study groups in a scientifically sound manner (gavage volume of 0.01 ml/2 g bw); 5 days/week for 13 weeks
Metric 9:	Reporting of Doses/Concentrations	High	All Outcomes: Administered doses were reported without ambiguity: 30, 60,125, 250, and 500 mg/kg. One analysis for dose concentration accuracy was performed; results were within +/- 10% of desired concentration.
Metric 10:	Exposure Frequency and Duration	High	All Outcomes: The exposure frequency and duration of exposure were reported and appropriate for this study type and evaluated outcomes (5 days/week, 13 weeks)
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: The number of exposure groups and dose spacing were justified by study authors; dose selections for this study were based on clinical toxicity and pathological findings observed in a previous repeated dose study (unspecified); suggested doses based on "death patterns, 1st repeat dose, and histopathology results, both repeat dose studies". The selected range sufficiently covered the full range of responses.
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Study Citation:	Battelle, (1978). Subchronic toxicity study - ortho-dichlorobenzene, B6C3F1 mice.			
Health Outcome(s):	Lung/Respiratory; Cardiovascular; Reproductive/Developmental; Musculoskeletal;			
Reported Health Effect(s):	Lung/Respiratory: lung weight, histopathology; Cardiovascular: heart weight, histopathology; Reproductive/Developmental: testicle weight (males), ovary and uterus weight (female), histopathology; Musculoskeletal: histopathology on skeletal muscle;			
Duration:	Subchronic (>30-91 days) 13 weeks			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	5278656			
Domain	Metric	Rating	Comments	
	Metric 12: Exposure Route and Method	High	All Outcomes: 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	All Outcomes: The test animal species, strain, sex, age (date of birth), and starting body weight were reported, and the test animal was obtained from a commercial source. The test species and strain were an appropriate animal model for the evaluation of the outcomes of interest.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: All husbandry conditions were reported (e.g., temperature, humidity, light- dark cycle, diet, water availability) and were adequate and the same for control and exposed populations.	
	Metric 15: Number of Animals per Group	Medium	All Outcomes: The number of animals per study group was reported (i.e., 10/sex/group) and were appropriate for the study type.	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	Medium	Lung/Respiratory: The outcome assessment methodology addressed the intended outcome of interest; surviving mice were terminated on day 91 with full necropsy, organ weights, and tissue collection. Mice who died early also underwent full necropsy and included measurement of organ weights. The assessment methodology for conducting histopathology was not reported; Cardiovascular: The outcome assessment methodology addressed the intended outcome of interest; surviving mice were terminated on day 91 with full necropsy, organ weights, and tissue collection. Mice who died early also underwent full necropsy and included measurement of organ weights. The assessment methodology for conducting histopathology was not reported; Reproductive/Developmental: The outcome assessment methodology addressed the intended outcome of interest; surviving mice were terminated on day 91 with full necropsy, organ weights (testes and ovary), and tissue collection. Mice who died early also underwent full necropsy and included measurement of organ weights. Microscopic examination of the ovary and testes was performed only on animals from the control and high dose groups.The assessment methodology for conducting histopathology was not clearly reported; Musculoskeletal: The outcome assessment methodology addressed the intended outcome of interest. Surviving mice were terminated on day 91 with full necropsy on all animals from all treatment groups. Microscopic examination of skeletal muscle was performed on animals from the control and two highest dose groups.The assessment methodology for conducting histopathology was not clearly reported	
	Metric 17: Consistency of Outcome Assessment	Medium	All Outcomes: Details of the outcome assessment protocol for most outcomes were reported and were assessed consistently across study groups. There was incomplete reporting of details of outcome assessment protocol execution, including methodology for conducting gross pathology and histopathology.	
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Study Citation:	Battelle, (1978). Subchronic toxicity study - ortho-dichlorobenzene, B6C3F1 mice.			
Health Outcome(s):	Lung/Respiratory; Cardiovascular; Reproductive/Developmental; Musculoskeletal;			
Reported Health Effect(s):	Lung/Respiratory: lung weight, histopathology; Cardiovascular: heart weight, histopathology; Reproductive/Developmental: testicle weight (males), ovary and uterus weight (female), histopathology; Musculoskeletal: histopathology on skeletal muscle;			
Duration:	Subchronic (>30-91 days) 13 weeks			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	5278656			
Domain	Metric	Rating	Comments	
	Metric 18: Sampling Adequacy	High	All Outcomes: Reported information indicates the study used adequate sampling for the outcome	
	Metric 19: Blinding of Assessors	N/A	All Outcomes: Not necessary for this study type or outcome.	
	Metric 20: Negative Control Response	High	Lung/Respiratory: The biological responses of the negative control group were adequate. Histopathologic examinations revealed a low incidence of lesions in the lung of two control females.; Cardiovascular: The biological responses of the negative control group were adequate.; Reproductive/Developmental: The biological responses of the negative control group were adequate.; Musculoskeletal: The biological responses of the negative control group were adequate.	
Domain 6: Confounding / Variable Control				
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	All Outcomes: The study reported body weight and food consumption changes. There were no differences in food consumption greater than 10% compared to controls. There were body weight changes (>10%) at the higher doses. Water intake was not reported.	
	Metric 22: Health Outcomes Unrelated to Exposure	Medium	All Outcomes: 2 mice of each sex were necropsied before random assignment to be tested for disease and none was found. There was no additional 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	Lung/Respiratory: Statistical analysis was not conducted; however, there are sufficient data to conduct statistical analysis on results for organ weights and incidence of pathological findings.; Cardiovascular: Statistical analysis was not conducted; however, there are sufficient data to conduct statistical analysis on results for organ weights and incidence of pathological findings.; Reproductive/Developmental: Statistical analysis was not conducted; however, there are sufficient data to conduct statistical analysis on results for organ weights and incidence of pathological findings.; Musculoskeletal: Statistical analysis was not conducted; however, there are sufficient data to conduct statistical analysis on histopathology results.	
	Metric 24: Reporting of Data	High	Lung/Respiratory: Data for exposure-related findings were presented for outcomes by exposure group and sex with quantal (incidence of pathological findings) and continuous outcomes (organ weights reported as mean +/-sd).; Cardiovascular: Data for exposure-related findings were presented for outcomes by exposure group and sex with quantal (incidence of pathological findings) and continuous outcomes (organ weights reported as mean +/-sd).; Reproductive/Developmental: Data for exposure-related findings were presented for outcomes by exposure group and sex with quantal (incidence of pathological findings) and continuous outcomes (organ weights reported as mean +/-sd).; Musculoskeletal: Incidence data for histopathologic findings were adequately reported by exposure group and sex.	
Additional Comments:	None			

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Study Citation:	Battelle, (1978). Subchronic toxicity study - ortho-dichlorobenzene, B6C3F1 mice.
Health Outcome(s):	Lung/Respiratory; Cardiovascular; Reproductive/Developmental; Musculoskeletal;
Reported Health Effect(s):	Lung/Respiratory: lung weight, histopathology; Cardiovascular: heart weight, histopathology; Reproductive/Developmental: testicle weight (males), ovary and uterus weight (female), histopathology; Musculoskeletal: histopathology on skeletal muscle;
Duration:	Subchronic (>30-91 days) 13 weeks
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	5278656

Domain	Metric	Rating	Comments
Overall Quality Determination		High	

Study Citation:	Battelle, (1978). Subchronic toxicity study - ortho-dichlorobenzene, B6C3F1 mice.		
Health Outcome(s):	Hepatic/Liver; Neurological/Behavioral;		
Reported Health Effect(s):	Hepatic/Liver: clinical chemistry (alkaline phosphatase, SGPT, GGTP), urinary porphyrin analysis, liver weight, histopathology; Neurological/Behavioral: brain weight;		
Duration:	Subchronic (>30-91 days) 13 weeks		
Chemical:	o-Dichlorobenzene- Parent compound		
HERO ID:	5278656		
Domain	Metric	Rating	Comments
Domain 1: Test Substance			
Metric 1:	Test Substance Identity	High	All Outcomes: The test substance was identified as ortho-dichlorobenzene. Chemical structure and molecular formula were provided.
Metric 2:	Test Substance Source	High	All Outcomes: The source of the test substance was reported (manufactured by Solvent Chemical Company, ICC Industries and obtained by Midwest Research Institute). The batch/lot number was identified (01/SC61377), and the chemical identity was verified by the source.
Metric 3:	Test Substance Purity	High	All Outcomes: Purity of the test substance was reported as 99% (label grade).
Domain 2: Test Design			
Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Study authors reported using an appropriate, concurrent negative control group (i.e., the control group was administered plain corn oil via gavage at the same volume as treatment groups).
Metric 5:	Positive Controls	N/A	All Outcomes: Not necessary for this study type.
Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: Animals were randomized to test groups by tables of random numbers; 60 mice/sex were randomly distributed to 12 cages (5 animals/cage), then the 12 cages were randomly assigned to the 5 dose groups and control group.
Domain 3: Exposure Characterization			
Metric 7:	Preparation and Storage of Test Substance	High	All Outcomes: Test substance preparation was described. "Prepared by placing a weighed portion of ortho-dichlorobenzene into a mixing graduated cylinder and adding corn oil to make up the proper volume for the highest dose of 500 mg/kg. this mixutre was stirred for 15 minutes. The remaining 4 doses were prepared by sequential dilutions of the stock..." Stability and homogeniety analysis was conducted. Storage conditions were specified.
Metric 8:	Consistency of Exposure Administration	High	All Outcomes: Details of exposure administration were reported and exposures were administered consistently across study groups in a scientifically sound manner (gavage volume of 0.01 ml/2 g bw); 5 days/week for 13 weeks
Metric 9:	Reporting of Doses/Concentrations	High	All Outcomes: Administered doses were reported without ambiguity: 30, 60,125, 250, and 500 mg/kg. One analysis for dose concentration accuracy was performed; results were within +/- 10% of desired concentration.
Metric 10:	Exposure Frequency and Duration	High	All Outcomes: The exposure frequency and duration of exposure were reported and appropriate for this study type and evaluated outcomes (5 days/week, 13 weeks)
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: The number of exposure groups and dose spacing were justified by study authors; dose selections for this study were based on clinical toxicity and pathological findings observed in a previous repeated dose study (unspecified); suggested doses based on "death patterns, 1st repeat dose, and histopathology results, both repeat dose studies". The selected range sufficiently covered the full range of responses.
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Study Citation:	Battelle, (1978). Subchronic toxicity study - ortho-dichlorobenzene, B6C3F1 mice.			
Health Outcome(s):	Hepatic/Liver; Neurological/Behavioral;			
Reported Health Effect(s):	Hepatic/Liver: clinical chemistry (alkaline phosphatase, SGPT, GGTP), urinary porphyrin analysis, liver weight, histopathology; Neurological/Behavioral: brain weight;			
Duration:	Subchronic (>30-91 days) 13 weeks			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	5278656			
Domain	Metric	Rating	Comments	
	Metric 12:	Exposure Route and Method	High	All Outcomes: 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	All Outcomes: The test animal species, strain, sex, age (date of birth), and starting body weight were reported, and the test animal was obtained from a commercial source. The test species and strain were an appropriate animal model for the evaluation of the outcomes of interest.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: All husbandry conditions were reported (e.g., temperature, humidity, light- dark cycle, diet, water availability) and were adequate and the same for control and exposed populations.
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: The number of animals per study group was reported (i.e., 10/sex/group) and were appropriate for the study type.
Domain 5: Outcome Assessment	Metric 16:	Outcome Assessment Methodology	Medium	Hepatic/Liver: The outcome assessment methodology addressed the intended outcome of interest; Surviving mice were terminated on day 91 with full necropsy, organ weights, and tissue collection. Mice who died early also underwent full necropsy and included measurement of organ weights. Clinical chemistry was conducted on all animals on the day of necropsy. Liver (all dose groups) and urine (control and high dose groups only) porphyrin analysis was conducted. The assessment methodology for conducting histopathology and clinical chemistry was not clearly reported; however the methodology for porphyrin analysis was adequately described.; Neurological/Behavioral: The outcome assessment methodology addressed the intended outcome of interest; Surviving mice were terminated on day 91 with full necropsy, organ weights, and tissue collection. Mice who died early also underwent full necropsy and included measurement of organ weights. Study authors state that microscopic examinations were performed on all tissues from the control and high dose groups, however, the brain is not listed in the pathology results tables, so there is uncertainty as to whether or not microscopic examinations were conducted. The assessment methodology for conducting histopathology was not clearly reported.
	Metric 17:	Consistency of Outcome Assessment	Medium	Hepatic/Liver: Urinary porphyrin analysis was conducted only in control animals and in the "highest surviving" dose during the week before sacrifice. It is unclear if this analysis occurred concurrently among the groups or on different days/times. There was incomplete reporting of details of outcome assessment protocol execution, including methodology for conducting histopathology and clinical chemistry.; Neurological/Behavioral: Details of the outcome assessment protocol for most outcomes were reported and were assessed consistently across study groups. There was incomplete reporting of details of outcome assessment protocol execution, including methodology for conducting gross pathology and histopathology.

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Study Citation:	Battelle, (1978). Subchronic toxicity study - ortho-dichlorobenzene, B6C3F1 mice.
Health Outcome(s):	Hepatic/Liver; Neurological/Behavioral;
Reported Health Effect(s):	Hepatic/Liver: clinical chemistry (alkaline phosphatase, SGPT, GGTP), urinary porphyrin analysis, liver weight, histopathology; Neurological/Behavioral: brain weight;
Duration:	Subchronic (>30-91 days) 13 weeks
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	5278656

Domain	Metric	Rating	Comments
	Metric 18: Sampling Adequacy	High	All Outcomes: Reported information indicates the study used adequate sampling for the outcome
	Metric 19: Blinding of Assessors	N/A	All Outcomes: Not necessary for this study type or outcome.
	Metric 20: Negative Control Response	High	All Outcomes: The biological responses of the negative control group were adequate.

Domain 6: Confounding / Variable Control

Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: The study reported body weight and food consumption changes. There were no differences in food consumption greater than 10% compared to controls. There were body weight changes (>10%) at the higher doses. Water intake was not reported.
Metric 22:	Health Outcomes Unrelated to Exposure	Medium	All Outcomes: 2 mice of each sex were necropsied before random assignment to be tested for disease and none was found. There was no additional 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	Hepatic/Liver: Statistical analysis was not conducted. Histopathologic findings, organ weight, clinical chemistry and porphyrin data were sufficiently reported to allow for independent statistical analysis.; Neurological/Behavioral: Statistical analysis was not conducted; however, there are sufficient data to conduct statistical analysis on results for organ weights.
Metric 24:	Reporting of Data	Medium	Hepatic/Liver: Histopathologic findings, organ weight (mean +/-SD, N), clinical chemistry parameter data (mean +/-SD, N), and liver and urine porphyrin analysis data (mean +/-SD, N) are adequately reported by sex and treatment group.; Neurological/Behavioral: Mean brain weight (+/-SD) is reported by sex and exposure group. Study authors state that microscopic examinations were performed on all tissues from the control and high dose groups, however, the brain is not listed in the pathology results tables, so there is uncertainty as to whether or not microscopic examinations were conducted.

Additional Comments: None

Overall Quality Determination**High**

Study Citation:	Battelle, (1978). Subchronic toxicity study - ortho-dichlorobenzene, B6C3F1 mice.		
Health Outcome(s):	Immune/Hematological		
Reported Health Effect(s):	Immune/Hematological: hematology (Hgb, HCT, WBC, RBC, MCV, platelet count, reticulocyte count), spleen weight, thymus weight, histopathology on thymus, pancreas, lymph nodes, spleen, bone marrow		
Duration:	Subchronic (>30-91 days) 13 weeks		
Chemical:	o-Dichlorobenzene- Parent compound		
HERO ID:	5278656		
Domain	Metric	Rating	Comments
Domain 1: Test Substance			
Metric 1:	Test Substance Identity	High	The test substance was identified as ortho-dichlorobenzene. Chemical structure and molecular formula were provided.
Metric 2:	Test Substance Source	High	The source of the test substance was reported (manufactured by Solvent Chemical Company, ICC Industries and obtained by Midwest Research Institute). The batch/lot number was identified (01/SC61377), and the chemical identity was verified by the source.
Metric 3:	Test Substance Purity	High	Purity of the test substance was reported as 99% (label grade).
Domain 2: Test Design			
Metric 4:	Negative and Vehicle Controls	High	Study authors reported using an appropriate, concurrent negative control group (i.e., the control group was administered plain corn oil via gavage at the same volume as treatment groups).
Metric 5:	Positive Controls	N/A	Not necessary for this study type.
Metric 6:	Randomized Allocation of Animals	Medium	Animals were randomized to test groups by tables of random numbers; 60 mice/sex were randomly distributed to 12 cages (5 animals/cage), then the 12 cages were randomly assigned to the 5 dose groups and control group.
Domain 3: Exposure Characterization			
Metric 7:	Preparation and Storage of Test Substance	High	Test substance preparation was described. "Prepared by placing a weighed portion of ortho-dichlorobenzene into a mixing graduated cylinder and adding corn oil to make up the proper volume for the highest dose of 500 mg/kg. this mixutre was stirred for 15 minutes. The remaining 4 doses were prepared by sequential dilutions of the stock..." Stability and homogeniety analysis was conducted. Storage conditions were specified.
Metric 8:	Consistency of Exposure Administration	High	Details of exposure administration were reported and exposures were administered consistently across study groups in a scientifically sound manner (gavage volume of 0.01 ml/2 g bw); 5 days/week for 13 weeks
Metric 9:	Reporting of Doses/Concentrations	High	Administered doses were reported without ambiguity: 30, 60,125, 250, and 500 mg/kg. One analysis for dose concentration accuracy was performed; results were within +/- 10% of desired concentration.
Metric 10:	Exposure Frequency and Duration	High	The exposure frequency and duration of exposure were reported and appropriate for this study type and evaluated outcomes (5 days/week, 13 weeks)
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The number of exposure groups and dose spacing were justified by study authors; dose selections for this study were based on clinical toxicity and pathological findings observed in a previous repeated dose study (unspecified); suggested doses based on "death patterns, 1st repeat dose, and histopathology results, both repeat dose studies". The selected range sufficiently covered the full range of responses.
Metric 12:	Exposure Route and Method	High	The route (oral) and method (gavage) of exposure were reported and were suited to the test substance

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Study Citation:	Battelle, (1978). Subchronic toxicity study - ortho-dichlorobenzene, B6C3F1 mice.		
Health Outcome(s):	Immune/Hematological		
Reported Health Effect(s):	Immune/Hematological: hematology (Hgb, HCT, WBC, RBC, MCV, platelet count, reticulocyte count), spleen weight, thymus weight, histopathology on thymus, pancreas, lymph nodes, spleen, bone marrow		
Duration:	Subchronic (>30-91 days) 13 weeks		
Chemical:	o-Dichlorobenzene- Parent compound		
HERO ID:	5278656		
Domain	Metric	Rating	Comments
Domain 4: Test Animals			
Metric 13:	Test Animal Characteristics	High	The test animal species, strain, sex, age (date of birth), and starting body weight were reported, and the test animal was obtained from a commercial source. The test species and strain were an appropriate animal model for the evaluation of the outcomes of interest.
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were reported (e.g., temperature, humidity, light- dark cycle, diet, water availability) and were adequate and the same for control and exposed populations.
Metric 15:	Number of Animals per Group	Medium	The number of animals per study group was reported (i.e., 10/sex/group) and were appropriate for the study type.
Domain 5: Outcome Assessment			
Metric 16:	Outcome Assessment Methodology	Medium	The outcome assessment methodology addressed the intended outcome of interest; Surviving mice were terminated on day 91 with full necropsy, organ weights, and tissue collection. Mice who died early also underwent full necropsy and included measurement of organ weights. Hematology was conducted in all animals the day before sacrifice. No further methodology information was provided. The assessment methodology for conducting histopathology methodology and hematology was not clearly reported.
Metric 17:	Consistency of Outcome Assessment	Medium	Details of the outcome assessment protocol for most outcomes were reported and most outcomes were assessed consistently across study groups. There was incomplete reporting of details of outcome assessment protocol execution, including methodology for conducting histopathology and hematology.
Metric 18:	Sampling Adequacy	High	Reported information indicates the study used adequate sampling for the outcome
Metric 19:	Blinding of Assessors	N/A	Not necessary for this study type or outcome.
Metric 20:	Negative Control Response	Medium	The biological responses of the negative control group were adequate for most hematological and immune endpoints including organ weights and hematology. It was noted that there were low white blood cell counts in male mice of the control group ("below those typically reported for normal mice in our laboratory and others." No historical control data were provided.
Domain 6: Confounding / Variable Control			
Metric 21:	Confounding Variables in Test Design and Procedures	Medium	The study reported body weight and food consumption changes. There were no differences in food consumption greater than 10% compared to controls. There were body weight changes (>10%) at the higher doses. Water intake was not reported.
Metric 22:	Health Outcomes Unrelated to Exposure	Medium	2 mice of each sex were necropsied before random assignment to be tested for disease and none was found. There was no additional information either to support or dismiss the suggestion that there were differences among groups in animal attrition or health outcomes unrelated to exposure
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Study Citation:	Battelle, (1978). Subchronic toxicity study - ortho-dichlorobenzene, B6C3F1 mice.
Health Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Immune/Hematological: hematology (Hgb, HCT, WBC, RBC, MCV, platelet count, reticulocyte count), spleen weight, thymus weight, histopathology on thymus, pancreas, lymph nodes, spleen, bone marrow
Duration:	Subchronic (>30-91 days) 13 weeks
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	5278656

Domain	Metric	Rating	Comments
	Metric 23: Data Presentation and Analysis	High	Statistical analysis was not conducted. However, there are sufficient data to conduct statistical analysis on results for hematological parameters, organ weights, and incidence of pathological findings.
	Metric 24: Reporting of Data	High	Data for exposure-related findings were presented for all outcomes by exposure group and sex with quantal (pathology findings) and continuous outcomes (organ weights and hematology results). Negative findings were reported qualitatively or quantitatively.

Additional Comments: None

Overall Quality Determination**High**

Study Citation:	Battelle, (1978). Subchronic toxicity study - ortho-dichlorobenzene, B6C3F1 mice.		
Health Outcome(s):	Gastrointestinal		
Reported Health Effect(s):	Gastrointestinal: Histopathology on salivary gland and stomach		
Duration:	Subchronic (>30-91 days) 13 weeks		
Chemical:	o-Dichlorobenzene- Parent compound		
HERO ID:	5278656		
Domain	Metric	Rating	Comments
Domain 1: Test Substance			
Metric 1:	Test Substance Identity	High	The test substance was identified as ortho-dichlorobenzene. Chemical structure and molecular formula were provided.
Metric 2:	Test Substance Source	High	The source of the test substance was reported (manufactured by Solvent Chemical Company, ICC Industries and obtained by Midwest Research Institute). The batch/lot number was identified (01/SC61377), and the chemical identity was verified by the source.
Metric 3:	Test Substance Purity	High	Purity of the test substance was reported as 99% (label grade).
Domain 2: Test Design			
Metric 4:	Negative and Vehicle Controls	High	Study authors reported using an appropriate, concurrent negative control group (i.e., the control group was administered plain corn oil via gavage at the same volume as treatment groups).
Metric 5:	Positive Controls	N/A	Not necessary for this study type.
Metric 6:	Randomized Allocation of Animals	Medium	Animals were randomized to test groups by tables of random numbers; 60 mice/sex were randomly distributed to 12 cages (5 animals/cage), then the 12 cages were randomly assigned to the 5 dose groups and control group.
Domain 3: Exposure Characterization			
Metric 7:	Preparation and Storage of Test Substance	High	Test substance preparation was described. "Prepared by placing a weighed portion of ortho-dichlorobenzene into a mixing graduated cylinder and adding corn oil to make up the proper volume for the highest dose of 500 mg/kg. this mixutre was stirred for 15 minutes. The remaining 4 doses were prepared by sequential dilutions of the stock..." Stability and homogeniety analysis was conducted. Storage conditions were specified.
Metric 8:	Consistency of Exposure Administration	High	Details of exposure administration were reported and exposures were administered consistently across study groups in a scientifically sound manner (gavage volume of 0.01 ml/2 g bw); 5 days/week for 13 weeks
Metric 9:	Reporting of Doses/Concentrations	High	Administered doses were reported without ambiguity: 30, 60,125, 250, and 500 mg/kg. One analysis for dose concentration accuracy was performed; results were within +/- 10% of desired concentration.
Metric 10:	Exposure Frequency and Duration	High	The exposure frequency and duration of exposure were reported and appropriate for this study type and evaluated outcomes (5 days/week, 13 weeks)
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The number of exposure groups and dose spacing were justified by study authors; dose selections for this study were based on clinical toxicity and pathological findings observed in a previous repeated dose study (unspecified); suggested doses based on "death patterns, 1st repeat dose, and histopathology results, both repeat dose studies". The selected range sufficiently covered the full range of responses.
Metric 12:	Exposure Route and Method	High	The route (oral) and method (gavage) of exposure were reported and were suited to the test substance

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Study Citation:	Battelle, (1978). Subchronic toxicity study - ortho-dichlorobenzene, B6C3F1 mice.		
Health Outcome(s):	Gastrointestinal		
Reported Health Effect(s):	Gastrointestinal: Histopathology on salivary gland and stomach		
Duration:	Subchronic (>30-91 days) 13 weeks		
Chemical:	o-Dichlorobenzene- Parent compound		
HERO ID:	5278656		
Domain	Metric	Rating	Comments
Domain 4: Test Animals			
Metric 13:	Test Animal Characteristics	High	The test animal species, strain, sex, age (date of birth), and starting body weight were reported, and the test animal was obtained from a commercial source. The test species and strain were an appropriate animal model for the evaluation of the outcomes of interest.
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were reported (e.g., temperature, humidity, light- dark cycle, diet, water availability) and were adequate and the same for control and exposed populations.
Metric 15:	Number of Animals per Group	Medium	The number of animals per study group was reported (i.e., 10/sex/group) and were appropriate for the study type.
Domain 5: Outcome Assessment			
Metric 16:	Outcome Assessment Methodology	Medium	The outcome assessment methodology addressed the intended outcome of interest. Surviving mice were terminated on day 91 with full necropsy on all animals from all treatment groups. Microscopic examination of GI-related tissues was performed only on animals from the control and high dose groups. The assessment methodology for conducting histopathology was not clearly reported
Metric 17:	Consistency of Outcome Assessment	Medium	Details of the outcome assessment protocol for most outcomes were reported and were assessed consistently across study groups. There was incomplete reporting of details of outcome assessment protocol execution, including methodology for conducting gross pathology and histopathology.
Metric 18:	Sampling Adequacy	Medium	Histopathology was performed for high-dose group and controls only. Some potential treatment-related changes were reported in the stomach and salivary gland of high dose females.
Metric 19:	Blinding of Assessors	N/A	Not necessary for this study type or outcome.
Metric 20:	Negative Control Response	High	The biological responses of the negative control group were adequate.
Domain 6: Confounding / Variable Control			
Metric 21:	Confounding Variables in Test Design and Procedures	Medium	The study reported body weight and food consumption changes. There were no differences in food consumption greater than 10% compared to controls. There were body weight changes (>10%) at the higher doses. Water intake was not reported.
Metric 22:	Health Outcomes Unrelated to Exposure	Medium	2 mice of each sex were necropsied before random assignment to be tested for disease and none was found. There was no additional 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 conducted; however, there are sufficient data to conduct statistical analysis on histopathology results.
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Study Citation:	Battelle, (1978). Subchronic toxicity study - ortho-dichlorobenzene, B6C3F1 mice.
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	Gastrointestinal: Histopathology on salivary gland and stomach
Duration:	Subchronic (>30-91 days) 13 weeks
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	5278656

Domain	Metric	Rating	Comments
	Metric 24: Reporting of Data	High	Incidence data for histopathologic findings were adequately reported by exposure group and sex.

Additional Comments: None

Overall Quality Determination**High**

Study Citation:	Eun-Sang, C., Yong-Soon, K., Hye-yeon, C., Kyung, R. (2023). Effect of inhaled 1,2-dichlorobenzene on cytochrome P450s and lipid peroxidation in B6C3F1 mice. Journal of Biomedical Translational Research 24(3):67-82.			
Health Outcome(s):	Neurological/Behavioral; Cardiovascular; Thyroid; Reproductive/Developmental; Gastrointestinal; Immune/Hematological; Hepatic/Liver; Mortality; Musculoskeletal; Ocular/Sensory; Renal/Kidney; Lung/Respiratory; Skin/Connective Tissue; Endocrine (Endocrine);			
Reported Health Effect(s):	Neurological/Behavioral: Brain weight; gross necropsy; histopathology (brain, optical nerve, sciatic nerve, spinal cord); Cardiovascular: Heart weight; gross necropsy; histopathology (heart, aorta); Thyroid: gross necropsy; histopathology (thyroid); Reproductive/Developmental: Testes, epididymides, uterus, and ovary weights; gross necropsy; histopathology (seminal vesicles, vagina, prostate, testes, epididymides, uterus, mammary gland, and ovary); Gastrointestinal: gross necropsy; histopathology (cecum, colon, duodenum, esophagus, gull bladder, ileum, jejunum, rectum, salivary glands, stomach, teeth tongue); Immune/Hematological: Hematology; spleen and thymus weights; gross necropsy; histopathology (bone marrow, lymph nodes, spleen, thymus); Hepatic/Liver: Liver weight, gross necropsy, histopathology (liver), serum chemistry (ALT, AST, ALP, total protein, albumin, globulin, triglycerides, total cholesterol, total bilirubin); Mortality: Mortality; Musculoskeletal: gross necropsy, histopathology (sternum, skeletal muscle, stifle joint, femur); Ocular/Sensory: gross necropsy, histopathology (eyes, Harderian glands); Renal/Kidney: Serum chemistry (BUN, creatinine, sodium, chloride, potassium, calcium, inorganic phosphorus), kidney weights, gross necropsy, histopathology (kidney, urinary bladder); Lung/Respiratory: Lung weights, gross necropsy, histopathology (lung, larynx, nasopharyngeal tissue); Skin/Connective Tissue: gross necropsy, histopathology (skin); Endocrine (Endocrine): Adrenal gland weights; gross necropsy, histopathology (adrenal glands, pancreas, parathyroids, pituitary);			
Duration:	Subchronic (>30-91 days) 13 weeks			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	13037009			
Domain		Metric	Rating	Comments
Domain 1: Test Substance				
	Metric 1:	Test Substance Identity	High	All Outcomes: The test substance was identified by name as 1,2-dichlorobenzene. A CASRN was provided.
	Metric 2:	Test Substance Source	High	All Outcomes: The test substance source (Samchun Pure Chemicals) was reported; a lot number was provided.
	Metric 3:	Test Substance Purity	High	All Outcomes: The reported purity is 99.0%
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Control animals were exposed to filtered air with all other conditions being equal to the test groups.
	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: Animals were randomly assigned into study groups; however, the method of allocation was not specified.
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and Storage of Test Substance	Medium	All Outcomes: Limited details were provided. Test atmospheres were generated using a liquid vapor generator. No further details were provided.
	Metric 8:	Consistency of Exposure Administration	Medium	All Outcomes: Some exposure administration details were provided. The chamber design was not described beyond indicating that animals were housed in individual wire mesh cages within the chambers. Based on the information provided, there is no information to suggest inconsistencies of exposure across groups.
	Metric 9:	Reporting of Doses/Concentrations	High	All Outcomes: Both nominal and analytical concentrations were reported. Test atmospheres were monitored every 30 minutes and samples were analyzed using gas chromatography. The study did not specify whether samples were collected from the breathing zone.

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Study Citation:	Eun-Sang, C., Yong-Soon, K., Hye-yeon, C., Kyung, R. (2023). Effect of inhaled 1,2-dichlorobenzene on cytochrome P450s and lipid peroxidation in B6C3F1 mice. Journal of Biomedical Translational Research 24(3):67-82.			
Health Outcome(s):	Neurological/Behavioral; Cardiovascular; Thyroid; Reproductive/Developmental; Gastrointestinal; Immune/Hematological; Hepatic/Liver; Mortality; Musculoskeletal; Ocular/Sensory; Renal/Kidney; Lung/Respiratory; Skin/Connective Tissue; Endocrine (Endocrine);			
Reported Health Effect(s):	Neurological/Behavioral: Brain weight; gross necropsy; histopathology (brain, optical nerve, sciatic nerve, spinal cord); Cardiovascular: Heart weight; gross necropsy; histopathology (heart, aorta); Thyroid: gross necropsy; histopathology (thyroid); Reproductive/Developmental: Testes, epididymides, uterus, and ovary weights; gross necropsy; histopathology (seminal vesicles, vagina, prostate, testes, epididymides, uterus, mammary gland, and ovary); Gastrointestinal: gross necropsy; histopathology (cecum, colon, duodenum, esophagus, gull bladder, ileum, jejunum, rectum, salivary glands, stomach, teeth tongue); Immune/Hematological: Hematology; spleen and thymus weights; gross necropsy; histopathology (bone marrow, lymph nodes, spleen, thymus); Hepatic/Liver: Liver weight, gross necropsy, histopathology (liver), serum chemistry (ALT, AST, ALP, total protein, albumin, globulin, triglycerides, total cholesterol, total bilirubin); Mortality: Mortality; Musculoskeletal: gross necropsy, histopathology (sternum, skeletal muscle, stifle joint, femur); Ocular/Sensory: gross necropsy, histopathology (eyes, Harderian glands); Renal/Kidney: Serum chemistry (BUN, creatinine, sodium, chloride, potassium, calcium, inorganic phosphorus), kidney weights, gross necropsy, histopathology (kidney, urinary bladder); Lung/Respiratory: Lung weights, gross necropsy, histopathology (lung, larynx, nasopharyngeal tissue); Skin/Connective Tissue: gross necropsy, histopathology (skin); Endocrine (Endocrine): Adrenal gland weights; gross necropsy, histopathology (adrenal glands, pancreas, parathyroids, pituitary);			
Duration:	Subchronic (>30-91 days) 13 weeks			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	13037009			
Domain	Metric	Rating	Comments	
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: The study generally followed OECD TG 413 and exposed animals 6 hrs/day, 5 days/week for 13 weeks.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	All Outcomes: The number of exposure groups (n=3 plus a control) is consistent with OECD recommendations. The concentrations were based on results from a preliminary subacute inhalation study (no further details provided). A study-wide NOAEC was not determined.
	Metric 12:	Exposure Route and Method	Low	All Outcomes: Animals were exposed whole-body. The study did not explicitly specify whether the chamber was static or dynamic and there were no details (e.g., air changes per hour) to infer a dynamic chamber.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Medium	All Outcomes: A standard test model was used. Animal species, strain, sex, age, and source was reported. Body weights were measured, but these data (including initial body weights) were not provided in the published study report.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: Chamber temperature and humidity were reported and monitored every 30 min. The photoperiod and illumination were reported. Animals were housed in individual cages. Food and water were available ad libitum.
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: The study included 10/sex/group which is consistent with OECD test guidelines for a subchronic duration study.
Domain 5: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	High	All Outcomes: Outcome assessment methods were generally consistent with OECD TG 413 and were sensitive to the outcomes of interest.
	Metric 17:	Consistency of Outcome Assessment	High	All Outcomes: The same protocols were applied across groups.
	Metric 18:	Sampling Adequacy	High	All Outcomes: Sampling was reported and adequate for all outcomes.
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding is not required for the outcomes of interest.
	Metric 20:	Negative Control Response	High	All Outcomes: Negative control responses were reported and appropriate.

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Study Citation:	Eun-Sang, C., Yong-Soon, K., Hye-yeon, C., Kyung, R. (2023). Effect of inhaled 1,2-dichlorobenzene on cytochrome P450s and lipid peroxidation in B6C3F1 mice. Journal of Biomedical Translational Research 24(3):67-82.
Health Outcome(s):	Neurological/Behavioral; Cardiovascular; Thyroid; Reproductive/Developmental; Gastrointestinal; Immune/Hematological; Hepatic/Liver; Mortality; Musculoskeletal; Ocular/Sensory; Renal/Kidney; Lung/Respiratory; Skin/Connective Tissue; Endocrine (Endocrine);
Reported Health Effect(s):	Neurological/Behavioral: Brain weight; gross necropsy; histopathology (brain, optical nerve, sciatic nerve, spinal cord); Cardiovascular: Heart weight; gross necropsy; histopathology (heart, aorta); Thyroid: gross necropsy; histopathology (thyroid); Reproductive/Developmental: Testes, epididymides, uterus, and ovary weights; gross necropsy; histopathology (seminal vesicles, vagina, prostate, testes, epididymides, uterus, mammary gland, and ovary); Gastrointestinal: gross necropsy; histopathology (cecum, colon, duodenum, esophagus, gull bladder, ileum, jejunum, rectum, salivary glands, stomach, teeth tongue); Immune/Hematological: Hematology; spleen and thymus weights; gross necropsy; histopathology (bone marrow, lymph nodes, spleen, thymus); Hepatic/Liver: Liver weight, gross necropsy, histopathology (liver), serum chemistry (ALT, AST, ALP, total protein, albumin, globulin, triglycerides, total cholesterol, total bilirubin); Mortality: Mortality; Musculoskeletal: gross necropsy, histopathology (sternum, skeletal muscle, stifle joint, femur); Ocular/Sensory: gross necropsy, histopathology (eyes, Harderian glands); Renal/Kidney: Serum chemistry (BUN, creatinine, sodium, chloride, potassium, calcium, inorganic phosphorus), kidney weights, gross necropsy, histopathology (kidney, urinary bladder); Lung/Respiratory: Lung weights, gross necropsy, histopathology (lung, larynx, nasopharyngeal tissue); Skin/Connective Tissue: gross necropsy, histopathology (skin); Endocrine (Endocrine): Adrenal gland weights; gross necropsy, histopathology (adrenal glands, pancreas, parathyroids, pituitary);
Duration:	Subchronic (>30-91 days) 13 weeks
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	13037009

Domain	Metric	Rating	Comments
Domain 6: Confounding / Variable Control			
	Metric 21: Confounding Variables in Test Design and Procedures	Low	All Outcomes: The test substance is a respiratory irritant. Respiratory rates or reflex bradypnea were not measured. There were no differences in body weights, food intake, or animal husbandry conditions that could confound the study results.
	Metric 22: Health Outcomes Unrelated to Exposure	High	All Outcomes: Details regarding animal attrition and health outcomes unrelated to exposure (e.g., infection) 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 reported and appropriate for the datasets.
	Metric 24: Reporting of Data	High	All Outcomes: All endpoints were reported quantitatively for each group and sex as incidences or means $\pm$ SD. Histopathology results were reported with severity. Only the organs/tissues in which a lesion was observed was included in the table provided.

Additional Comments: None

Overall Quality Determination**High**

Study Citation:	Eun-Sang, C., Yong-Soon, K., Hye-yeon, C., Kyung, R. (2023). Effect of inhaled 1,2-dichlorobenzene on cytochrome P450s and lipid peroxidation in B6C3F1 mice. Journal of Biomedical Translational Research 24(3):67-82.		
Health Outcome(s):	Nutritional/Metabolic		
Reported Health Effect(s):	Nutritional/Metabolic: Body weights, food intake		
Duration:	Subchronic (>30-91 days) 13 weeks		
Chemical:	o-Dichlorobenzene- Parent compound		
HERO ID:	13037009		
Domain	Metric	Rating	Comments
Domain 1: Test Substance			
	Metric 1: Test Substance Identity	High	The test substance was identified by name as 1,2-dichlorobenzene. A CASRN was provided.
	Metric 2: Test Substance Source	High	The test substance source (Samchun Pure Chemicals) was reported; a lot number was provided.
	Metric 3: Test Substance Purity	High	The reported purity is 99.0%
Domain 2: Test Design			
	Metric 4: Negative and Vehicle Controls	High	Control animals were exposed to filtered air with all other conditions being equal to the test groups.
	Metric 5: Positive Controls	N/A	Positive controls are not required for the study type.
	Metric 6: Randomized Allocation of Animals	Medium	Animals were randomly assigned into study groups; however, the method of allocation was not specified.
Domain 3: Exposure Characterization			
	Metric 7: Preparation and Storage of Test Substance	Medium	Limited details were provided. Test atmospheres were generated using a liquid vapor generator. No further details were provided.
	Metric 8: Consistency of Exposure Administration	Medium	Some exposure administration details were provided. The chamber design was not described beyond indicating that animals were housed in individual wire mesh cages within the chambers. Based on the information provided, there is no information to suggest inconsistencies of exposure across groups.
	Metric 9: Reporting of Doses/Concentrations	High	Both nominal and analytical concentrations were reported. Test atmospheres were monitored every 30 minutes and samples were analyzed using gas chromatography. The study did not specify whether samples were collected from the breathing zone.
	Metric 10: Exposure Frequency and Duration	High	The study generally followed OECD TG 413 and exposed animals 6 hrs/day, 5 days/week for 13 weeks.
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	Medium	The number of exposure groups (n=3 plus a control) is consistent with OECD recommendations. The concentrations were based on results from a preliminary subacute inhalation study (no further details provided). A study-wide NOAEC was not determined.
	Metric 12: Exposure Route and Method	Low	Animals were exposed whole-body. The study did not explicitly specify whether the chamber was static or dynamic and there were no details (e.g., air changes per hour) to infer a dynamic chamber.
Domain 4: Test Animals			
	Metric 13: Test Animal Characteristics	Medium	A standard test model was used. Animal species, strain, sex, age, and source was reported. Body weights were measured, but these data (including initial body weights) were not provided in the published study report.
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Study Citation:	Eun-Sang, C., Yong-Soon, K., Hye-yeon, C., Kyung, R. (2023). Effect of inhaled 1,2-dichlorobenzene on cytochrome P450s and lipid peroxidation in B6C3F1 mice. Journal of Biomedical Translational Research 24(3):67-82.			
Health Outcome(s):	Nutritional/Metabolic			
Reported Health Effect(s):	Nutritional/Metabolic: Body weights, food intake			
Duration:	Subchronic (>30-91 days) 13 weeks			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	13037009			
Domain	Metric	Rating	Comments	
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	Chamber temperature and humidity were reported and monitored every 30 min. The photoperiod and illumination were reported. Animals were housed in individual cages. Food and water were available ad libitum.
	Metric 15:	Number of Animals per Group	Medium	The study included 10/sex/group which is consistent with OECD test guidelines for a subchronic duration study.
Domain 5: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	High	Outcome assessment methods were generally consistent with OECD TG 413 and were sensitive to the outcomes of interest.
	Metric 17:	Consistency of Outcome Assessment	High	The same protocols were applied across groups.
	Metric 18:	Sampling Adequacy	High	Sampling was reported and adequate for all outcomes.
	Metric 19:	Blinding of Assessors	N/A	Blinding is not required for the outcomes of interest.
	Metric 20:	Negative Control Response	High	Negative control responses were reported and appropriate.
Domain 6: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Low	The test substance is a respiratory irritant. Respiratory rates or reflex bradypnea were not measured. There were no differences in body weights, food intake, or animal husbandry conditions that could confound the study results.
	Metric 22:	Health Outcomes Unrelated to Exposure	High	Details regarding animal attrition and health outcomes unrelated to exposure (e.g., infection) 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 reported and appropriate for the datasets.
	Metric 24:	Reporting of Data	Medium	Body weights were measured throughout the study, but only terminal body weights were quantitatively reported. Negative findings (no changes) in food consumption were qualitatively reported in the text. Individual animal data are not provided.
Additional Comments:	None			

Overall Quality Determination**High**

Study Citation:	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.		
Health Outcome(s):	Nutritional/Metabolic		
Reported Health Effect(s):	Nutritional/Metabolic: Body weight		
Duration:	Subchronic (>30-91 days) 13 weeks Rat		
Chemical:	o-Dichlorobenzene- Parent compound		
HERO ID:	1944492		
Domain	Metric	Rating	Comments
Domain 1: Test Substance			
	Metric 1: Test Substance Identity	High	Test substance was identified by nomenclature, CAS number, and structure
	Metric 2: Test Substance Source	High	Test substance was obtained from a commercial source: " ICC solvent Chemical Company (New York, NY) Lot number SC61377 and analytically verified.
	Metric 3: Test Substance Purity	High	Test substance was >99% purity verified analytically. Impurities were reported "Acidic components (assumed to be hydrochloric acid) were found to be present at a concentration of 10.8 ppm. one impurity with an area that was approximately 0.7% of the major peak area; this impurity, identified as 1 ,4-dichlorobenzene"
Domain 2: Test Design			
	Metric 4: Negative and Vehicle Controls	High	Concurrent vehicle control was used and appropriate for the study
	Metric 5: Positive Controls	N/A	Not necessary for the study type
	Metric 6: Randomized Allocation of Animals	Medium	The study reported the random allocation of animals into groups
Domain 3: Exposure Characterization			
	Metric 7: Preparation and Storage of Test Substance	High	Dose preparation and storage were reported "adding a weighed amount of 1 ,2-dichlorobenzene to the appropriate volume of corn oil and mixing for 15 minutes" then doses solutions were prepared by dilution. The mixture was stable at room temp for 7 days and solutions were stored no longer than 14 days at 4 degrees C
	Metric 8: Consistency of Exposure Administration	High	Details of exposure administration were reported and consistent. Gavage volume was not excessive 5ml/kg.
	Metric 9: Reporting of Doses/Concentrations	High	Doses were reported clearly
	Metric 10: Exposure Frequency and Duration	High	Exposure frequency (5 days/week) and duration (13 weeks) were appropriate for the study type
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	Number of exposure groups was adequate and consisted of 5 treated groups and a control. Spacing was sufficient to encompass a full range of response
	Metric 12: Exposure Route and Method	High	Exposure route and method were suited to the test substance: gavage is appropriate
Domain 4: Test Animals			
	Metric 13: Test Animal Characteristics	High	Species, strain, sex, and age were all reported in table 1. Initial body weight was reported in the results
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were reported in table 1: temperature, humidity, light- dark cycle, diet, water availability and were adequate and consistent across all groups

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Study Citation:	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.
Health Outcome(s):	Nutritional/Metabolic
Reported Health Effect(s):	Nutritional/Metabolic: Body weight
Duration:	Subchronic (>30-91 days) 13 weeks Rat
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	1944492

Domain	Metric	Rating	Comments
	Metric 15: Number of Animals per Group	Medium	The number of animals per group was reported and appropriate for the study type: 10/sex/group for subchronic

Domain 5: Outcome Assessment

Metric 16:	Outcome Assessment Methodology	High	Outcome assessment was sensitive and appropriate for the outcome
Metric 17:	Consistency of Outcome Assessment	High	Outcome was assessed consistently across groups
Metric 18:	Sampling Adequacy	High	Sampling was adequate
Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary for the study type
Metric 20:	Negative Control Response	High	Control group responded adequately

Domain 6: Confounding / Variable Control

Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Reported information did not identify differences in confounding factors
Metric 22:	Health Outcomes Unrelated to Exposure	Low	Premature death due to gavage error was reported in 1 male in each the control, 30, and 125 mg/kg/day groups. An additional one male in the 250 mg/kg/day group was removed due to being missexed.
Metric 23:	Data Presentation and Analysis	High	Statistical methods were reported and appropriate for the data
Metric 24:	Reporting of Data	High	Data were reported for all outcomes by group and sex

Additional Comments: None

Overall Quality Determination**High**

Study Citation:	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.
Health Outcome(s):	Cardiovascular; Lung/Respiratory; Immune/Hematological; Hepatic/Liver; Cardiovascular; Lung/Respiratory; Nutritional/Metabolic; Mortality; Mortality; Hepatic/Liver; Renal/Kidney;
Reported Health Effect(s):	Cardiovascular: Heart weight, cholesterol, triglycerides; Lung/Respiratory: Lung weight and histology; Immune/Hematological: Organ weight (spleen, thymus), hematology (hgb, hct, RBC, WBC, MCV, platelets, reticulocytes), Histology (thymus, spleen, bone marrow, and lymph node); histopathology (thymus (rats only) & spleen (rats and mice); Hepatic/Liver: Liver weight, histopathology, clinical chemistry (Mice & rats: ALP, GGT, and glutamic pyruvic transaminase; Rats only: bilirubin, cholesterol, triglycerides, BUN, glucose, total protein); Cardiovascular: Heart weight, cholesterol, triglycerides; Lung/Respiratory: Lung weight and histology; Nutritional/Metabolic: Body weight; Mortality: Death; Mortality: Death; Hepatic/Liver: Liver weight, histopathology, clinical chemistry (Mice & rats: ALP, GGT, and glutamic pyruvic transaminase; Rats only: bilirubin, cholesterol, triglycerides, BUN, glucose, total protein); Renal/Kidney: clinical chemistry (BUN (rats only)), kidney weight, histology;
Duration:	Subchronic (>30-91 days) 13 weeks Mouse
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	1944492

Domain	Metric	Rating	Comments
Domain 1: Test Substance			
	Metric 1: Test Substance Identity	High	All Outcomes: Test substance was identified by nomenclature, CAS number, and structure
	Metric 2: Test Substance Source	High	Cardiovascular: Test substance was obtained from a commercial source: "ICC solvent Chemical Company (New York, NY) Lot number SC61377 and analytically verified.; Lung/Respiratory: Test substance was obtained from a commercial source: " ICC solvent Chemical Company (New York, NY) Lot number SC61377 and analytically verified.; Immune/Hematological: Test substance was obtained from a commercial source: " ICC solvent Chemical Company (New York, NY) Lot number SC61377 and analytically verified.; Hepatic/Liver: Test substance was obtained from a commercial source: " ICC solvent Chemical Company (New York, NY) Lot number SC61377 and analytically verified.; Cardiovascular: Test substance was obtained from a commercial source: " ICC solvent Chemical Company (New York, NY) Lot number SC61377 and analytically verified.; Lung/Respiratory: Test substance was obtained from a commercial source: " ICC solvent Chemical Company (New York, NY) Lot number SC61377 and analytically verified.; Nutritional/Metabolic: Test substance was obtained from a commercial source: " ICC solvent Chemical Company (New York, NY) Lot number SC61377 and analytically verified.; Mortality: Test substance was obtained from a commercial source: "ICC solvent Chemical Company (New York, NY) Lot number SC61377 and analytically verified.; Mortality: Test substance was obtained from a commercial source: " ICC solvent Chemical Company (New York, NY) Lot number SC61377 and analytically verified.; Hepatic/Liver: Test substance was obtained from a commercial source: "ICC solvent Chemical Company (New York, NY) Lot number SC61377 and analytically verified.; Renal/Kidney: Test substance was obtained from a commercial source: "ICC solvent Chemical Company (New York, NY) Lot number SC61377 and analytically verified.

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Study Citation:	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.
Health Outcome(s):	Cardiovascular; Lung/Respiratory; Immune/Hematological; Hepatic/Liver; Cardiovascular; Lung/Respiratory; Nutritional/Metabolic; Mortality; Mortality; Hepatic/Liver; Renal/Kidney;
Reported Health Effect(s):	Cardiovascular: Heart weight, cholesterol, triglycerides; Lung/Respiratory: Lung weight and histology; Immune/Hematological: Organ weight (spleen, thymus), hematology (hgb, hct, RBC, WBC, MCV, platelets, reticulocytes), Histology (thymus, spleen, bone marrow, and lymph node); histopathology (thymus (rats only) & spleen (rats and mice); Hepatic/Liver: Liver weight, histopathology, clinical chemistry (Mice & rats: ALP, GGT, and glutamic pyruvic transaminase; Rats only: bilirubin, cholesterol, triglycerides, BUN, glucose, total protein); Cardiovascular: Heart weight, cholesterol, triglycerides; Lung/Respiratory: Lung weight and histology; Nutritional/Metabolic: Body weight; Mortality: Death; Mortality: Death; Hepatic/Liver: Liver weight, histopathology, clinical chemistry (Mice & rats: ALP, GGT, and glutamic pyruvic transaminase; Rats only: bilirubin, cholesterol, triglycerides, BUN, glucose, total protein); Renal/Kidney: clinical chemistry (BUN (rats only)), kidney weight, histology;
Duration:	Subchronic (>30-91 days) 13 weeks Mouse
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	1944492

Domain	Metric	Rating	Comments
Metric 3:	Test Substance Purity	High	Cardiovascular: Test substance was >99% purity verified analytically. Impurities were reported "Acidic components (assumed to be hydrochloric acid) were found to be present at a concentration of 10.8 ppm. One impurity with an area that was approximately 0.7% of the major peak area; this impurity, identified as 1 ,4-dichlorobenzene"; Lung/Respiratory: Test substance was >99% purity verified analytically. impurities were reported "Acidic components (assumed to be hydrochloric acid) were found to be present at a concentration of 10.8 ppm. one impurity with an area that was approximately 0.7% of the major peak area; this impurity, identified as 1 ,4-dichlorobenzene"; Immune/Hematological: Test substance was >99% purity verified analytically. impurities were reported "Acidic components (assumed to be hydrochloric acid) were found to be present at a concentration of 10.8 ppm. one impurity with an area that was approximately 0.7% of the major peak area; this impurity, identified as 1 ,4-dichlorobenzene"; Hepatic/Liver: Test substance was >99% purity verified analytically. impurities were reported "Acidic components (assumed to be hydrochloric acid) were found to be present at a concentration of 10.8 ppm. one impurity with an area that was approximately 0.7% of the major peak area; this impurity, identified as 1 ,4-dichlorobenzene"; Cardiovascular: Test substance was >99% purity verified analytically. impurities were reported "Acidic components (assumed to be hydrochloric acid) were found to be present at a concentration of 10.8 ppm. one impurity with an area that was approximately 0.7% of the major peak area; this impurity, identified as 1 ,4-dichlorobenzene"; Lung/Respiratory: Test substance was >99% purity verified analytically. impurities were reported "Acidic components (assumed to be hydrochloric acid) were found to be present at a concentration of 10.8 ppm. one impurity with an area that was approximately 0.7% of the major peak area; this impurity, identified as 1 ,4-dichlorobenzene"; Nutritional/Metabolic: Test substance was >99% purity verified analytically. Impurities were reported "Acidic components (assumed to be hydrochloric acid) were found to be present at a concentration of 10.8 ppm. One impurity with an area that was approximately 0.7% of the major peak area; this impurity, identified as 1 ,4-dichlorobenzene"; Mortality: Test substance was >99% purity verified analytically. impurities were reported "Acidic components (assumed to be hydrochloric acid) were found to be present at a concentration of 10.8 ppm. one impurity with an area that was approximately 0.7% of the major peak area; this impurity, identified as 1 ,4-dichlorobenzene"; Hepatic/Liver: Test substance was >99% purity verified analytically; impurities were reported "Acidic components (assumed to be hydrochloric acid) were found to be present at a concentration of 10.8 ppm. one impurity with an area that was approximately 0.7% of the major peak area; this impurity, identified as 1 ,4-dichlorobenzene";

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Study Citation:	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.
Health Outcome(s):	Cardiovascular; Lung/Respiratory; Immune/Hematological; Hepatic/Liver; Cardiovascular; Lung/Respiratory; Nutritional/Metabolic; Mortality; Mortality; Hepatic/Liver; Renal/Kidney;
Reported Health Effect(s):	Cardiovascular: Heart weight, cholesterol, triglycerides; Lung/Respiratory: Lung weight and histology; Immune/Hematological: Organ weight (spleen, thymus), hematology (hgb, hct, RBC, WBC, MCV, platelets, reticulocytes), Histology (thymus, spleen, bone marrow, and lymph node); histopathology (thymus (rats only) & spleen (rats and mice); Hepatic/Liver: Liver weight, histopathology, clinical chemistry (Mice & rats: ALP, GGT, and glutamic pyruvic transaminase; Rats only: bilirubin, cholesterol, triglycerides, BUN, glucose, total protein); Cardiovascular: Heart weight, cholesterol, triglycerides; Lung/Respiratory: Lung weight and histology; Nutritional/Metabolic: Body weight; Mortality: Death; Mortality: Death; Hepatic/Liver: Liver weight, histopathology, clinical chemistry (Mice & rats: ALP, GGT, and glutamic pyruvic transaminase; Rats only: bilirubin, cholesterol, triglycerides, BUN, glucose, total protein); Renal/Kidney: clinical chemistry (BUN (rats only)), kidney weight, histology;
Duration:	Subchronic (>30-91 days) 13 weeks Mouse
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	1944492

Domain	Metric	Rating	Comments
Domain 2: Test Design	Metric 4: Negative and Vehicle Controls	High	All Outcomes: Concurrent vehicle control was used and appropriate for the study
	Metric 5: Positive Controls	N/A	All Outcomes: Not necessary for the study type
	Metric 6: Randomized Allocation of Animals	Medium	All Outcomes: The study reported the random allocation of animals into groups
Domain 3: Exposure Characterization	Metric 7: Preparation and Storage of Test Substance	High	All Outcomes: Dose preparation and storage were reported "adding a weighed amount of 1,2-dichlorobenzene to the appropriate volume of corn oil and mixing for 15 minutes" then doses solutions were prepared by dilution. The mixture was stable at room temp for 7 days and solutions were stored no longer than 14 days at 4 degrees C
	Metric 8: Consistency of Exposure Administration	High	Cardiovascular: Details of exposure administration were reported and consistent; gavage volume was not excessive 5ml/kg.; Lung/Respiratory: Details of exposure administration were reported and consistent. gavage volume was not excessive 5ml/kg.; Immune/Hematological: Details of exposure administration were reported and consistent. gavage volume was not excessive 5ml/kg.; Hepatic/Liver: Details of exposure administration were reported and consistent. gavage volume was not excessive 5ml/kg.; Cardiovascular: Details of exposure administration were reported and consistent. gavage volume was not excessive 5ml/kg.; Lung/Respiratory: Details of exposure administration were reported and consistent. gavage volume was not excessive 5ml/kg.; Nutritional/Metabolic: Details of exposure administration were reported and consistent; gavage volume was not excessive 5ml/kg.; Mortality: Details of exposure administration were reported and consistent. Gavage volume was not excessive 5ml/kg.; Mortality: Details of exposure administration were reported and consistent. gavage volume was not excessive 5ml/kg.; Hepatic/Liver: Details of exposure administration were reported and consistent; gavage volume was not excessive 5ml/kg.; Renal/Kidney: Details of exposure administration were reported and consistent; gavage volume was not excessive 5ml/kg.
	Metric 9: Reporting of Doses/Concentrations	High	All Outcomes: Doses were reported clearly

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Study Citation:	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.
Health Outcome(s):	Cardiovascular; Lung/Respiratory; Immune/Hematological; Hepatic/Liver; Cardiovascular; Lung/Respiratory; Nutritional/Metabolic; Mortality; Mortality; Hepatic/Liver; Renal/Kidney;
Reported Health Effect(s):	Cardiovascular: Heart weight, cholesterol, triglycerides; Lung/Respiratory: Lung weight and histology; Immune/Hematological: Organ weight (spleen, thymus), hematology (hgb, hct, RBC, WBC, MCV, platelets, reticulocytes), Histology (thymus, spleen, bone marrow, and lymph node); histopathology (thymus (rats only) & spleen (rats and mice); Hepatic/Liver: Liver weight, histopathology, clinical chemistry (Mice & rats: ALP, GGT, and glutamic pyruvic transaminase; Rats only: bilirubin, cholesterol, triglycerides, BUN, glucose, total protein); Cardiovascular: Heart weight, cholesterol, triglycerides; Lung/Respiratory: Lung weight and histology; Nutritional/Metabolic: Body weight; Mortality: Death; Mortality: Death; Hepatic/Liver: Liver weight, histopathology, clinical chemistry (Mice & rats: ALP, GGT, and glutamic pyruvic transaminase; Rats only: bilirubin, cholesterol, triglycerides, BUN, glucose, total protein); Renal/Kidney: clinical chemistry (BUN (rats only)), kidney weight, histology;
Duration:	Subchronic (>30-91 days) 13 weeks Mouse
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	1944492

Domain	Metric	Rating	Comments
Metric 10:	Exposure Frequency and Duration	High	Cardiovascular: Exposure frequency (5days/week) and duration (13 weeks) were appropriate for the study type; Lung/Respiratory: Exposure frequency (5days/week) and duration (13 weeks) were appropriate for the study type; Immune/Hematological: Exposure frequency (5days/week) and duration (13 weeks) were appropriate for the study type; Hepatic/Liver: Exposure frequency (5days/week) and duration (13 weeks) were appropriate for the study type; Cardiovascular: Exposure frequency (5days/week) and duration (13 weeks) were appropriate for the study type; Lung/Respiratory: Exposure frequency (5days/week) and duration (13 weeks) were appropriate for the study type; Nutritional/Metabolic: Exposure frequency (5days/week) and duration (13 weeks) were appropriate for the study type; Mortality: Exposure frequency (5 days/week) and duration (13 weeks) were appropriate for the study type; Mortality: Exposure frequency (5days/week) and duration (13 weeks) were appropriate for the study type; Hepatic/Liver: Exposure frequency (5days/week) and duration (13 weeks) were appropriate for the study type; Renal/Kidney: Exposure frequency (5days/week) and duration (13 weeks) were appropriate for the study type

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Study Citation:	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.			
Health Outcome(s):	Cardiovascular; Lung/Respiratory; Immune/Hematological; Hepatic/Liver; Cardiovascular; Lung/Respiratory; Nutritional/Metabolic; Mortality; Mortality; Hepatic/Liver; Renal/Kidney;			
Reported Health Effect(s):	Cardiovascular: Heart weight, cholesterol, triglycerides; Lung/Respiratory: Lung weight and histology; Immune/Hematological: Organ weight (spleen, thymus), hematology (hgb, hct, RBC, WBC, MCV, platlets, reticulocytes), Histology (thymus, spleen, bone marrow, and lymph node); histopathology (thymus (rats only) & spleen (rats and mice); Hepatic/Liver: Liver weight, histopathology, vlinical chemistry (Mice & rats: ALP, GGT, and glutamic pyruvic transaminase; Rats only: bilirubin, cholesterol, triglycerides, BUN, glucose, total protein); Cardiovascular: Heart weight, cholesterol, triglycerides; Lung/Respiratory: Lung weight and histology; Nutritional/Metabolic: Body weight; Mortality: Death; Mortality: Death; Hepatic/Liver: Liver weight, histopathology, vlinical chemistry (Mice & rats: ALP, GGT, and glutamic pyruvic transaminase; Rats only: bilirubin, cholesterol, triglycerides, BUN, glucose, total protein); Renal/Kidney: clinical chemistry (BUN (rats only)), kidney weight, histology;			
Duration:	Subchronic (>30-91 days) 13 weeks Mouse			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	1944492			
Domain	Metric	Rating	Comments	
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	Cardiovascular: Number of exposure groups was adequate and consisted of 5 treated groups and a control. Spacing was justified using the results of the short term study.; Lung/Respiratory: Number of exposure groups was adequate and consisted of 5 treated groups and a control. Spacing was justified based on the results of the short term study.; Immune/Hematological: Number of exposure groups was adequate and consisted of 5 treated groups and a control. Spacing was sufficient to encompass a full range of response; Hepatic/Liver: Number of exposure groups was adequate and consisted of 5 treated groups and a control. Spacing was sufficient to encompass a full range of response; Cardiovascular: Number of exposure groups was adequate and consisted of 5 treated groups and a control. Spacing was justified by previous short term study; Lung/Respiratory: Number of exposure groups was adequate and consisted of 5 treated groups and a control. Spacing was sufficient to encompass a full range of response; Nutritional/Metabolic: Number of exposure groups was adequate and consisted of 5 treated groups and a control. Spacing was sufficient to encompass a full range of response; Mortality: Number of exposure groups was adequate and consisted of 5 treated groups and a control. Spacing was sufficient to encompass a full range of response; Mortality: Number of exposure groups was adequate and consisted of 5 treated groups and a control. Spacing was sufficient to encompass a full range of response; Hepatic/Liver: Number of exposure groups was adequate and consisted of 5 treated groups and a control. Spacing was sufficient to encompass a full range of response; Renal/Kidney: Number of exposure groups was adequate and consisted of 5 treated groups and a control. Spacing was Justified based on the results from the short term study.	
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Study Citation:	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.
Health Outcome(s):	Cardiovascular; Lung/Respiratory; Immune/Hematological; Hepatic/Liver; Cardiovascular; Lung/Respiratory; Nutritional/Metabolic; Mortality; Mortality; Hepatic/Liver; Renal/Kidney;
Reported Health Effect(s):	Cardiovascular: Heart weight, cholesterol, triglycerides; Lung/Respiratory: Lung weight and histology; Immune/Hematological: Organ weight (spleen, thymus), hematology (hgb, hct, RBC, WBC, MCV, platelets, reticulocytes), Histology (thymus, spleen, bone marrow, and lymph node); histopathology (thymus (rats only) & spleen (rats and mice); Hepatic/Liver: Liver weight, histopathology, clinical chemistry (Mice & rats: ALP, GGT, and glutamic pyruvic transaminase; Rats only: bilirubin, cholesterol, triglycerides, BUN, glucose, total protein); Cardiovascular: Heart weight, cholesterol, triglycerides; Lung/Respiratory: Lung weight and histology; Nutritional/Metabolic: Body weight; Mortality: Death; Mortality: Death; Hepatic/Liver: Liver weight, histopathology, clinical chemistry (Mice & rats: ALP, GGT, and glutamic pyruvic transaminase; Rats only: bilirubin, cholesterol, triglycerides, BUN, glucose, total protein); Renal/Kidney: clinical chemistry (BUN (rats only)), kidney weight, histology;
Duration:	Subchronic (>30-91 days) 13 weeks Mouse
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	1944492

Domain	Metric	Rating	Comments
	Metric 12: Exposure Route and Method	High	Cardiovascular: Exposure route and method were suited to the test substance: gavage is appropriate; Lung/Respiratory: Exposure route and method were suited to the test substance: gavage is appropriate; Immune/Hematological: Exposure route and method were suited to the test substance: gavage is appropriate; Hepatic/Liver: Exposure route and method were suited to the test substance: gavage is appropriate; Cardiovascular: Exposure route and method were suited to the test substance: gavage is appropriate; Lung/Respiratory: Exposure route and method were suited to the test substance: gavage is appropriate; Nutritional/Metabolic: Exposure route and method were suited to the test substance: gavage is appropriate; Mortality: Exposure route and method were suited to the test substance: gavage is appropriate; Mortality: Exposure route and method were suited to the test substance: gavage is appropriate; Hepatic/Liver: Exposure route and method were suited to the test substance: gavage is appropriate; Renal/Kidney: Exposure route and method were suited to the test substance: gavage is appropriate
Domain 4: Test Animals			
	Metric 13: Test Animal Characteristics	High	All Outcomes: Species, strain, sex, and age were all reported in table 1. Initial body weight was reported in the results
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: All husbandry conditions were reported in table 1: temperature, humidity, light- dark cycle, diet, water availability and were adequate and consistent across all groups

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Study Citation:	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.
Health Outcome(s):	Cardiovascular; Lung/Respiratory; Immune/Hematological; Hepatic/Liver; Cardiovascular; Lung/Respiratory; Nutritional/Metabolic; Mortality; Mortality; Hepatic/Liver; Renal/Kidney;
Reported Health Effect(s):	Cardiovascular: Heart weight, cholesterol, triglycerides; Lung/Respiratory: Lung weight and histology; Immune/Hematological: Organ weight (spleen, thymus), hematology (hgb, hct, RBC, WBC, MCV, platelets, reticulocytes), Histology (thymus, spleen, bone marrow, and lymph node); histopathology (thymus (rats only) & spleen (rats and mice); Hepatic/Liver: Liver weight, histopathology, clinical chemistry (Mice & rats: ALP, GGT, and glutamic pyruvic transaminase; Rats only: bilirubin, cholesterol, triglycerides, BUN, glucose, total protein); Cardiovascular: Heart weight, cholesterol, triglycerides; Lung/Respiratory: Lung weight and histology; Nutritional/Metabolic: Body weight; Mortality: Death; Mortality: Death; Hepatic/Liver: Liver weight, histopathology, clinical chemistry (Mice & rats: ALP, GGT, and glutamic pyruvic transaminase; Rats only: bilirubin, cholesterol, triglycerides, BUN, glucose, total protein); Renal/Kidney: clinical chemistry (BUN (rats only)), kidney weight, histology;
Duration:	Subchronic (>30-91 days) 13 weeks Mouse
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	1944492

Domain	Metric	Rating	Comments
Metric 15:	Number of Animals per Group	Medium	Cardiovascular: The number of animals per group was reported and appropriate for the study type: 10/sex/group for subchronic; Lung/Respiratory: The number of animals per group was reported and appropriate for the study type: 10/sex/group for subchronic; Immune/Hematological: The number of animals per group was reported and appropriate for the study type: 10/sex/group for subchronic; Hepatic/Liver: The number of animals per group was reported and appropriate for the study type: 10/sex/group for subchronic; Cardiovascular: The number of animals per group was reported and appropriate for the study type: 10/sex/group for subchronic (8-10 after deaths); Lung/Respiratory: The number of animals per group was reported and appropriate for the study type: 10/sex/group for subchronic; Nutritional/Metabolic: The number of animals per group was reported and appropriate for the study type: 10/sex/group for subchronic; Mortality: The number of animals per group was reported and appropriate for the study type: 10/sex/group for subchronic; Mortality: The number of animals per group was reported and appropriate for the study type: 10/sex/group for subchronic; Hepatic/Liver: The number of animals per group was reported and appropriate for the study type: 10/sex/group for subchronic; Renal/Kidney: The number of animals per group was reported and appropriate for the study type: 10/sex/group for subchronic

Domain 5: Outcome Assessment

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Study Citation:	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.
Health Outcome(s):	Cardiovascular; Lung/Respiratory; Immune/Hematological; Hepatic/Liver; Cardiovascular; Lung/Respiratory; Nutritional/Metabolic; Mortality; Mortality; Hepatic/Liver; Renal/Kidney;
Reported Health Effect(s):	Cardiovascular: Heart weight, cholesterol, triglycerides; Lung/Respiratory: Lung weight and histology; Immune/Hematological: Organ weight (spleen, thymus), hematology (hgb, hct, RBC, WBC, MCV, platelets, reticulocytes), Histology (thymus, spleen, bone marrow, and lymph node); histopathology (thymus (rats only) & spleen (rats and mice); Hepatic/Liver: Liver weight, histopathology, clinical chemistry (Mice & rats: ALP, GGT, and glutamic pyruvic transaminase; Rats only: bilirubin, cholesterol, triglycerides, BUN, glucose, total protein); Cardiovascular: Heart weight, cholesterol, triglycerides; Lung/Respiratory: Lung weight and histology; Nutritional/Metabolic: Body weight; Mortality: Death; Mortality: Death; Hepatic/Liver: Liver weight, histopathology, clinical chemistry (Mice & rats: ALP, GGT, and glutamic pyruvic transaminase; Rats only: bilirubin, cholesterol, triglycerides, BUN, glucose, total protein); Renal/Kidney: clinical chemistry (BUN (rats only)), kidney weight, histology;
Duration:	Subchronic (>30-91 days) 13 weeks Mouse
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	1944492

Domain	Metric	Rating	Comments
	Metric 16: Outcome Assessment Methodology	High	Cardiovascular: Outcome assessment was sensitive and appropriate for the outcome but limited to organ weight and histology; Lung/Respiratory: Outcome assessment was sensitive and appropriate for the outcome but limited to organ weight and histology; Immune/Hematological: Outcome assessment was sensitive and appropriate for the outcome; Hepatic/Liver: Outcome assessment was sensitive and appropriate for the outcome. clinical chemistry panel tested ALT, GGT, ALP, bili, chol, and TG, but does not include AST; Cardiovascular: Outcome assessment was sensitive and appropriate for the outcome and include organ weight and histopathology; Lung/Respiratory: Outcome assessment was sensitive and appropriate for the outcome but limited to organ weight and histology; Nutritional/Metabolic: Outcome assessment was sensitive and appropriate for the outcome; Mortality: Outcome assessment was sensitive and appropriate for the outcome; Mortality: Outcome assessment was sensitive and appropriate for the outcome of interest.; Hepatic/Liver: Outcome assessment was sensitive and appropriate for the outcome of interest: organ weight, histology, and clinical chemistry values of ALT, ggt, bilirubin etc. were included. AST was not included.; Renal/Kidney: Outcome assessment was sensitive and appropriate for the outcome, but was limited to organ weight and histology, clinical chemistry (BUN)
	Metric 17: Consistency of Outcome Assessment	High	All Outcomes: Outcome was assessed consistently across groups
	Metric 18: Sampling Adequacy	High	All Outcomes: Sampling was adequate
	Metric 19: Blinding of Assessors	N/A	All Outcomes: Blinding was not necessary for the study type
	Metric 20: Negative Control Response	High	All Outcomes: Control group responded adequately
Domain 6: Confounding / Variable Control			
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	All Outcomes: Reported information did not identify differences in confounding factors

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Study Citation:	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.
Health Outcome(s):	Cardiovascular; Lung/Respiratory; Immune/Hematological; Hepatic/Liver; Cardiovascular; Lung/Respiratory; Nutritional/Metabolic; Mortality; Mortality; Hepatic/Liver; Renal/Kidney;
Reported Health Effect(s):	Cardiovascular: Heart weight, cholesterol, triglycerides; Lung/Respiratory: Lung weight and histology; Immune/Hematological: Organ weight (spleen, thymus), hematology (hgb, hct, RBC, WBC, MCV, platelets, reticulocytes), Histology (thymus, spleen, bone marrow, and lymph node); histopathology (thymus (rats only) & spleen (rats and mice); Hepatic/Liver: Liver weight, histopathology, clinical chemistry (Mice & rats: ALP, GGT, and glutamic pyruvic transaminase; Rats only: bilirubin, cholesterol, triglycerides, BUN, glucose, total protein); Cardiovascular: Heart weight, cholesterol, triglycerides; Lung/Respiratory: Lung weight and histology; Nutritional/Metabolic: Body weight; Mortality: Death; Mortality: Death; Hepatic/Liver: Liver weight, histopathology, clinical chemistry (Mice & rats: ALP, GGT, and glutamic pyruvic transaminase; Rats only: bilirubin, cholesterol, triglycerides, BUN, glucose, total protein); Renal/Kidney: clinical chemistry (BUN (rats only)), kidney weight, histology;
Duration:	Subchronic (>30-91 days) 13 weeks Mouse
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	1944492

Domain	Metric	Rating	Comments
Metric 22:	Health Outcomes Unrelated to Exposure	Medium	Cardiovascular: Insufficient information provided to support or dismiss whether there were differences among groups.; Lung/Respiratory: Insufficient information provided to support or dismiss whether there were differences among groups.; Immune/Hematological: Premature death due to gavage error was reported in 1 male in the control, 30, and 125 mg/kg/day groups. An additional one male in the 250 mg/kg/day group was removed due to being missexed.; Hepatic/Liver: Premature death due to gavage error was reported in 1 male in the control, 30, and 125 mg/kg/day groups. An additional one male in the 250 mg/kg/day group was removed due to being missexed. Remaining animals were used for outcome; Cardiovascular: Premature death due to gavage error was reported in 1 male in the control, 30, and 125 mg/kg/day groups. An additional one male in the 250 mg/kg/day group was removed due to being missexed.; Lung/Respiratory: Premature death due to gavage error was reported in 1 male in the control, 30, and 125 mg/kg/day groups. An additional one male in the 250 mg/kg/day group was removed due to being missexed.; Nutritional/Metabolic: Insufficient information provided to support or dismiss whether there were differences among groups.; Mortality: Premature death due to gavage error was reported in 1 male in the control, 30, and 125 mg/kg/day groups. An additional one male in the 250 mg/kg/day group was removed due to being missexed.; Mortality: Insufficient information provided to support or dismiss whether there were differences among groups.; Hepatic/Liver: Insufficient information provided to support or dismiss whether there were differences among groups.; Renal/Kidney: Insufficient information provided to support or dismiss whether there were differences among groups.
Metric 23:	Data Presentation and Analysis	High	All Outcomes: Statistical methods were reported and appropriate for the data
Metric 24:	Reporting of Data	High	All Outcomes: Data were reported for all outcomes by group and sex

Additional Comments: None

Overall Quality Determination**High**

Study Citation:	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.			
Health Outcome(s):	Immune/Hematological			
Reported Health Effect(s):	Immune/Hematological: Organ weight (spleen, thymus), hematology (hgb, hct, RBC, WBC, MCV, platlets, reticulocytes), Histology (thymus, spleen, bone marrow, and lymph node); histopathology (thymus (rats only) & spleen (rats and mice)			
Duration:	Subchronic (>30-91 days) 13 weeks Mouse			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	1944492			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1:	Test Substance Identity	High	Test substance was identified by nomenclature, CAS number, and structure
	Metric 2:	Test Substance Source	High	Test substance was obtained from a commercial source: " ICC solvent Chemical Company (New York, NY) Lot number SC61377 and analytically verified.
	Metric 3:	Test Substance Purity	High	Test substance was >99% purity verified analytically. Impurities were reported "Acidic components (assumed to be hydrochloric acid) were found to be present at a concentration of 10.8 ppm. One impurity with an area that was approximately 0.7% of the major peak area; this impurity, identified as 1 ,4-dichlorobenzene"
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	Concurrent vehicle control was used and appropriate for the study
	Metric 5:	Positive Controls	N/A	Not necessary for the study type
	Metric 6:	Randomized Allocation of Animals	Medium	The study reported the random allocation of animals into groups
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and Storage of Test Substance	High	Dose preparation and storage were reported "adding a weighed amount of 1 ,2-dichlorobenzene to the appropriate volume of corn oil and mixing for 15 minutes" then doses solutions were prepared by dilution. The mixture was stable at room temp for 7 days and solutions were stored no longer than 14 days at 4 degrees C
	Metric 8:	Consistency of Exposure Administration	High	Details of exposure administration were reported and consistent. gavage volume was not excessive 5ml/kg.
	Metric 9:	Reporting of Doses/Concentrations	High	Doses were reported clearly
	Metric 10:	Exposure Frequency and Duration	High	Exposure frequency (5days/week) and duration (13 weeks) were appropriate for the study type
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	Number of exposure groups was adequate and consisted of 5 treated groups and a control. Spacing was sufficient to encompass a full range of response
	Metric 12:	Exposure Route and Method	High	Exposure route and method were suited to the test substance: gavage is appropriate
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	High	Species, strain, sex, and age were all reported in table 1. Initial body weight was reported in the results
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were reported in table 1: temperature, humidity, light- dark cycle, diet, water availability and were adequate and consistent across all groups
	Metric 15:	Number of Animals per Group	Medium	The number of animals per group was reported and appropriate for the study type: 10/sex/group for subchronic
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Study Citation:	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.			
Health Outcome(s):	Immune/Hematological			
Reported Health Effect(s):	Immune/Hematological: Organ weight (spleen, thymus), hematology (hgb, hct, RBC, WBC, MCV, platlets, reticulocytes), Histology (thymus, spleen, bone marrow, and lymph node); histopathology (thymus (rats only) & spleen (rats and mice)			
Duration:	Subchronic (>30-91 days) 13 weeks Mouse			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	1944492			
Domain	Metric	Rating	Comments	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	High	Outcome assessment was sensitive and appropriate for the outcome	
	Metric 17: Consistency of Outcome Assessment	High	Outcome was assessed consistently across groups	
	Metric 18: Sampling Adequacy	High	Sampling was adequate	
	Metric 19: Blinding of Assessors	N/A	Blinding was not necessary for the study type	
	Metric 20: Negative Control Response	Medium	Control group responded appropriately in organ weights, histopathology, and numerous hematological parameters, however, it was noted that the male control group WBC were lower than observed historically, but still within historic range.	
Domain 6: Confounding / Variable Control				
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	Reported information did not identify differences in confounding factors	
	Metric 22: Health Outcomes Unrelated to Exposure	Medium	Insufficient information provided to support or dismiss whether there were differences among groups.	
	Metric 23: Data Presentation and Analysis	High	Statistical methods were reported and appropriate for the data	
	Metric 24: Reporting of Data	High	Data were reported for all outcomes by group and sex	
Additional Comments: None				
Overall Quality Determination		High		

Study Citation:	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.			
Health Outcome(s):	Renal/Kidney			
Reported Health Effect(s):	Renal/Kidney: clinical chemistry (BUN (rats only)), kidney weight, histology			
Duration:	Subchronic (>30-91 days) 13 weeks Rat			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	1944492			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	Test substance was identified by nomenclature, CAS number, and structure	
	Metric 2: Test Substance Source	High	Test substance was obtained from a commercial source: " ICC solvent Chemical Company (New York, NY) Lot number SC61377 and analytically verified.	
	Metric 3: Test Substance Purity	High	Test substance was >99% purity verified analytically. impurities were reported "Acidic components (assumed to be hydrochloric acid) were found to be present at a concentration of 10.8 ppm. one impurity with an area that was approximately 0.7% of the major peak area; this impurity, identified as 1 ,4-dichlorobenzene"	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	Concurrent vehicle control was used and appropriate for the study	
	Metric 5: Positive Controls	N/A	Not necessary for the study type	
	Metric 6: Randomized Allocation of Animals	Medium	The study reported the random allocation of animals into groups	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	High	Dose preparation and storage were reported "adding a weighed amount of 1 ,2-dichlorobenzene to the appropriate volume of corn oil and mixing for 15 minutes" then doses solutions were prepared by dilution. The mixture was stable at room temp for 7 days and solutions were stored no longer than 14 days at 4 degrees C	
	Metric 8: Consistency of Exposure Administration	High	Details of exposure administration were reported and consistent. gavage volume was not excessive 5ml/kg.	
	Metric 9: Reporting of Doses/Concentrations	High	Doses were reported clearly	
	Metric 10: Exposure Frequency and Duration	High	Exposure frequency (5days/week) and duration (13 weeks) were appropriate for the study type	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	Number of exposure groups was adequate and consisted of 5 treated groups and a control. Spacing was sufficient to encompass a full range of response	
	Metric 12: Exposure Route and Method	High	Exposure route and method were suited to the test substance: gavage is appropriate	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	High	Species, strain, sex, and age were all reported in table 1. Initial body weight was reported in the results	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were reported in table 1: temperature, humidity, light- dark cycle, diet, water availability and were adequate and consistent across all groups	
	Metric 15: Number of Animals per Group	Medium	The number of animals per group was reported and appropriate for the study type: 10/sex/group for subchronic	
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Study Citation:	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Renal/Kidney: clinical chemistry (BUN (rats only)), kidney weight, histology
Duration:	Subchronic (>30-91 days) 13 weeks Rat
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	1944492

Domain	Metric	Rating	Comments
Domain 5: Outcome Assessment			
Metric 16:	Outcome Assessment Methodology	Medium	The outcome assessment was sensitive and appropriate for the outcome of interest but was limited to gross and histopathological examination.
Metric 17:	Consistency of Outcome Assessment	High	Outcome was assessed consistently across groups
Metric 18:	Sampling Adequacy	High	Sampling was adequate
Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary for the study type
Metric 20:	Negative Control Response	High	Control group responded adequately
Domain 6: Confounding / Variable Control			
Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Reported information did not identify differences in confounding factors
Metric 22:	Health Outcomes Unrelated to Exposure	Medium	Premature death due to gavage error was reported in 1 male in the control, 30, and 125 mg/kg/day groups. An additional one male in the 250 mg/kg/day group was removed due to being missexed.
Metric 23:	Data Presentation and Analysis	High	Statistical methods were reported and appropriate for the data
Metric 24:	Reporting of Data	High	Data were reported for all outcomes by group and sex

Additional Comments: None

Overall Quality Determination**High**

Study Citation:	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.
Health Outcome(s):	Skin/Connective Tissue; Gastrointestinal; Endocrine (Endocrine); Thyroid; Gastrointestinal; Endocrine (Endocrine); Skin/Connective Tissue; Thyroid;
Reported Health Effect(s):	Skin/Connective Tissue: Skin histology; Gastrointestinal: Histology of salivary gland, esophagus, stomach, small intestine, large intestine; Endocrine (Endocrine): Parathyroid, pituitary, pancreas, adrenals histology; Thyroid: Thyroid histology; Gastrointestinal: Histology of salivary gland, esophagus, stomach, small intestine, large intestine; Endocrine (Endocrine): Parathyroid, pituitary, pancreas, adrenals histology; Skin/Connective Tissue: Skin histology; Thyroid: Thyroid histology;
Duration:	Subchronic (>30-91 days) 13 weeks Mouse
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	1944492

Domain	Metric	Rating	Comments
Domain 1: Test Substance			
	Metric 1: Test Substance Identity	High	All Outcomes: Test substance was identified by nomenclature, CAS number, and structure
	Metric 2: Test Substance Source	High	All Outcomes: Test substance was obtained from a commercial source: " ICC solvent Chemical Company (New York, NY) Lot number SC61377 and analytically verified.
	Metric 3: Test Substance Purity	High	Skin/Connective Tissue: Test substance was >99% purity verified analytically. impurities were reported "Acidic components (assumed to be hydrochloric acid) were found to be present at a concentration of 10.8 ppm. one impurity with an area that was approximately 0.7% of the major peak area; this impurity, identified as 1 ,4-dichlorobenzene"; Gastrointestinal: Test substance was >99% purity verified analytically. Impurities were reported "Acidic components (assumed to be hydrochloric acid) were found to be present at a concentration of 10.8 ppm. One impurity with an area that was approximately 0.7% of the major peak area; this impurity, identified as 1 ,4-dichlorobenzene"; Endocrine (Endocrine): Test substance was >99% purity verified analytically. impurities were reported "Acidic components (assumed to be hydrochloric acid) were found to be present at a concentration of 10.8 ppm. one impurity with an area that was approximately 0.7% of the major peak area; this impurity, identified as 1 ,4-dichlorobenzene"; Thyroid: Test substance was >99% purity verified analytically. impurities were reported "Acidic components (assumed to be hydrochloric acid) were found to be present at a concentration of 10.8 ppm. one impurity with an area that was approximately 0.7% of the major peak area; this impurity, identified as 1 ,4-dichlorobenzene"; Gastrointestinal: Test substance was >99% purity verified analytically. impurities were reported "Acidic components (assumed to be hydrochloric acid) were found to be present at a concentration of 10.8 ppm. one impurity with an area that was approximately 0.7% of the major peak area; this impurity, identified as 1 ,4-dichlorobenzene"; Endocrine (Endocrine): Test substance was >99% purity verified analytically. impurities were reported "Acidic components (assumed to be hydrochloric acid) were found to be present at a concentration of 10.8 ppm. one impurity with an area that was approximately 0.7% of the major peak area; this impurity, identified as 1 ,4-dichlorobenzene"; Skin/Connective Tissue: Test substance was >99% purity verified analytically. impurities were reported "Acidic components (assumed to be hydrochloric acid) were found to be present at a concentration of 10.8 ppm. one impurity with an area that was approximately 0.7% of the major peak area; this impurity, identified as 1 ,4-dichlorobenzene"; Thyroid: Test substance was >99% purity verified analytically. Impurities were reported "Acidic components (assumed to be hydrochloric acid) were found to be present at a concentration of 10.8 ppm. one impurity with an area that was approximately 0.7% of the major peak area; this impurity, identified as 1 ,4-dichlorobenzene"

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Study Citation:	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.
Health Outcome(s):	Skin/Connective Tissue; Gastrointestinal; Endocrine (Endocrine); Thyroid; Gastrointestinal; Endocrine (Endocrine); Skin/Connective Tissue; Thyroid;
Reported Health Effect(s):	Skin/Connective Tissue: Skin histology; Gastrointestinal: Histology of salivary gland, esophagus, stomach, small intestine, large intestine; Endocrine (Endocrine): Parathyroid, pituitary, pancreas, adrenals histology; Thyroid: Thyroid histology; Gastrointestinal: Histology of salivary gland, esophagus, stomach, small intestine, large intestine; Endocrine (Endocrine): Parathyroid, pituitary, pancreas, adrenals histology; Skin/Connective Tissue: Skin histology; Thyroid: Thyroid histology;
Duration:	Subchronic (>30-91 days) 13 weeks Mouse
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	1944492

Domain	Metric	Rating	Comments
Domain 2: Test Design			
	Metric 4: Negative and Vehicle Controls	High	All Outcomes: Concurrent vehicle control was used and appropriate for the study
	Metric 5: Positive Controls	N/A	All Outcomes: Not necessary for the study type
	Metric 6: Randomized Allocation of Animals	Medium	All Outcomes: The study reported the random allocation of animals into groups
Domain 3: Exposure Characterization			
	Metric 7: Preparation and Storage of Test Substance	High	All Outcomes: Dose preparation and storage were reported "adding a weighed amount of 1 ,2-dichlorobenzene to the appropriate volume of corn oil and mixing for 15 minutes" then doses solutions were prepared by dilution. The mixture was stable at room temp for 7 days and solutions were stored no longer than 14 days at 4 degrees C
	Metric 8: Consistency of Exposure Administration	High	All Outcomes: Details of exposure administration were reported and consistent. gavage volume was not excessive 5ml/kg.
	Metric 9: Reporting of Doses/Concentrations	High	All Outcomes: Doses were reported clearly
	Metric 10: Exposure Frequency and Duration	High	All Outcomes: Exposure frequency (5days/week) and duration (13 weeks) were appropriate for the study type
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	Skin/Connective Tissue: Number of exposure groups was adequate and consisted of 5 treated groups and a control. Spacing was justified based on the results of the short term study; Gastrointestinal: Number of exposure groups was adequate and consisted of 5 treated groups and a control. Spacing was justified based on the results of the short term study; Endocrine (Endocrine): Number of exposure groups was adequate and consisted of 5 treated groups and a control. Spacing was justified based on the results of the short term study; Thyroid: Number of exposure groups was adequate and consisted of 5 treated groups and a control. Spacing was justified based on results of the short term study; Gastrointestinal: Number of exposure groups was adequate and consisted of 5 treated groups and a control. Spacing was justified based on the results of the short term study; Endocrine (Endocrine): Number of exposure groups was adequate and consisted of 5 treated groups and a control. Spacing was justified based on the results of the short term study.; Skin/Connective Tissue: Number of exposure groups was adequate and consisted of 5 treated groups and a control. Spacing was justified based on the results of the short term study.; Thyroid: Number of exposure groups was adequate and consisted of 5 treated groups and a control. Spacing was sufficient to encompass a full range of response
	Metric 12: Exposure Route and Method	High	All Outcomes: Exposure route and method were suited to the test substance: gavage is appropriate

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Study Citation:	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.			
Health Outcome(s):	Skin/Connective Tissue; Gastrointestinal; Endocrine (Endocrine); Thyroid; Gastrointestinal; Endocrine (Endocrine); Skin/Connective Tissue; Thyroid;			
Reported Health Effect(s):	Skin/Connective Tissue: Skin histology; Gastrointestinal: Histology of salivary gland, esophagus, stomach, small intestine, large intestine; Endocrine (Endocrine): Parathyroid, pituitary, pancreas, adrenals histology; Thyroid: Thyroid histology; Gastrointestinal: Histology of salivary gland, esophagus, stomach, small intestine, large intestine; Endocrine (Endocrine): Parathyroid, pituitary, pancreas, adrenals histology; Skin/Connective Tissue: Skin histology; Thyroid: Thyroid histology;			
Duration:	Subchronic (>30-91 days) 13 weeks Mouse			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	1944492			
Domain		Metric	Rating	Comments
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	High	All Outcomes: Species, strain, sex, and age were all reported in table 1. Initial body weight was reported in the results
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: All husbandry conditions were reported in table 1: temperature, humidity, light- dark cycle, diet, water availability and were adequate and consistent across all groups
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: The number of animals per group was reported and appropriate for the study type: 10/sex/group for subchronic
Domain 5: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	Medium	Skin/Connective Tissue: Outcome assessment was sensitive and appropriate for the outcome but limited to histology; Gastrointestinal: Outcome assessment was sensitive and appropriate for the outcome but limited to histology; Endocrine (Endocrine): Outcome assessment was sensitive and appropriate for the outcome but was limited to histopathology of endocrine organs; Thyroid: Outcome assessment was sensitive and appropriate for the outcome, however it was limited to thyroid histopathology only. Organ weight and thyroid hormones were not measured.; Gastrointestinal: Outcome assessment was sensitive and appropriate for the outcome but was limited to histopathology; Endocrine (Endocrine): Outcome assessment was sensitive and appropriate for the outcome but was limited to histopathology of endocrine organs; Skin/Connective Tissue: Outcome assessment was sensitive and appropriate for the outcome, but was limited to histopathology; Thyroid: Outcome assessment was sensitive and appropriate for the outcome, however it was limited to thyroid histopathology only. Organ weight and thyroid hormones were not measured.
	Metric 17:	Consistency of Outcome Assessment	High	All Outcomes: Outcome was assessed consistently across groups
	Metric 18:	Sampling Adequacy	High	All Outcomes: Sampling was adequate
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding was not necessary for the study type
	Metric 20:	Negative Control Response	High	All Outcomes: Control group responded adequately
Domain 6: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: Reported information did not identify differences in confounding factors
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Study Citation:	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.
Health Outcome(s):	Skin/Connective Tissue; Gastrointestinal; Endocrine (Endocrine); Thyroid; Gastrointestinal; Endocrine (Endocrine); Skin/Connective Tissue; Thyroid;
Reported Health Effect(s):	Skin/Connective Tissue: Skin histology; Gastrointestinal: Histology of salivary gland, esophagus, stomach, small intestine, large intestine; Endocrine (Endocrine): Parathyroid, pituitary, pancreas, adrenals histology; Thyroid: Thyroid histology; Gastrointestinal: Histology of salivary gland, esophagus, stomach, small intestine, large intestine; Endocrine (Endocrine): Parathyroid, pituitary, pancreas, adrenals histology; Skin/Connective Tissue: Skin histology; Thyroid: Thyroid histology;
Duration:	Subchronic (>30-91 days) 13 weeks Mouse
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	1944492

Domain	Metric	Rating	Comments
	Metric 22: Health Outcomes Unrelated to Exposure	Medium	Skin/Connective Tissue: Insufficient information provided to support or dismiss whether there were differences among groups.; Gastrointestinal: Insufficient information provided to support or dismiss whether there were differences among groups.; Endocrine (Endocrine): Insufficient information provided to support or dismiss whether there were differences among groups.; Thyroid: Premature death due to gavage error was reported in 1 male in the control, 30, and 125 mg/kg/day groups. An additional one male in the 250 mg/kg/day group was removed due to being missexed.; Gastrointestinal: Premature death due to gavage error was reported in 1 male in the control, 30, and 125 mg/kg/day groups. An additional one male in the 250 mg/kg/day group was removed due to being missexed.; Endocrine (Endocrine): Premature death due to gavage error was reported in 1 male in the control, 30, and 125 mg/kg/day groups. An additional one male in the 250 mg/kg/day group was removed due to being missexed.; Skin/Connective Tissue: Premature death due to gavage error was reported in 1 male in the control, 30, and 125 mg/kg/day groups. An additional one male in the 250 mg/kg/day group was removed due to being missexed.; Thyroid: Insufficient information provided to support or dismiss whether there were differences among groups.
	Metric 23: Data Presentation and Analysis	High	All Outcomes: Statistical methods were reported and appropriate for the data
	Metric 24: Reporting of Data	Low	Skin/Connective Tissue: histology tables were not presented for 13 week data. Negative histology data were implied in text.; Gastrointestinal: histology tables were not presented for 13 week data. Negative histology data were implied in text.; Endocrine (Endocrine): Histology tables were not presented for 13 week data. Negative histology data were implied in text.; Thyroid: Histology tables were not presented for 13 week data. Negative histology data were implied in text.; Gastrointestinal: histology tables were not presented for 13 week data. Negative histology data were implied in text.; Endocrine (Endocrine): Histology tables were not presented for 13 week data. Negative histology data were implied in text.; Skin/Connective Tissue: Histology tables were not presented for 13 week data. Negative histology data were implied in text.; Thyroid: Histology tables were not presented for 13 week data. Negative histology data were implied in text.

Additional Comments: None

Overall Quality Determination**High**

Study Citation:	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.			
Health Outcome(s):	Reproductive/Developmental; Neurological/Behavioral; Reproductive/Developmental; Neurological/Behavioral;			
Reported Health Effect(s):	Reproductive/Developmental: Organ weight (testis, ovary, uterus); Histology (testis, ovary, uterus); Neurological/Behavioral: Brain weight and histology;			
Duration:	Subchronic (>30-91 days) 13 weeks Mouse			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	1944492			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	All Outcomes: Test substance was identified by nomenclature, CAS number, and structure	
	Metric 2: Test Substance Source	High	All Outcomes: Test substance was obtained from a commercial source: " ICC solvent Chemical Company (New York, NY) Lot number SC61377 and analytically verified.	
	Metric 3: Test Substance Purity	High	Reproductive/Developmental: Test substance was >99% purity verified analytically. Impurities were reported "Acidic components (assumed to be hydrochloric acid) were found to be present at a concentration of 10.8 ppm. One impurity with an area that was approximately 0.7% of the major peak area; this impurity, identified as 1 ,4-dichlorobenzene"; Neurological/Behavioral: Test substance was >99% purity verified analytically. impurities were reported "Acidic components (assumed to be hydrochloric acid) were found to be present at a concentration of 10.8 ppm. one impurity with an area that was approximately 0.7% of the major peak area; this impurity, identified as 1 ,4-dichlorobenzene"; Reproductive/Developmental: Test substance was >99% purity verified analytically. impurities were reported "Acidic components (assumed to be hydrochloric acid) were found to be present at a concentration of 10.8 ppm. one impurity with an area that was approximately 0.7% of the major peak area; this impurity, identified as 1 ,4-dichlorobenzene"; Neurological/Behavioral: Test substance was >99% purity verified analytically. impurities were reported "Acidic components (assumed to be hydrochloric acid) were found to be present at a concentration of 10.8 ppm. one impurity with an area that was approximately 0.7% of the major peak area; this impurity, identified as 1 ,4-dichlorobenzene"	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	All Outcomes: Concurrent vehicle control was used and appropriate for the study	
	Metric 5: Positive Controls	N/A	All Outcomes: Not necessary for the study type	
	Metric 6: Randomized Allocation of Animals	Medium	All Outcomes: The study reported the random allocation of animals into groups	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	High	All Outcomes: Dose preparation and storage were reported "adding a weighed amount of 1 ,2-dichlorobenzene to the appropriate volume of corn oil and mixing for 15 minutes" then doses solutions were prepared by dilution. The mixture was stable at room temp for 7 days and solutions were stored no longer than 14 days at 4 degrees C	
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Study Citation:	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.
Health Outcome(s):	Reproductive/Developmental; Neurological/Behavioral; Reproductive/Developmental; Neurological/Behavioral;
Reported Health Effect(s):	Reproductive/Developmental: Organ weight (testis, ovary, uterus); Histology (testis, ovary, uterus); Neurological/Behavioral: Brain weight and histology;
Duration:	Subchronic (>30-91 days) 13 weeks Mouse
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	1944492

Domain	Metric	Rating	Comments
	Metric 8: Consistency of Exposure Administration	High	Reproductive/Developmental: Details of exposure administration were reported and consistent. gavage volume was not excessive 5ml/kg.; Neurological/Behavioral: Details of exposure administration were reported and consistent. gavage volume was not excessive 5ml/kg.; Reproductive/Developmental: Details of exposure administration were reported and consistent. gavage volume was not excessive 5ml/kg.; Neurological/Behavioral: Details of exposure administration were reported and consistent. Gavage volume was not excessive 5ml/kg.
	Metric 9: Reporting of Doses/Concentrations	High	All Outcomes: Doses were reported clearly
	Metric 10: Exposure Frequency and Duration	High	Reproductive/Developmental: Exposure frequency (5days/week) and duration (13 weeks) were appropriate for the study type; Neurological/Behavioral: Exposure frequency (5days/week) and duration (13 weeks) were appropriate for the study type; Reproductive/Developmental: Exposure frequency (5days/week) and duration (13 weeks) were appropriate for the study type; Neurological/Behavioral: Exposure frequency (5 days/week) and duration (13 weeks) were appropriate for the study type
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	Reproductive/Developmental: Number of exposure groups was adequate and consisted of 5 treated groups and a control. Spacing was sufficient to encompass a full range of response; Neurological/Behavioral: Number of exposure groups was adequate and consisted of 5 treated groups and a control. Spacing was justified based on the results of the short term study.; Reproductive/Developmental: Number of exposure groups was adequate and consisted of 5 treated groups and a control. Spacing was sufficient to encompass a full range of response; Neurological/Behavioral: Number of exposure groups was adequate and consisted of 5 treated groups and a control. Spacing was justified based on the results of the short term study.
	Metric 12: Exposure Route and Method	High	All Outcomes: Exposure route and method were suited to the test substance: gavage is appropriate
Domain 4: Test Animals			
	Metric 13: Test Animal Characteristics	High	All Outcomes: Species, strain, sex, and age were all reported in table 1. Initial body weight was reported in the results
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: All husbandry conditions were reported in table 1: temperature, humidity, light- dark cycle, diet, water availability and were adequate and consistent across all groups
	Metric 15: Number of Animals per Group	Medium	All Outcomes: The number of animals per group was reported and appropriate for the study type: 10/sex/group for subchronic

Domain 5: Outcome Assessment

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Study Citation:	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.
Health Outcome(s):	Reproductive/Developmental; Neurological/Behavioral; Reproductive/Developmental; Neurological/Behavioral;
Reported Health Effect(s):	Reproductive/Developmental: Organ weight (testis, ovary, uterus); Histology (testis, ovary, uterus); Neurological/Behavioral: Brain weight and histology;
Duration:	Subchronic (>30-91 days) 13 weeks Mouse
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	1944492

Domain	Metric	Rating	Comments
	Metric 16: Outcome Assessment Methodology	Medium	Reproductive/Developmental: Outcome assessment was limited to reproductive organ weights and histopathology; Neurological/Behavioral: Outcome assessment was sensitive and appropriate for the outcome but limited to organ weight and histology; Reproductive/Developmental: Outcome assessment was limited to reproductive organ weight and histopathology; Neurological/Behavioral: Outcome assessment was sensitive and appropriate for the outcome, however, it was limited to histopathological evaluation of brain and nervous tissue
	Metric 17: Consistency of Outcome Assessment	High	All Outcomes: Outcome was assessed consistently across groups
	Metric 18: Sampling Adequacy	High	All Outcomes: Sampling was adequate
	Metric 19: Blinding of Assessors	N/A	All Outcomes: Blinding was not necessary for the study type
	Metric 20: Negative Control Response	High	All Outcomes: Control group responded adequately

Domain 6: Confounding / Variable Control

Metric 21:	Confounding Variables in Test Design and Procedures	Medium	All Outcomes: Reported information did not identify differences in confounding factors
Metric 22:	Health Outcomes Unrelated to Exposure	Medium	Reproductive/Developmental: Insufficient information provided to support or dismiss whether there were differences among groups.; Neurological/Behavioral: Insufficient information provided to support or dismiss whether there were differences among groups.; Reproductive/Developmental: Premature death due to gavage error was reported in 1 male in the control, 30, and 125 mg/kg/day groups. An additional one male in the 250 mg/kg/day group was removed due to being missexed.; Neurological/Behavioral: Premature death due to gavage error was reported in 1 male in the control, 30, and 125 mg/kg/day groups. An additional one male in the 250 mg/kg/day group was removed due to being missexed.
Metric 23:	Data Presentation and Analysis	High	All Outcomes: Statistical methods were reported and appropriate for the data
Metric 24:	Reporting of Data	Medium	Reproductive/Developmental: Organ weight data were reported by group and sex. Histology data was not reported for the 13-week studies.; Neurological/Behavioral: Organ weight data was presented for species and sex. Histology tables were not presented for 13 week data.; Reproductive/Developmental: Organ weight data were reported by group and sex. Histology data was not reported for the 13-week studies.; Neurological/Behavioral: Organ weight data was presented for species and sex. Histology tables were not presented for 13 week data.

Additional Comments: None

Overall Quality Determination

High

Study Citation:	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.			
Health Outcome(s):	Musculoskeletal; Musculoskeletal;			
Reported Health Effect(s):	Musculoskeletal: Histologic examination of femur, sternebrae, vertebrae, thigh muscle; Musculoskeletal: Histologic examination of femur, sternebrae, vertebrae, thigh muscle;			
Duration:	Subchronic (>30-91 days) 13 weeks Mouse			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	1944492			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
Metric 1:	Test Substance Identity	High	All Outcomes: Test substance was identified by nomenclature, CAS number, and structure	
Metric 2:	Test Substance Source	High	All Outcomes: Test substance was obtained from a commercial source: " ICC solvent Chemical Company (New York, NY) Lot number SC61377 and analytically verified.	
Metric 3:	Test Substance Purity	High	All Outcomes: Test substance was >99% purity verified analytically. impurities were reported "Acidic components (assumed to be hydrochloric acid) were found to be present at a concentration of 10.8 ppm. one impurity with an area that was approximately 0.7% of the major peak area; this impurity, identified as 1 ,4-dichlorobenzene"	
Domain 2: Test Design				
Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Concurrent vehicle control was used and appropriate for the study	
Metric 5:	Positive Controls	N/A	All Outcomes: Not necessary for the study type	
Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: The study reported the random allocation of animals into groups	
Domain 3: Exposure Characterization				
Metric 7:	Preparation and Storage of Test Substance	High	All Outcomes: Dose preparation and storage were reported "adding a weighed amount of 1 ,2-dichlorobenzene to the appropriate volume of corn oil and mixing for 15 minutes" then doses solutions were prepared by dilution. The mixture was stable at room temp for 7 days and solutions were stored no longer than 14 days at 4 degrees C	
Metric 8:	Consistency of Exposure Administration	High	All Outcomes: Details of exposure administration were reported and consistent. gavage volume was not excessive 5ml/kg.	
Metric 9:	Reporting of Doses/Concentrations	High	All Outcomes: Doses were reported clearly	
Metric 10:	Exposure Frequency and Duration	High	All Outcomes: Exposure frequency (5days/week) and duration (13 weeks) were appropriate for the study type	
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	All Outcomes: Number of exposure groups was adequate and consisted of 5 treated groups and a control. Spacing was justified based on the results of the short term study.	
Metric 12:	Exposure Route and Method	High	All Outcomes: Exposure route and method were suited to the test substance: gavage is appropriate	
Domain 4: Test Animals				
Metric 13:	Test Animal Characteristics	High	All Outcomes: Species, strain, sex, and age were all reported in table 1. Initial body weight was reported in the results	
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: All husbandry conditions were reported in table 1: temperature, humidity, light- dark cycle, diet, water availability and were adequate and consistent across all groups	
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Study Citation:	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.
Health Outcome(s):	Musculoskeletal; Musculoskeletal;
Reported Health Effect(s):	Musculoskeletal: Histologic examination of femur, sternebrae, vertebrae, thigh muscle; Musculoskeletal: Histologic examination of femur, sternebrae, vertebrae, thigh muscle;
Duration:	Subchronic (>30-91 days) 13 weeks Mouse
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	1944492

Domain	Metric	Rating	Comments
	Metric 15: Number of Animals per Group	Medium	All Outcomes: The number of animals per group was reported and appropriate for the study type: 10/sex/group for subchronic
Domain 5: Outcome Assessment			
	Metric 16: Outcome Assessment Methodology	Medium	Musculoskeletal: Outcome assessment was sensitive and appropriate for the outcome but limited to histology; Musculoskeletal: Outcome assessment was sensitive and appropriate for the outcome but was limited to histopathology
	Metric 17: Consistency of Outcome Assessment	High	All Outcomes: Outcome was assessed consistently across groups
	Metric 18: Sampling Adequacy	High	All Outcomes: Sampling was adequate
	Metric 19: Blinding of Assessors	N/A	All Outcomes: Blinding was not necessary for the study type
	Metric 20: Negative Control Response	High	All Outcomes: Control group responded adequately
Domain 6: Confounding / Variable Control			
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	All Outcomes: Reported information did not identify differences in confounding factors
	Metric 22: Health Outcomes Unrelated to Exposure	Medium	Musculoskeletal: Insufficient information provided to support or dismiss whether there were differences among groups.; Musculoskeletal: Premature death due to gavage error was reported in 1 male in the control, 30, and 125 mg/kg/day groups. An additional one male in the 250 mg/kg/day group was removed due to being missexed.
	Metric 23: Data Presentation and Analysis	High	All Outcomes: Statistical methods were reported and appropriate for the data
	Metric 24: Reporting of Data	Low	Musculoskeletal: Histology tables were not presented for 13 week data. Negative histology data were implied in text.; Musculoskeletal: histology tables were not presented for 13 week data. Negative histology data were implied in text.

Additional Comments: None

Overall Quality Determination**High**

Study Citation:	Robinson, M., Bercz, J. P., Ringhand, H. P., Condie, L. W., Parnell, M. J. (1991). Ten- and ninety-day toxicity studies of 1,2-dichlorobenzene administered by oral gavage to Sprague-Dawley rats. Drug and Chemical Toxicology 14(1-2):83-112.			
Health Outcome(s):	Hepatic/Liver; Renal/Kidney; Reproductive/Developmental; Immune/Hematological; Cardiovascular; Ocular/Sensory; Lung/Respiratory;			
Reported Health Effect(s):	Hepatic/Liver: Liver weights and liver-to-weight body ratios; microscopic hepatocellular changes.; Renal/Kidney: Urinalysis: Samples were analyzed for pH, glucose, protein, bilirubin, urobilinogen, and occult blood. Increased kidney weight and kidney-to-body weight ratio and increased BUN levels.; Reproductive/Developmental: Organ weights for testes/ovaries.; Immune/Hematological: Hematological parameters, consisting of hemoglobin (Hgb), hematocrit (Hct), red blood cell (RBC) count, white blood cell (WBC)count, and mean cell volume (MCV); organ weights for thymus and spleen.; Cardiovascular: Heart organ weight.; Ocular/Sensory: Ophthalmoscopic examinations were performed.; Lung/Respiratory: Lung organ weight;			
Duration:	Subchronic (>30-91 days) 90-day			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	5099073			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	All Outcomes: Chemical identified by nomenclature,	
	Metric 2: Test Substance Source	High	All Outcomes: 1,2-Dichlorobenzene (Lot AM/9202 PL) was obtained from Aldrich-Chemical Company (Milwaukee, WI).	
	Metric 3: Test Substance Purity	High	All Outcomes: specified as 99% pure by the vendor, was analyzed for purity by mass spectrometry prior to use in these studies. There were no impurities present	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	All Outcomes: Appropriate vehicle control (corn oil) used	
	Metric 5: Positive Controls	N/A	Hepatic/Liver: Missing Comment ; Renal/Kidney: Missing Comment ; Reproductive/Developmental: Missing Comment ; Immune/Hematological: Missing Comment ; Cardiovascular: Missing Comment ; Ocular/Sensory: Missing Comment ; Lung/Respiratory: Missing Comment	
	Metric 6: Randomized Allocation of Animals	Medium	All Outcomes: animals randomly assigned to vehicle and treatment groups using a computer-generated table of random numbers.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Low	All Outcomes: Preparation and storage was not adequately described. The authors noted that dosing formulations were made using corn oil and administered by oral gavage with a 20-gauge intubating needle attached to a 1-mL disposable syringe. All doses of DCB were delivered at a constant volume of 1.0 mL/kg. Control animals received corn oil at the samevolume.	
	Metric 8: Consistency of Exposure Administration	High	All Outcomes: Details of exposure administration were reported and exposures were administered consistently across study groups.	
	Metric 9: Reporting of Doses/Concentrations	High	All Outcomes: All doses are reported	
	Metric 10: Exposure Frequency and Duration	High	All Outcomes: The exposure frequency and duration of exposure were reported and appropriate for this study type.	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: The number of exposure groups were adequate.	
	Metric 12: Exposure Route and Method	High	All Outcomes: The route and method of exposure were reported and were suited to the test substance.	

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Study Citation:	Robinson, M., Bercz, J. P., Ringhand, H. P., Condie, L. W., Parnell, M. J. (1991). Ten- and ninety-day toxicity studies of 1,2-dichlorobenzene administered by oral gavage to Sprague-Dawley rats. Drug and Chemical Toxicology 14(1-2):83-112.			
Health Outcome(s):	Hepatic/Liver; Renal/Kidney; Reproductive/Developmental; Immune/Hematological; Cardiovascular; Ocular/Sensory; Lung/Respiratory;			
Reported Health Effect(s):	Hepatic/Liver: Liver weights and liver-to-weight body ratios; microscopic hepatocellular changes.; Renal/Kidney: Urinalysis: Samples were analyzed for pH, glucose, protein, bilirubin, urobilinogen, and occult blood. Increased kidney weight and kidney-to-body weight ratio and increased BUN levels.; Reproductive/Developmental: Organ weights for testes/ovaries.; Immune/Hematological: Hematological parameters, consisting of hemoglobin (Hgb), hematocrit (Hct), red blood cell (RBC) count, white blood cell (WBC)count, and mean cell volume (MCV); organ weights for thymus and spleen.; Cardiovascular: Heart organ weight.; Ocular/Sensory: Ophthalmoscopic examinations were performed.; Lung/Respiratory: Lung organ weight;			
Duration:	Subchronic (>30-91 days) 90-day			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	5099073			
Domain	Metric	Rating	Comments	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	High	All Outcomes: Age and starting body weight were not reported.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: All husbandry conditions were reported (e.g., temperature, humidity, light- dark cycle, diet, water availability) and were adequate.	
	Metric 15: Number of Animals per Group	Medium	All Outcomes: Appropriate number of animals used to observe toxicological effects	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	Medium	All Outcomes: Histopathological analyses were only conducted for controls and high dose animals.	
	Metric 17: Consistency of Outcome Assessment	Medium	All Outcomes: Details about timing of sampling collections were not provided	
	Metric 18: Sampling Adequacy	Medium	All Outcomes: Some treatment-related changes were observed at the high dose. A significant increase in the incidence of hepatocellular necrosis was seen in the 300 mg/kg group of males compared to controls; Males also displayed significant increases in ALT (300 mg/kg) and increased hepatocellular lesions	
	Metric 19: Blinding of Assessors	N/A	Hepatic/Liver: Missing Comment ; Renal/Kidney: Missing Comment ; Reproductive/Developmental: Missing Comment ; Immune/Hematological: Missing Comment ; Cardiovascular: Missing Comment ; Ocular/Sensory: Missing Comment ; Lung/Respiratory: Missing Comment	
	Metric 20: Negative Control Response	High	All Outcomes: The biological responses of the negative control groups 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.	
	Metric 22: Health Outcomes Unrelated to Exposure	High	All Outcomes: No information suggesting 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: Appropriate statistical analyses were performed; data on males and females were analyzed separately	
	Metric 24: Reporting of Data	Low	All Outcomes: All outcomes and results were not presented	
Additional Comments:	None			

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Study Citation:	Robinson, M., Bercz, J. P., Ringhand, H. P., Condie, L. W., Parnell, M. J. (1991). Ten- and ninety-day toxicity studies of 1,2-dichlorobenzene administered by oral gavage to Sprague-Dawley rats. Drug and Chemical Toxicology 14(1-2):83-112.
Health Outcome(s):	Hepatic/Liver; Renal/Kidney; Reproductive/Developmental; Immune/Hematological; Cardiovascular; Ocular/Sensory; Lung/Respiratory;
Reported Health Effect(s):	Hepatic/Liver: Liver weights and liver-to-weight body ratios; microscopic hepatocellular changes.; Renal/Kidney: Urinalysis: Samples were analyzed for pH, glucose, protein, bilirubin, urobilinogen, and occult blood. Increased kidney weight and kidney-to-body weight ratio and increased BUN levels.; Reproductive/Developmental: Organ weights for testes/ovaries.; Immune/Hematological: Hematological parameters, consisting of hemoglobin (Hgb), hematocrit (Hct), red blood cell (RBC) count, white blood cell (WBC)count, and mean cell volume (MCV); organ weights for thymus and spleen.; Cardiovascular: Heart organ weight.; Ocular/Sensory: Ophthalmoscopic examinations were performed.; Lung/Respiratory: Lung organ weight;
Duration:	Subchronic (>30-91 days) 90-day
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	5099073

Domain	Metric	Rating	Comments
Overall Quality Determination		High	

Study Citation:	Robinson, M., Bercz, J. P., Ringhand, H. P., Condie, L. W., Parnell, M. J. (1991). Ten- and ninety-day toxicity studies of 1,2-dichlorobenzene administered by oral gavage to Sprague-Dawley rats. Drug and Chemical Toxicology 14(1-2):83-112.			
Health Outcome(s):	Mortality; Nutritional/Metabolic;			
Reported Health Effect(s):	Mortality: Animals were checked twice daily. No deaths were observed.; Nutritional/Metabolic: Body weight changes and food and water consumption;			
Duration:	Subchronic (>30-91 days) 90-day			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	5099073			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	All Outcomes: Chemical identified by nomenclature,	
	Metric 2: Test Substance Source	High	All Outcomes: 1,2-Dichlorobenzene (Lot AM/9202 PL) was obtained from Aldrich-Chemical Company (Milwaukee, WI).	
	Metric 3: Test Substance Purity	High	All Outcomes: specified as 99% pure by the vendor, was analyzed for purity by mass spectrometry prior to use in these studies. There were no impurities present	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	All Outcomes: Appropriate vehicle control (corn oil) used	
	Metric 5: Positive Controls	N/A	Mortality: Missing Comment ; Nutritional/Metabolic: Missing Comment	
	Metric 6: Randomized Allocation of Animals	Medium	All Outcomes: animals randomly assigned to vehicle and treatment groups using a computer-generated table of random numbers.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Low	All Outcomes: Preparation and storage was not adequately described. The authors noted that dosing formulations were made using corn oil and administered by oral gavage with a 20-gauge intubating needle attached to a 1-mL disposable syringe. All doses of DCB were delivered at a constant volume of 1.0 mL/kg. Control animals received corn oil at the same volume.	
	Metric 8: Consistency of Exposure Administration	High	All Outcomes: Details of exposure administration were reported and exposures were administered consistently across study groups.	
	Metric 9: Reporting of Doses/Concentrations	High	All Outcomes: All doses are reported	
	Metric 10: Exposure Frequency and Duration	High	All Outcomes: The exposure frequency and duration of exposure were reported and appropriate for this study type.	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: The number of exposure groups were adequate.	
	Metric 12: Exposure Route and Method	High	All Outcomes: The route and method of exposure were reported and were suited to the test substance.	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	Medium	All Outcomes: Age and starting body weight were not reported.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: All husbandry conditions were reported (e.g., temperature, humidity, light- dark cycle, diet, water availability) and were adequate.	
	Metric 15: Number of Animals per Group	Medium	All Outcomes: Appropriate number of animals used to observe toxicological effects	
Domain 5: Outcome Assessment				
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Study Citation:	Robinson, M., Bercz, J. P., Ringhand, H. P., Condie, L. W., Parnell, M. J. (1991). Ten- and ninety-day toxicity studies of 1,2-dichlorobenzene administered by oral gavage to Sprague-Dawley rats. Drug and Chemical Toxicology 14(1-2):83-112.
Health Outcome(s):	Mortality; Nutritional/Metabolic;
Reported Health Effect(s):	Mortality: Animals were checked twice daily. No deaths were observed.; Nutritional/Metabolic: Body weight changes and food and water consumption;
Duration:	Subchronic (>30-91 days) 90-day
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	5099073

Domain	Metric	Rating	Comments
	Metric 16: Outcome Assessment Methodology	High	All Outcomes: The outcome assessment methodology addressed the intended outcome.
	Metric 17: Consistency of Outcome Assessment	Medium	All Outcomes: Details about timing of sampling collections were not provided
	Metric 18: Sampling Adequacy	High	All Outcomes: Reported information indicates the study used adequate sampling for the outcome.
	Metric 19: Blinding of Assessors	N/A	Mortality: Missing Comment ; Nutritional/Metabolic: Missing Comment
	Metric 20: Negative Control Response	High	All Outcomes: The biological responses of the negative control groups 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.
	Metric 22: Health Outcomes Unrelated to Exposure	High	All Outcomes: No information suggesting 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	All Outcomes: No statistical analyses needed as no mortality occurred
	Metric 24: Reporting of Data	High	All Outcomes: No mortality was reported.

Additional Comments: None

Overall Quality Determination**High**

Study Citation:	Hollingsworth, R. L., Rowe, V. K., Oyen, F., Torkelson, T. R., Adams, E. M. (1958). Toxicity of o-dichlorobenzene: Studies on animals and industrial experience. AMA Archives of Industrial Health 17(3):180-187.			
Health Outcome(s):	all studies (Oral chronic: mortality, body weights, organ weights (heart, liver, kidney, spleen), gross and microscopic examinations.)			
Reported Health Effect(s):	all studies (Oral chronic: mortality, body weights, organ weights (heart, liver, kidney, spleen), gross and microscopic examinations.): Acute inhalation - Lethality experiments: Mortality; "gross response" (drowsiness, unsteadiness, eye irritation, difficulty breathing, anaesthesia); weight loss.Acute inhalation - Organ injury experiments: Organ weights (liver, kidney), gross and microscopic examinations (liver and kidney).Inhalation Chronic experiments: Mortality, observations of gross appearance and behavior, growth/body weights, organ weights (lungs, heart, liver, kidney, spleen, testes), hematology (rabbits and monkeys), urine tests (blood, sugar, albumin, sediment in females), serum BUN (female guinea pig and rabbits), gross and microscopic examinations. Acute oral: mortality, body weight gain.Oral chronic: mortality, body weights, organ weights (heart, liver, kidney, spleen), gross and microscopic examinations.Eye irritation: eye irritation.			
Duration:	Chronic (>91 days) Chronic oral: 192 days			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	2962108			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
Metric 1:	Test Substance Identity	High	The test substance was identified by name as o-dichlorobenzene. Physical chemical properties were provided. A CASRN was not reported.	
Metric 2:	Test Substance Source	Low	The original source was not described; the test substance was a re-distillation of a commercial product and was not analytically verified by the performing laboratory.	
Metric 3:	Test Substance Purity	High	The purity was ≥99% based on physical properties	
Domain 2: Test Design				
Metric 4:	Negative and Vehicle Controls	High	Control animals were administered a similar quantity of oil-acacia emulsion alone.	
Metric 5:	Positive Controls	N/A	Positive controls are not required for the study type	
Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated into study groups.	
Domain 3: Exposure Characterization				
Metric 7:	Preparation and Storage of Test Substance	Low	The test substance was added to an olive oil solution that was emulsified with with 2 mL of a 5% to 10% acacia solusion. No further details were provided. Frequency of preparation, stability and homogeneity, and storage details were not reported.	
Metric 8:	Consistency of Exposure	Low	Animals were dosed via gavage. The gavage volume was not reported.	
Metric 9:	Administration Reporting of Doses/Concentrations	Low	Doses were reported in mg/kg. It was not specified whether these were target or nominal doses. It was not reported whether concentrations of the test substance in the test solutions were analytically verified. No animal body weights were provided.	
Metric 10:	Exposure Frequency and Duration	Medium	Animals were dosed 5 days per week for a total of 138 doses in 192 days. No justification was provided for the selected duration, which is shorter than a standard chronic oral toxicity study.	
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The study included 3 dose groups plus a control. No justification was provided for the selected doses and dose spacing, but spacing was adequate to identify NOAEL and LOAEL values.	
Metric 12:	Exposure Route and Method	High	Animals were dose via gavage which is an appropriate exposure method for the test substance.	

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Study Citation:	Hollingsworth, R. L., Rowe, V. K., Oyen, F., Torkelson, T. R., Adams, E. M. (1958). Toxicity of o-dichlorobenzene: Studies on animals and industrial experience. AMA Archives of Industrial Health 17(3):180-187.			
Health Outcome(s):	all studies (Oral chronic: mortality, body weights, organ weights (heart, liver, kidney, spleen), gross and microscopic examinations.)			
Reported Health Effect(s):	all studies (Oral chronic: mortality, body weights, organ weights (heart, liver, kidney, spleen), gross and microscopic examinations.): Acute inhalation - Lethality experiments: Mortality; "gross response" (drowsiness, unsteadiness, eye irritation, difficulty breathing, anaesthesia); weight loss.Acute inhalation - Organ injury experiments: Organ weights (liver, kidney), gross and microscopic examinations (liver and kidney).Inhalation Chronic experiments: Mortality, observations of gross appearance and behavior, growth/body weights, organ weights (lungs, heart, liver, kidney, spleen, testes), hematology (rabbits and monkeys), urine tests (blood, sugar, albumin, sediment in females), serum BUN (female guinea pig and rabbits), gross and microscopic examinations. Acute oral: mortality, body weight gain.Oral chronic: mortality, body weights, organ weights (heart, liver, kidney, spleen), gross and microscopic examinations.Eye irritation: eye irritation.			
Duration:	Chronic (>91 days) Chronic oral: 192 days			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	2962108			
Domain	Metric	Rating	Comments	
Domain 4: Test Animals				
Metric 13:	Test Animal Characteristics	Low	Details were provided in a citation (Spencer et al. 1951). The animals (rats) were from in-house colonies, although the original source of rats was also specified. Strains, initial body weights, and age were not reported. Based on the text, it appears that only female rats were used. No justification was provided.	
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Low	A citation was provided specifying the animal diets. No other animal husbandry details were provided.	
Metric 15:	Number of Animals per Group	Low	Treatment groups contained 10 females/group. The control group contained 20 females. Generally, chronic studies require at least 20 animals per sex.	
Domain 5: Outcome Assessment				
Metric 16:	Outcome Assessment Methodology	Low	The outcomes measured were reported, but no methodological details were provided. Animals were sacrificed one day following the last dose.	
Metric 17:	Consistency of Outcome Assessment	Low	Details of outcome assessment methods were limited. The frequencies of observations were not provided, so consistency across groups is unclear.	
Metric 18:	Sampling Adequacy	Low	Most of the results are qualitatively described, and sample sizes were not specified. For endpoints with quantitative data (organ weights), sample sizes were shown and were sufficient for statistical analysis. The sample sizes varied because it was based on the number of surviving animals at the end of the study.	
Metric 19:	Blinding of Assessors	N/A	Blinding is not required for the outcomes of interest.	
Metric 20:	Negative Control Response	Low	Most results were qualitatively described, and control responses were not mentioned. When quantitative data are shown, control responses appear to be 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 (or identified only minor differences) among study groups in the above listed confounding factors.	
Metric 22:	Health Outcomes Unrelated to Exposure	Low	The text indicates that the deaths that occurred were due to "respiratory infection in nearly every instance." However, the deaths were purportedly evenly distributed across groups, which should not significantly impact the study results. It is unclear whether surviving animals also had respiratory infections.	

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Study Citation:	Hollingsworth, R. L., Rowe, V. K., Oyen, F., Torkelson, T. R., Adams, E. M. (1958). Toxicity of o-dichlorobenzene: Studies on animals and industrial experience. AMA Archives of Industrial Health 17(3):180-187.
Health Outcome(s):	all studies (Oral chronic: mortality, body weights, organ weights (heart, liver, kidney, spleen), gross and microscopic examinations.)
Reported Health Effect(s):	all studies (Oral chronic: mortality, body weights, organ weights (heart, liver, kidney, spleen), gross and microscopic examinations.): Acute inhalation - Lethality experiments: Mortality; "gross response" (drowsiness, unsteadiness, eye irritation, difficulty breathing, anaesthesia); weight loss. Acute inhalation - Organ injury experiments: Organ weights (liver, kidney), gross and microscopic examinations (liver and kidney). Inhalation Chronic experiments: Mortality, observations of gross appearance and behavior, growth/body weights, organ weights (lungs, heart, liver, kidney, spleen, testes), hematology (rabbits and monkeys), urine tests (blood, sugar, albumin, sediment in females), serum BUN (female guinea pig and rabbits), gross and microscopic examinations. Acute oral: mortality, body weight gain. Oral chronic: mortality, body weights, organ weights (heart, liver, kidney, spleen), gross and microscopic examinations. Eye irritation: eye irritation.
Duration:	Chronic (>91 days) Chronic oral: 192 days
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	2962108

Domain	Metric	Rating	Comments
	Metric 23: Data Presentation and Analysis	Low	The study specified using a T-test. A T-test may not be suitable for all of the endpoints. For some datasets, an ANOVA would be more appropriate. In several cases, statistical analysis was not shown, and data enabling an independent analysis were not provided (eg, means without measures of variance, or only qualitative descriptions). Therefore, the results of most endpoints may not be usable.
	Metric 24: Reporting of Data	Low	Body weight and organ weight data were quantitatively reported as means without measures of variance. Statistical significance is shown. All other results, including effects related to treatment, were qualitatively described for each dose group, minus the control.

Additional Comments: None

Overall Quality Determination**Low**

Study Citation:	Hollingsworth, R. L., Rowe, V. K., Oyen, F., Torkelson, T. R., Adams, E. M. (1958). Toxicity of o-dichlorobenzene: Studies on animals and industrial experience. AMA Archives of Industrial Health 17(3):180-187.			
Health Outcome(s):	all studies (Inhalation Chronic experiments: Mortality, observations of gross appearance and behavior, growth/body weights, organ weights (lungs, heart, liver, kidney, spleen, testes))			
Reported Health Effect(s):	all studies (Inhalation Chronic experiments: Mortality, observations of gross appearance and behavior, growth/body weights, organ weights (lungs, heart, liver, kidney, spleen, testes)): Acute inhalation - Lethality experiments: Mortality; "gross response" (drowsiness, unsteadiness, eye irritation, difficulty breathing, anaesthesia); weight loss.Acute inhalation - Organ injury experiments: Organ weights (liver, kidney), gross and microscopic examinations (liver and kidney).Inhalation Chronic experiments: Mortality, observations of gross appearance and behavior, growth/body weights, organ weights (lungs, heart, liver, kidney, spleen, testes), hematology (rabbits and monkeys), urine tests (blood, sugar, albumin, sediment in females), serum BUN (female guinea pig and rabbits), gross and microscopic examinations. Acute oral: mortality, body weight gain.Oral chronic: mortality, body weights, organ weights (heart, liver, kidney, spleen), gross and microscopic examinations.Eye irritation: eye irritation.			
Duration:	Chronic (>91 days) Chronic inhalation (6-7 months)			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	2962108			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	The test substance was identified by name as o-dichlorobenzene. Physical chemical properties were provided. A CASRN was not reported.	
	Metric 2: Test Substance Source	Low	The original source was not described; the test substance was a re-distillation of a commercial product and was not analytically verified by the performing laboratory.	
	Metric 3: Test Substance Purity	High	The purity was ≥99% based on physical properties	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	High	Air-exposed control animals were "well matched with experimental animals in respect to number, age, sex, and body weight."	
	Metric 5: Positive Controls	N/A	Positive controls are not required for the study type	
	Metric 6: Randomized Allocation of Animals	Low	The study did not report how animals were allocated into study groups.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Medium	The methods of atmosphere generation were briefly described with further details in a cited reference (Adams et al., 1951), which was viewed for this review. The method of vapor generation was appropriate.	
	Metric 8: Consistency of Exposure Administration	Low	Details of the exposure chamber were provided in a cited reference (Adams et al., 1951). Air flow rates were between 15 and 30 liters/min in the cited reference, but it is difficult to know whether all of the details were similar in the current study. The number of animals per cage was not reported. Different chamber designs were used for different exposure groups, although these were run as separate experiments. A 1700 L chamber was used for exposures at 93 ppm, and 450 L chambers were used for exposures at 49 ppm.	
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Study Citation:	Hollingsworth, R. L., Rowe, V. K., Oyen, F., Torkelson, T. R., Adams, E. M. (1958). Toxicity of o-dichlorobenzene: Studies on animals and industrial experience. AMA Archives of Industrial Health 17(3):180-187.
Health Outcome(s):	all studies (Inhalation Chronic experiments: Mortality, observations of gross appearance and behavior, growth/body weights, organ weights (lungs, heart, liver, kidney, spleen, testes))
Reported Health Effect(s):	all studies (Inhalation Chronic experiments: Mortality, observations of gross appearance and behavior, growth/body weights, organ weights (lungs, heart, liver, kidney, spleen, testes)): Acute inhalation - Lethality experiments: Mortality; "gross response" (drowsiness, unsteadiness, eye irritation, difficulty breathing, anaesthesia); weight loss. Acute inhalation - Organ injury experiments: Organ weights (liver, kidney), gross and microscopic examinations (liver and kidney). Inhalation Chronic experiments: Mortality, observations of gross appearance and behavior, growth/body weights, organ weights (lungs, heart, liver, kidney, spleen, testes), hematology (rabbits and monkeys), urine tests (blood, sugar, albumin, sediment in females), serum BUN (female guinea pig and rabbits), gross and microscopic examinations. Acute oral: mortality, body weight gain. Oral chronic: mortality, body weights, organ weights (heart, liver, kidney, spleen), gross and microscopic examinations. Eye irritation: eye irritation.
Duration:	Chronic (>91 days) Chronic inhalation (6-7 months)
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	2962108

Domain	Metric	Rating	Comments
	Metric 9: Reporting of Doses/Concentrations	Medium	Vapor concentrations were analytically determined "by combustion of samples of the chamber atmosphere, absorption of combustion products in dilute sodium carbonate-sodium formate solution, and titration of the chloride by the micro Volhard method. " This is an antiquated method, but it was likely appropriate, and all that was available at the time the study was published (1958). The frequency of measurements was not explicitly reported, but the number of samples was indicated, and it was noted that concentrations were "checked repeatedly at intervals during the experimental period." It was not specified where the air samples were taken from. The study reported nominal concentrations, and measured concentrations were reported as a range and as an average.
	Metric 10: Exposure Frequency and Duration	Low	Animals were generally exposed 7 hrs/day 5 days/week. The study included multiple experiments, all with different durations that fall under the chronic duration category. No justification was provided for any of the study design. For rats, the number of days of exposure were slightly different between control and exposed animals (e.g., 182 days for exposed male rats and 184 days for control male rats).
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	Low	In each experiment, only a single concentration was tested in repeated exposure chronic studies, precluding the ability to identify a dose-response. No justification for the concentration tested was provided.
	Metric 12: Exposure Route and Method	Low	Animals were exposed, whole body, in dynamic exposure chambers. Nose-only exposures are preferred. The number of air changes per hour was not reported; however, the flow rate was indicated, suggesting a dynamic chamber was used. Different chamber sizes were used for different exposure concentrations. It is unclear if the chamber sizes were appropriate for the number of animals.
Domain 4: Test Animals			
	Metric 13: Test Animal Characteristics	Low	Details were provided in a citation (Spencer et al. 1951). The animals (rats, GP, and rabbits) were from in-house colonies, although the original source of rats was also specified. Monkeys were imported (no further details). Strains, sex, initial body weights, and age were not reported.
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were not sufficiently reported.
	Metric 15: Number of Animals per Group	Medium	The number of animals used in each acute exposure experiment ranged from 5 to 20. It is unclear why some exposure scenarios used more rats than others, but the numbers were appropriate for assessing lethality.

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Study Citation:	Hollingsworth, R. L., Rowe, V. K., Oyen, F., Torkelson, T. R., Adams, E. M. (1958). Toxicity of o-dichlorobenzene: Studies on animals and industrial experience. AMA Archives of Industrial Health 17(3):180-187.
Health Outcome(s):	all studies (Inhalation Chronic experiments: Mortality, observations of gross appearance and behavior, growth/body weights, organ weights (lungs, heart, liver, kidney, spleen, testes))
Reported Health Effect(s):	all studies (Inhalation Chronic experiments: Mortality, observations of gross appearance and behavior, growth/body weights, organ weights (lungs, heart, liver, kidney, spleen, testes)): Acute inhalation - Lethality experiments: Mortality; "gross response" (drowsiness, unsteadiness, eye irritation, difficulty breathing, anaesthesia); weight loss. Acute inhalation - Organ injury experiments: Organ weights (liver, kidney), gross and microscopic examinations (liver and kidney). Inhalation Chronic experiments: Mortality, observations of gross appearance and behavior, growth/body weights, organ weights (lungs, heart, liver, kidney, spleen, testes), hematology (rabbits and monkeys), urine tests (blood, sugar, albumin, sediment in females), serum BUN (female guinea pig and rabbits), gross and microscopic examinations. Acute oral: mortality, body weight gain. Oral chronic: mortality, body weights, organ weights (heart, liver, kidney, spleen), gross and microscopic examinations. Eye irritation: eye irritation.
Duration:	Chronic (>91 days) Chronic inhalation (6-7 months)
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	2962108

Domain	Metric	Rating	Comments
Domain 5: Outcome Assessment			
	Metric 16: Outcome Assessment Methodology	Low	It is confusing which outcomes are assessed in which inhalation experiment. Outcome assessment methods were generally described for inhalation studies of different durations, and were often vague. Animals were assessed for mortality, gross appearance, behavior, body weights, select organ weights, hematology (rabbits and monkeys only), qualitative urine tests on females (all species), serum BUN (female rats, GP, and rabbits), and gross and microscopic examination of tissues. In general, these outcomes are consistent with those assessed in repeated dose studies and (if all performed) are sensitive for assessing the outcomes of interest.
	Metric 17: Consistency of Outcome Assessment	Low	Insufficient details were provided to determine consistency in outcome assessments. Details on the frequencies of observations were not provided.
	Metric 18: Sampling Adequacy	Low	Most of the results are qualitatively described, and sample sizes were not specified. For endpoints with quantitative data (organ weights), sample sizes were shown and were sufficient for statistical analysis. The sample sizes varied because they were based on the number of surviving animals at the end of the study.
	Metric 19: Blinding of Assessors	N/A	Blinding is not required for the outcomes of interest.
	Metric 20: Negative Control Response	Low	Most results were qualitatively described, and control responses were not mentioned. When quantitative data are shown, control responses appear to be 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 (or identified only minor differences) among study groups in the above listed confounding factors.
	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	Low	The study specified using a T-test. A T-test may not be suitable for all of the endpoints. For some datasets, an ANOVA would be more appropriate. In several cases, statistical analysis was not shown, and data enabling an independent analysis were not provided (e.g., means without measures of variance, or only qualitative descriptions). Therefore, the results of most endpoints may not be usable.
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Study Citation:	Hollingsworth, R. L., Rowe, V. K., Oyen, F., Torkelson, T. R., Adams, E. M. (1958). Toxicity of o-dichlorobenzene: Studies on animals and industrial experience. AMA Archives of Industrial Health 17(3):180-187.
Health Outcome(s):	all studies (Inhalation Chronic experiments: Mortality, observations of gross appearance and behavior, growth/body weights, organ weights (lungs, heart, liver, kidney, spleen, testes))
Reported Health Effect(s):	all studies (Inhalation Chronic experiments: Mortality, observations of gross appearance and behavior, growth/body weights, organ weights (lungs, heart, liver, kidney, spleen, testes)): Acute inhalation - Lethality experiments: Mortality; "gross response" (drowsiness, unsteadiness, eye irritation, difficulty breathing, anaesthesia); weight loss. Acute inhalation - Organ injury experiments: Organ weights (liver, kidney), gross and microscopic examinations (liver and kidney). Inhalation Chronic experiments: Mortality, observations of gross appearance and behavior, growth/body weights, organ weights (lungs, heart, liver, kidney, spleen, testes), hematology (rabbits and monkeys), urine tests (blood, sugar, albumin, sediment in females), serum BUN (female guinea pig and rabbits), gross and microscopic examinations. Acute oral: mortality, body weight gain. Oral chronic: mortality, body weights, organ weights (heart, liver, kidney, spleen), gross and microscopic examinations. Eye irritation: eye irritation.
Duration:	Chronic (>91 days) Chronic inhalation (6-7 months)
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	2962108

Domain	Metric	Rating	Comments
Metric 24:	Reporting of Data	Low	Quantitative results were provided for only organ weights. These data were reported as means without measures of variance. Statistical significance was shown. All other results were qualitatively reported and did not explicitly differentiate between species or experiment.

Additional Comments: None

Overall Quality Determination**Low**

Study Citation:	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.		
Health Outcome(s):	Mortality		
Reported Health Effect(s):	Mortality: Death		
Duration:	Chronic (>91 days) 2 years Rat		
Chemical:	o-Dichlorobenzene- Parent compound		
HERO ID:	1944492		
Domain	Metric	Rating	Comments
Domain 1: Test Substance			
Metric 1:	Test Substance Identity	High	Test substance was identified by nomenclature, CAS number, and structure
Metric 2:	Test Substance Source	High	Test substance was obtained from a commercial source: "ICC solvent Chemical Company (New York, NY) Lot number SC61377 and analytically verified.
Metric 3:	Test Substance Purity	High	Test substance was >99% purity verified analytically. Impurities were reported "Acidic components (assumed to be hydrochloric acid) were found to be present at a concentration of 10.8 ppm. one impurity with an area that was approximately 0.7% of the major peak area; this impurity, identified as 1 ,4-dichlorobenzene"
Domain 2: Test Design			
Metric 4:	Negative and Vehicle Controls	High	Concurrently treated vehicle control was used and appropriate for the study
Metric 5:	Positive Controls	N/A	Positive control not required for study type
Metric 6:	Randomized Allocation of Animals	Medium	The study reported the random allocation of animals into groups
Domain 3: Exposure Characterization			
Metric 7:	Preparation and Storage of Test Substance	High	Dose preparation and storage were reported "adding a weighed amount of 1 ,2-dichlorobenzene to the appropriate volume of corn oil and mixing for 15 minutes" then dose solutions were prepared by dilution. The mixture was stable at room temp for 7 days and solutions were stored no longer than 14 days at 4 degrees C
Metric 8:	Consistency of Exposure Administration	High	Details of exposure administration were reported and consistent. gavage volume was not excessive 5ml/kg.
Metric 9:	Reporting of Doses/Concentrations	High	Doses were reported clearly
Metric 10:	Exposure Frequency and Duration	High	Exposure frequency and duration were appropriate for the study type at 5 days a week for 103 weeks
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	Number of exposure groups was fewer than recommended at 2 exposure groups and one control. Spacing was appropriate and covered a range of response
Metric 12:	Exposure Route and Method	High	Exposure route and method were suited to the test substance: gavage is appropriate
Domain 4: Test Animals			
Metric 13:	Test Animal Characteristics	High	Species, strain, sex, and age were all reported in table 1 and starting body weight was reported in results
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All husbandry conditions were reported in table 1: temperature, humidity, light- dark cycle, diet, water availability and were adequate and consistent across all groups

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Study Citation:	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.			
Health Outcome(s):	Mortality			
Reported Health Effect(s):	Mortality: Death			
Duration:	Chronic (>91 days) 2 years Rat			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	1944492			
Domain	Metric	Rating	Comments	
	Metric 15:	Number of Animals per Group	Medium	The number of animals per group was reported and appropriate for the study type: 50/group for chronic
Domain 5: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	High	The outcome assessment was sensitive and appropriate for the outcome of interest. Animals were observed twice daily for mortality.
	Metric 17:	Consistency of Outcome Assessment	High	Outcome assessment was reported and was consistent across groups
	Metric 18:	Sampling Adequacy	High	Sampling was adequate and was for each animal
	Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary as mortality is not subjective
	Metric 20:	Negative Control Response	High	Control animals responded appropriately
Domain 6: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	Information was incompletely reported but did not identify differences among groups
	Metric 22:	Health Outcomes Unrelated to Exposure	Low	Retrospective audit of the survival data indicated numerous probable or possible gavage-related deaths that were disproportionately in the male high dose group.
	Metric 23:	Data Presentation and Analysis	High	Statistical methods were reported and appropriate for the data
	Metric 24:	Reporting of Data	High	Data was presented as Kaplan-Meier Survival Curves for both sexes.
Additional Comments: None				

Overall Quality Determination**High**

Study Citation:	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.			
Health Outcome(s):	Nutritional/Metabolic; Nutritional/Metabolic; Mortality; Cardiovascular;			
Reported Health Effect(s):	Nutritional/Metabolic: Body weight; Nutritional/Metabolic: Body weight; Mortality: Death; Cardiovascular: Heart weight, cholesterol, triglycerides;			
Duration:	Chronic (>91 days) 2 years Rat			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	1944492			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
Metric 1:	Test Substance Identity	High	All Outcomes: Test substance was identified by nomenclature, CAS number, and structure	
Metric 2:	Test Substance Source	High	All Outcomes: Test substance was obtained from a commercial source: "ICC solvent Chemical Company (New York, NY) Lot number SC61377 and analytically verified.	
Metric 3:	Test Substance Purity	High	Nutritional/Metabolic: Test substance was >99% purity verified analytically. Impurities were reported "Acidic components (assumed to be hydrochloric acid) were found to be present at a concentration of 10.8 ppm. one impurity with an area that was approximately 0.7% of the major peak area; this impurity, identified as 1 ,4-dichlorobenzene"; Nutritional/Metabolic: Test substance was >99% purity verified analytically. Impurities were reported "Acidic components (assumed to be hydrochloric acid) were found to be present at a concentration of 10.8 ppm. one impurity with an area that was approximately 0.7% of the major peak area; this impurity, identified as 1 ,4-dichlorobenzene"; Mortality: Test substance was >99% purity verified analytically. Impurities were reported "Acidic components (assumed to be hydrochloric acid) were found to be present at a concentration of 10.8 ppm. one impurity with an area that was approximately 0.7% of the major peak area; this impurity, identified as 1 ,4-dichlorobenzene"; Cardiovascular: Test substance was >99% purity verified analytically. impurities were reported "Acidic components (assumed to be hydrochloric acid) were found to be present at a concentration of 10.8 ppm. one impurity with an area that was approximately 0.7% of the major peak area; this impurity, identified as 1 ,4-dichlorobenzene"	
Domain 2: Test Design				
Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Concurrently treated vehicle control was used and appropriate for the study	
Metric 5:	Positive Controls	N/A	Nutritional/Metabolic: A positive control was not necessary for this study type; Nutritional/Metabolic: A positive control was not necessary for this study type; Mortality: Positive control not required for study type; Cardiovascular: A positive control was not necessary for this study type	
Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: The study reported the random allocation of animals into groups	
Domain 3: Exposure Characterization				
Metric 7:	Preparation and Storage of Test Substance	High	All Outcomes: Dose preparation and storage were reported "adding a weighed amount of 1 ,2-dichlorobenzene to the appropriate volume of corn oil and mixing for 15 minutes" then dose solutions were prepared by dilution. The mixture was stable at room temp for 7 days and solutions were stored no longer than 14 days at 4 degrees C	
Metric 8:	Consistency of Exposure Administration	High	All Outcomes: Details of exposure administration were reported and consistent. gavage volume was not excessive 5ml/kg.	
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Study Citation:	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.
Health Outcome(s):	Nutritional/Metabolic; Nutritional/Metabolic; Mortality; Cardiovascular;
Reported Health Effect(s):	Nutritional/Metabolic: Body weight; Nutritional/Metabolic: Body weight; Mortality: Death; Cardiovascular: Heart weight, cholesterol, triglycerides;
Duration:	Chronic (>91 days) 2 years Rat
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	1944492

Domain	Metric	Rating	Comments
	Metric 9: Reporting of Doses/Concentrations	High	All Outcomes: Doses were reported clearly
	Metric 10: Exposure Frequency and Duration	High	All Outcomes: Exposure frequency and duration were appropriate for the study type at 5 days a week for 103 weeks
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	Medium	Nutritional/Metabolic: Number of exposure groups was fewer than recommended at 2 exposure groups and one control. Spacing was appropriate and covered a range of response; Nutritional/Metabolic: Number of exposure groups was fewer than recommended at 2 exposure groups and one control. Spacing was appropriate and covered a range of response; Mortality: Number of exposure groups was fewer than recommended at 2 exposure groups and one control. Spacing was justified based on the results of the previous 13 week study but it is unclear if the highest dose is high enough; Cardiovascular: Number of exposure groups was fewer than recommended at 2 exposure groups and one control. Spacing was appropriate and covered a range of response
	Metric 12: Exposure Route and Method	High	All Outcomes: Exposure route and method were suited to the test substance: gavage is appropriate
Domain 4: Test Animals			
	Metric 13: Test Animal Characteristics	High	All Outcomes: Species, strain, sex, and age were all reported in table 1 and starting body weight was reported in results
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: All husbandry conditions were reported in table 1: temperature, humidity, light- dark cycle, diet, water availability and were adequate and consistent across all groups
	Metric 15: Number of Animals per Group	Medium	All Outcomes: The number of animals per group was reported and appropriate for the study type: 50/group for chronic
Domain 5: Outcome Assessment			
	Metric 16: Outcome Assessment Methodology	High	Nutritional/Metabolic: The outcome assessment was sensitive and appropriate for the outcome of interest; Nutritional/Metabolic: The outcome assessment was sensitive and appropriate for the outcome of interest; Mortality: The outcome assessment was sensitive and appropriate for the outcome of interest. Animals were observed twice daily for mortality.; Cardiovascular: The outcome assessment was sensitive and appropriate for the outcome of interest, and included gross and histopathological examination.
	Metric 17: Consistency of Outcome Assessment	High	Nutritional/Metabolic: Outcome assessment was reported and was consistent across groups; Nutritional/Metabolic: Outcome assessment was reported and was consistent across groups; Mortality: Outcome assessment was consistent and reported; Cardiovascular: Outcome assessment was reported and was consistent across groups

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Study Citation:	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.
Health Outcome(s):	Nutritional/Metabolic; Nutritional/Metabolic; Mortality; Cardiovascular;
Reported Health Effect(s):	Nutritional/Metabolic: Body weight; Nutritional/Metabolic: Body weight; Mortality: Death; Cardiovascular: Heart weight, cholesterol, triglycerides;
Duration:	Chronic (>91 days) 2 years Rat
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	1944492

Domain	Metric	Rating	Comments
	Metric 18: Sampling Adequacy	High	Nutritional/Metabolic: Sampling was adequate (body weight recorded for each animal); Nutritional/Metabolic: Sampling was adequate (body weight recorded for each animal); Mortality: Sampling was adequate and was for each animal; Cardiovascular: Sampling was adequate
	Metric 19: Blinding of Assessors	N/A	Nutritional/Metabolic: Blinding not required: quantitative measure; Nutritional/Metabolic: Blinding was reported for re-evaluation of histology slides; Mortality: Blinding was not necessary as mortality is not subjective; Cardiovascular: Blinding was reported for re-evaluation of histology slides
	Metric 20: Negative Control Response	High	All Outcomes: Control animals responded appropriately
Domain 6: Confounding / Variable Control			
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	All Outcomes: Information was incompletely reported but did not identify differences among groups
	Metric 22: Health Outcomes Unrelated to Exposure	Medium	All Outcomes: Information provided was not sufficient to either support or dismiss the idea that there were differences unrelated to exposure
	Metric 23: Data Presentation and Analysis	High	All Outcomes: Statistical methods were reported and appropriate for the data
	Metric 24: Reporting of Data	High	Nutritional/Metabolic: Data were reported for all outcomes by group and sex; Nutritional/Metabolic: Data were reported for all outcomes by group and sex; Mortality: Data was presented as Kaplan-Meier Survival Curves for both sexes.; Cardiovascular: Data were reported for all outcomes by group and sex

Additional Comments: None

Overall Quality Determination**High**

Study Citation:	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.
Health Outcome(s):	Cancer/Carcinogenesis; Cancer/Carcinogenesis;
Reported Health Effect(s):	Cancer/Carcinogenesis: Neoplastic nodules; Cancer/Carcinogenesis: Neoplastic nodules;
Duration:	Chronic (>91 days) 2 years Rat
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	1944492

Domain	Metric	Rating	Comments
Domain 1: Test Substance			
Metric 1:	Test Substance Identity	High	All Outcomes: Test substance was identified by nomenclature, CAS number, and structure
Metric 2:	Test Substance Source	High	All Outcomes: Test substance was obtained from a commercial source: "ICC solvent Chemical Company (New York, NY) Lot number SC61377 and analytically verified.
Metric 3:	Test Substance Purity	High	All Outcomes: Test substance was >99% purity verified analytically. Impurities were reported "Acidic components (assumed to be hydrochloric acid) were found to be present at a concentration of 10.8 ppm. one impurity with an area that was approximately 0.7% of the major peak area; this impurity, identified as 1 ,4-dichlorobenzene"
Domain 2: Test Design			
Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Concurrently treated vehicle control was used and appropriate for the study
Metric 5:	Positive Controls	N/A	Cancer/Carcinogenesis: A positive control was not necessary for this study type; Cancer/Carcinogenesis: Not needed for the study type
Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: The study reported the random allocation of animals into groups
Domain 3: Exposure Characterization			
Metric 7:	Preparation and Storage of Test Substance	High	All Outcomes: Dose preparation and storage were reported "adding a weighed amount of 1 ,2-dichlorobenzene to the appropriate volume of corn oil and mixing for 15 minutes" then dose solutions were prepared by dilution. The mixture was stable at room temp for 7 days and solutions were stored no longer than 14 days at 4 degrees C
Metric 8:	Consistency of Exposure Administration	High	All Outcomes: Details of exposure administration were reported and consistent. gavage volume was not excessive 5ml/kg.
Metric 9:	Reporting of Doses/Concentrations	High	All Outcomes: Doses were reported clearly
Metric 10:	Exposure Frequency and Duration	High	All Outcomes: Exposure frequency and duration were appropriate for the study type at 5 days a week for 103 weeks
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	Medium	Cancer/Carcinogenesis: Number of exposure groups was fewer than recommended at 2 exposure groups and one control. Spacing was appropriate and covered a range of response; Cancer/Carcinogenesis: Number of exposure groups was fewer than recommended at 2 exposure groups and one control. Spacing was justified based on results from 13 week study and covered a range of response
Metric 12:	Exposure Route and Method	High	All Outcomes: Exposure route and method were suited to the test substance: gavage is appropriate
Domain 4: Test Animals			

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Study Citation:	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.
Health Outcome(s):	Cancer/Carcinogenesis; Cancer/Carcinogenesis;
Reported Health Effect(s):	Cancer/Carcinogenesis: Neoplastic nodules; Cancer/Carcinogenesis: Neoplastic nodules;
Duration:	Chronic (>91 days) 2 years Rat
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	1944492

Domain	Metric	Rating	Comments
	Metric 13: Test Animal Characteristics	High	All Outcomes: Species, strain, sex, and age were all reported in table 1 and starting body weight was reported in results
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: All husbandry conditions were reported in table 1: temperature, humidity, light-dark cycle, diet, water availability and were adequate and consistent across all groups
	Metric 15: Number of Animals per Group	Medium	All Outcomes: The number of animals per group was reported and appropriate for the study type: 50/group for chronic
Domain 5: Outcome Assessment			
	Metric 16: Outcome Assessment Methodology	High	All Outcomes: The outcome assessment was sensitive and appropriate for the outcome of interest
	Metric 17: Consistency of Outcome Assessment	High	Cancer/Carcinogenesis: Outcome assessment was reported and was consistent across groups; Cancer/Carcinogenesis: The outcome assessment was described and applied consistently across groups
	Metric 18: Sampling Adequacy	High	Cancer/Carcinogenesis: Sampling was adequate and was for each animal; Cancer/Carcinogenesis: Sampling was adequate for the outcome
	Metric 19: Blinding of Assessors	High	All Outcomes: Histopathology re evaluations were blinded
	Metric 20: Negative Control Response	High	All Outcomes: Control animals responded appropriately
Domain 6: Confounding / Variable Control			
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	All Outcomes: Information was incompletely reported but did not identify differences among groups
	Metric 22: Health Outcomes Unrelated to Exposure	Medium	All Outcomes: Information provided was not sufficient to either support or dismiss the idea that there were differences unrelated to exposure
	Metric 23: Data Presentation and Analysis	High	All Outcomes: Statistical methods were reported and appropriate for the data
	Metric 24: Reporting of Data	High	All Outcomes: Data were reported for all outcomes by group and sex

Additional Comments: None

Overall Quality Determination**High**

Study Citation:	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.
Health Outcome(s):	Hepatic/Liver; Cardiovascular; Immune/Hematological; Lung/Respiratory; Skin/Connective Tissue; Gastrointestinal; Renal/Kidney; Thyroid; Endocrine (Endocrine); Reproductive/Developmental; Musculoskeletal; Neurological/Behavioral; Neurological/Behavioral; Hepatic/Liver; Immune/Hematological; Reproductive/Developmental; Gastrointestinal; Thyroid; Renal/Kidney; Musculoskeletal; Lung/Respiratory; Skin/Connective Tissue; Endocrine (Endocrine);
Reported Health Effect(s):	Hepatic/Liver: Liver weight, histopathology, vlinical chemistry (Mice & rats: ALP, GGT, and glutamic pyruvic transaminase; Rats only: bilirubin, cholesterol, triglycerides, BUN, glucose, total protein); Cardiovascular: Heart weight, cholesterol, triglycerides; Immune/Hematological: Organ weight (spleen, thymus), hematology (hgb, hct, RBC, WBC, MCV, platlets, reticulocytes), Histology (thymus, spleen, bone marrow, and lymph node); histopathology (thymus (rats only) & spleen (rats and mice); Lung/Respiratory: Lung weight and histology; Skin/Connective Tissue: Skin histology; Gastrointestinal: Histology of salivary gland, esophagus, stomach, small intestine, large intestine; Renal/Kidney: clinical chemistry (BUN (rats only)), kidney weight, histology; Thyroid: Thyroid histology; Endocrine (Endocrine): Parathyroid, pituitary, pancreas, adrenals histology; Reproductive/Developmental: Organ weight (testis, ovary, uterus); Histology (testis, ovary, uterus); Musculoskeletal: Histologic examination of femur, sternebrae, vertebrae, thigh muscle; Neurological/Behavioral: Brain weight and histology; Neurological/Behavioral: Brain weight and histology; Hepatic/Liver: Liver weight, histopathology, vlinical chemistry (Mice & rats: ALP, GGT, and glutamic pyruvic transaminase; Rats only: bilirubin, cholesterol, triglycerides, BUN, glucose, total protein); Immune/Hematological: Organ weight (spleen, thymus), hematology (hgb, hct, RBC, WBC, MCV, platlets, reticulocytes), Histology (thymus, spleen, bone marrow, and lymph node); histopathology (thymus (rats only) & spleen (rats and mice); Reproductive/Developmental: Organ weight (testis, ovary, uterus); Histology (testis, ovary, uterus); Gastrointestinal: Histology of salivary gland, esophagus, stomach, small intestine, large intestine; Thyroid: Thyroid histology; Renal/Kidney: clinical chemistry (BUN (rats only)), kidney weight, histology; Musculoskeletal: Histologic examination of femur, sternebrae, vertebrae, thigh muscle; Lung/Respiratory: Lung weight and histology; Skin/Connective Tissue: Skin histology; Endocrine (Endocrine): Parathyroid, pituitary, pancreas, adrenals histology;
Duration:	Chronic (>91 days) 2 years Rat
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	1944492

Domain	Metric	Rating	Comments
Domain 1: Test Substance			

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Study Citation:	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.
Health Outcome(s):	Hepatic/Liver; Cardiovascular; Immune/Hematological; Lung/Respiratory; Skin/Connective Tissue; Gastrointestinal; Renal/Kidney; Thyroid; Endocrine (Endocrine); Reproductive/Developmental; Musculoskeletal; Neurological/Behavioral; Neurological/Behavioral; Hepatic/Liver; Immune/Hematological; Reproductive/Developmental; Gastrointestinal; Thyroid; Renal/Kidney; Musculoskeletal; Lung/Respiratory; Skin/Connective Tissue; Endocrine (Endocrine);
Reported Health Effect(s):	Hepatic/Liver: Liver weight, histopathology, vlinical chemistry (Mice & rats: ALP, GGT, and glutamic pyruvic transaminase; Rats only: bilirubin, cholesterol, triglycerides, BUN, glucose, total protein); Cardiovascular: Heart weight, cholesterol, triglycerides; Immune/Hematological: Organ weight (spleen, thymus), hematology (hgb, hct, RBC, WBC, MCV, platlets, reticulocytes), Histology (thymus, spleen, bone marrow, and lymph node); histopathology (thymus (rats only) & spleen (rats and mice); Lung/Respiratory: Lung weight and histology; Skin/Connective Tissue: Skin histology; Gastrointestinal: Histology of salivary gland, esophagus, stomach, small intestine, large intestine; Renal/Kidney: clinical chemistry (BUN (rats only)), kidney weight, histology; Thyroid: Thyroid histology; Endocrine (Endocrine): Parathyroid, pituitary, pancreas, adrenals histology; Reproductive/Developmental: Organ weight (testis, ovary, uterus); Histology (testis, ovary, uterus); Musculoskeletal: Histologic examination of femur, sternebrae, vertebrae, thigh muscle; Neurological/Behavioral: Brain weight and histology; Neurological/Behavioral: Brain weight and histology; Hepatic/Liver: Liver weight, histopathology, vlinical chemistry (Mice & rats: ALP, GGT, and glutamic pyruvic transaminase; Rats only: bilirubin, cholesterol, triglycerides, BUN, glucose, total protein); Immune/Hematological: Organ weight (spleen, thymus), hematology (hgb, hct, RBC, WBC, MCV, platlets, reticulocytes), Histology (thymus, spleen, bone marrow, and lymph node); histopathology (thymus (rats only) & spleen (rats and mice); Reproductive/Developmental: Organ weight (testis, ovary, uterus); Histology (testis, ovary, uterus); Gastrointestinal: Histology of salivary gland, esophagus, stomach, small intestine, large intestine; Thyroid: Thyroid histology; Renal/Kidney: clinical chemistry (BUN (rats only)), kidney weight, histology; Musculoskeletal: Histologic examination of femur, sternebrae, vertebrae, thigh muscle; Lung/Respiratory: Lung weight and histology; Skin/Connective Tissue: Skin histology; Endocrine (Endocrine): Parathyroid, pituitary, pancreas, adrenals histology;
Duration:	Chronic (>91 days) 2 years Rat
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	1944492

Domain	Metric	Rating	Comments
Metric 1:	Test Substance Identity	High	Hepatic/Liver: Test substance was identified by nomenclature, CAS number, and structure; Cardiovascular: Test substance was identified by nomenclature, CAS number, and structure; Immune/Hematological: Test substance was identified by nomenclature, CAS number, and structure; Lung/Respiratory: Test substance was identified by nomenclature, CAS number, and structure; Skin/Connective Tissue: Test substance was identified by nomenclature, CAS number, and structure; Gastrointestinal: Test substance was identified by nomenclature, CAS number, and structure; Renal/Kidney: Test substance was identified by nomenclature, CAS number, and structure; Thyroid: Test substance was identified by nomenclature, CAS number, and structure; Endocrine (Endocrine): Test substance was identified by nomenclature, CAS number, and structure; Reproductive/Developmental: Test substance was identified by nomenclature, CAS number, and structure; Musculoskeletal: Test substance was identified by nomenclature, CAS number, and structure; Neurological/Behavioral: Test substance was identified by nomenclature, CAS number, and structure; Neurological/Behavioral: Test substance was identified by nomenclature, CAS number, and structure; Hepatic/Liver: Test substance was identified by nomenclature, CAS number, and structure; Immune/Hematological: Test substance was identified by nomenclature, CAS number, and structure; Reproductive/Developmental: Test substance was identified by nomenclature, CAS number, and structure; Gastrointestinal: test substance was identified by nomenclature, CAS number, and structure; Thyroid: Test substance was identified by nomenclature, CAS number, and structure; Renal/Kidney: test substance was identified by nomenclature, CAS number, and structure; Musculoskeletal: Test substance was identified by nomenclature, CAS number, and structure; Lung/Respiratory: Test substance was identified by nomenclature, CAS number, and structure; Skin/Connective Tissue: Test substance was identified by nomenclature, CAS number, and structure; Endocrine (Endocrine): Test substance was identified by nomenclature, CAS number, and structure

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Study Citation:	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.
Health Outcome(s):	Hepatic/Liver; Cardiovascular; Immune/Hematological; Lung/Respiratory; Skin/Connective Tissue; Gastrointestinal; Renal/Kidney; Thyroid; Endocrine (Endocrine); Reproductive/Developmental; Musculoskeletal; Neurological/Behavioral; Neurological/Behavioral; Hepatic/Liver; Immune/Hematological; Reproductive/Developmental; Gastrointestinal; Thyroid; Renal/Kidney; Musculoskeletal; Lung/Respiratory; Skin/Connective Tissue; Endocrine (Endocrine);
Reported Health Effect(s):	Hepatic/Liver: Liver weight, histopathology, vlinical chemistry (Mice & rats: ALP, GGT, and glutamic pyruvic transaminase; Rats only: bilirubin, cholesterol, triglycerides, BUN, glucose, total protein); Cardiovascular: Heart weight, cholesterol, triglycerides; Immune/Hematological: Organ weight (spleen, thymus), hematology (hgb, hct, RBC, WBC, MCV, platlets, reticulocytes), Histology (thymus, spleen, bone marrow, and lymph node); histopathology (thymus (rats only) & spleen (rats and mice); Lung/Respiratory: Lung weight and histology; Skin/Connective Tissue: Skin histology; Gastrointestinal: Histology of salivary gland, esophagus, stomach, small intestine, large intestine; Renal/Kidney: clinical chemistry (BUN (rats only)), kidney weight, histology; Thyroid: Thyroid histology; Endocrine (Endocrine): Parathyroid, pituitary, pancreas, adrenals histology; Reproductive/Developmental: Organ weight (testis, ovary, uterus); Histology (testis, ovary, uterus); Musculoskeletal: Histologic examination of femur, sternebrae, vertebrae, thigh muscle; Neurological/Behavioral: Brain weight and histology; Neurological/Behavioral: Brain weight and histology; Hepatic/Liver: Liver weight, histopathology, vlinical chemistry (Mice & rats: ALP, GGT, and glutamic pyruvic transaminase; Rats only: bilirubin, cholesterol, triglycerides, BUN, glucose, total protein); Immune/Hematological: Organ weight (spleen, thymus), hematology (hgb, hct, RBC, WBC, MCV, platlets, reticulocytes), Histology (thymus, spleen, bone marrow, and lymph node); histopathology (thymus (rats only) & spleen (rats and mice); Reproductive/Developmental: Organ weight (testis, ovary, uterus); Histology (testis, ovary, uterus); Gastrointestinal: Histology of salivary gland, esophagus, stomach, small intestine, large intestine; Thyroid: Thyroid histology; Renal/Kidney: clinical chemistry (BUN (rats only)), kidney weight, histology; Musculoskeletal: Histologic examination of femur, sternebrae, vertebrae, thigh muscle; Lung/Respiratory: Lung weight and histology; Skin/Connective Tissue: Skin histology; Endocrine (Endocrine): Parathyroid, pituitary, pancreas, adrenals histology;
Duration:	Chronic (>91 days) 2 years Rat
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	1944492

Domain	Metric	Rating	Comments
Metric 2:	Test Substance Source	High	Hepatic/Liver: Test substance was obtained from a commercial source: "ICC solvent Chemical Company (New York, NY) Lot number SC61377 and analytically verified.; Cardiovascular: Test substance was obtained from a commercial source: "ICC solvent Chemical Company (New York, NY) Lot number SC61377 and analytically verified.; Immune/Hematological: Test substance was obtained from a commercial source: "ICC solvent Chemical Company (New York, NY) Lot number SC61377 and analytically verified.; Lung/Respiratory: Test substance was obtained from a commercial source: "ICC solvent Chemical Company (New York, NY) Lot number SC61377 and analytically verified.; Skin/Connective Tissue: Test substance was obtained from a commercial source: "ICC solvent Chemical Company (New York, NY) Lot number SC61377 and analytically verified.; Gastrointestinal: Test substance was obtained from a commercial source: "ICC solvent Chemical Company (New York, NY) Lot number SC61377 and analytically verified.; Renal/Kidney: Test substance was obtained from a commercial source: "ICC solvent Chemical Company (New York, NY) Lot number SC61377 and analytically verified.; Thyroid: Test substance was obtained from a commercial source: "ICC solvent Chemical Company (New York, NY) Lot number SC61377 and analytically verified.; Endocrine (Endocrine): Test substance was obtained from a commercial source: "ICC solvent Chemical Company (New York, NY) Lot number SC61377 and analytically verified.; Reproductive/Developmental: Test substance was obtained from a commercial source: "ICC solvent Chemical Company (New York, NY) Lot number SC61377 and analytically verified.; Musculoskeletal: Test substance was obtained from a commercial source: "ICC solvent Chemical Company (New York, NY) Lot number SC61377 and analytically verified.; Neurological/Behavioral: Test substance was obtained from a commercial source: "ICC solvent Chemical Company (New York, NY) Lot number SC61377 and analytically verified.; Neurological/Behavioral: Test substance was obtained from a commercial source: "ICC solvent Chemical Company (New York, NY) Lot number SC61377 and analytically verified.; Hepatic/Liver: Test substance was obtained from a commercial source: "ICC solvent Chemical Company (New York, NY) Lot number SC61377 and analytically verified.;

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Study Citation:	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.
Health Outcome(s):	Hepatic/Liver; Cardiovascular; Immune/Hematological; Lung/Respiratory; Skin/Connective Tissue; Gastrointestinal; Renal/Kidney; Thyroid; Endocrine (Endocrine); Reproductive/Developmental; Musculoskeletal; Neurological/Behavioral; Neurological/Behavioral; Hepatic/Liver; Immune/Hematological; Reproductive/Developmental; Gastrointestinal; Thyroid; Renal/Kidney; Musculoskeletal; Lung/Respiratory; Skin/Connective Tissue; Endocrine (Endocrine);
Reported Health Effect(s):	Hepatic/Liver: Liver weight, histopathology, vlinical chemistry (Mice & rats: ALP, GGT, and glutamic pyruvic transaminase; Rats only: bilirubin, cholesterol, triglycerides, BUN, glucose, total protein); Cardiovascular: Heart weight, cholesterol, triglycerides; Immune/Hematological: Organ weight (spleen, thymus), hematology (hgb, hct, RBC, WBC, MCV, platlets, reticulocytes), Histology (thymus, spleen, bone marrow, and lymph node); histopathology (thymus (rats only) & spleen (rats and mice); Lung/Respiratory: Lung weight and histology; Skin/Connective Tissue: Skin histology; Gastrointestinal: Histology of salivary gland, esophagus, stomach, small intestine, large intestine; Renal/Kidney: clinical chemistry (BUN (rats only)), kidney weight, histology; Thyroid: Thyroid histology; Endocrine (Endocrine): Parathyroid, pituitary, pancreas, adrenals histology; Reproductive/Developmental: Organ weight (testis, ovary, uterus); Histology (testis, ovary, uterus); Musculoskeletal: Histologic examination of femur, sternebrae, vertebrae, thigh muscle; Neurological/Behavioral: Brain weight and histology; Neurological/Behavioral: Brain weight and histology; Hepatic/Liver: Liver weight, histopathology, vlinical chemistry (Mice & rats: ALP, GGT, and glutamic pyruvic transaminase; Rats only: bilirubin, cholesterol, triglycerides, BUN, glucose, total protein); Immune/Hematological: Organ weight (spleen, thymus), hematology (hgb, hct, RBC, WBC, MCV, platlets, reticulocytes), Histology (thymus, spleen, bone marrow, and lymph node); histopathology (thymus (rats only) & spleen (rats and mice); Reproductive/Developmental: Organ weight (testis, ovary, uterus); Histology (testis, ovary, uterus); Gastrointestinal: Histology of salivary gland, esophagus, stomach, small intestine, large intestine; Thyroid: Thyroid histology; Renal/Kidney: clinical chemistry (BUN (rats only)), kidney weight, histology; Musculoskeletal: Histologic examination of femur, sternebrae, vertebrae, thigh muscle; Lung/Respiratory: Lung weight and histology; Skin/Connective Tissue: Skin histology; Endocrine (Endocrine): Parathyroid, pituitary, pancreas, adrenals histology;
Duration:	Chronic (>91 days) 2 years Rat
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	1944492

Domain	Metric	Rating	Comments
Metric 3:	Test Substance Purity	High	Hepatic/Liver: Test substance was >99% purity verified analytically. impurities were reported "Acidic components (assumed to be hydrochloric acid) were found to be present at a concentration of 10.8 ppm. one impurity with an area that was approximately 0.7% of the major peak area; this impurity, identified as 1 ,4-dichlorobenzene"; Cardiovascular: Test substance was >99% purity verified analytically. Impurities were reported "Acidic components (assumed to be hydrochloric acid) were found to be present at a concentration of 10.8 ppm. one impurity with an area that was approximately 0.7% of the major peak area; this impurity, identified as 1 ,4-dichlorobenzene"; Immune/Hematological: Test substance was >99% purity verified analytically. Impurities were reported "Acidic components (assumed to be hydrochloric acid) were found to be present at a concentration of 10.8 ppm. one impurity with an area that was approximately 0.7% of the major peak area; this impurity, identified as 1 ,4-dichlorobenzene"; Lung/Respiratory: Test substance was >99% purity verified analytically. Impurities were reported "Acidic components (assumed to be hydrochloric acid) were found to be present at a concentration of 10.8 ppm. one impurity with an area that was approximately 0.7% of the major peak area; this impurity, identified as 1 ,4-dichlorobenzene"; Skin/Connective Tissue: Test substance was >99% purity verified analytically. impurities were reported "Acidic components (assumed to be hydrochloric acid) were found to be present at a concentration of 10.8 ppm. one impurity with an area that was approximately 0.7% of the major peak area; this impurity, identified as 1 ,4-dichlorobenzene"; Gastrointestinal: Test substance was >99% purity verified analytically. Impurities were reported "Acidic components (assumed to be hydrochloric acid) were found to be present at a concentration of 10.8 ppm. one impurity with an area that was approximately 0.7% of the major peak area; this impurity, identified as 1 ,4-dichlorobenzene"; Renal/Kidney: Test substance was >99% purity verified analytically. Impurities were reported "Acidic components (assumed to be hydrochloric acid) were found to be present at a concentration of 10.8 ppm. one impurity with an area that was approximately 0.7% of the major peak area; this impurity, identified as 1 ,4-dichlorobenzene";

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Study Citation:	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.
Health Outcome(s):	Hepatic/Liver; Cardiovascular; Immune/Hematological; Lung/Respiratory; Skin/Connective Tissue; Gastrointestinal; Renal/Kidney; Thyroid; Endocrine (Endocrine); Reproductive/Developmental; Musculoskeletal; Neurological/Behavioral; Neurological/Behavioral; Hepatic/Liver; Immune/Hematological; Reproductive/Developmental; Gastrointestinal; Thyroid; Renal/Kidney; Musculoskeletal; Lung/Respiratory; Skin/Connective Tissue; Endocrine (Endocrine);
Reported Health Effect(s):	Hepatic/Liver: Liver weight, histopathology, vlinical chemistry (Mice & rats: ALP, GGT, and glutamic pyruvic transaminase; Rats only: bilirubin, cholesterol, triglycerides, BUN, glucose, total protein); Cardiovascular: Heart weight, cholesterol, triglycerides; Immune/Hematological: Organ weight (spleen, thymus), hematology (hgb, hct, RBC, WBC, MCV, platlets, reticulocytes), Histology (thymus, spleen, bone marrow, and lymph node); histopathology (thymus (rats only) & spleen (rats and mice); Lung/Respiratory: Lung weight and histology; Skin/Connective Tissue: Skin histology; Gastrointestinal: Histology of salivary gland, esophagus, stomach, small intestine, large intestine; Renal/Kidney: clinical chemistry (BUN (rats only)), kidney weight, histology; Thyroid: Thyroid histology; Endocrine (Endocrine): Parathyroid, pituitary, pancreas, adrenals histology; Reproductive/Developmental: Organ weight (testis, ovary, uterus); Histology (testis, ovary, uterus); Musculoskeletal: Histologic examination of femur, sternebrae, vertebrae, thigh muscle; Neurological/Behavioral: Brain weight and histology; Neurological/Behavioral: Brain weight and histology; Hepatic/Liver: Liver weight, histopathology, vlinical chemistry (Mice & rats: ALP, GGT, and glutamic pyruvic transaminase; Rats only: bilirubin, cholesterol, triglycerides, BUN, glucose, total protein); Immune/Hematological: Organ weight (spleen, thymus), hematology (hgb, hct, RBC, WBC, MCV, platlets, reticulocytes), Histology (thymus, spleen, bone marrow, and lymph node); histopathology (thymus (rats only) & spleen (rats and mice); Reproductive/Developmental: Organ weight (testis, ovary, uterus); Histology (testis, ovary, uterus); Gastrointestinal: Histology of salivary gland, esophagus, stomach, small intestine, large intestine; Thyroid: Thyroid histology; Renal/Kidney: clinical chemistry (BUN (rats only)), kidney weight, histology; Musculoskeletal: Histologic examination of femur, sternebrae, vertebrae, thigh muscle; Lung/Respiratory: Lung weight and histology; Skin/Connective Tissue: Skin histology; Endocrine (Endocrine): Parathyroid, pituitary, pancreas, adrenals histology;
Duration:	Chronic (>91 days) 2 years Rat
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	1944492

Domain	Metric	Rating	Comments
Domain 2: Test Design	Metric 4: Negative and Vehicle Controls	High	All Outcomes: Concurrently treated vehicle control was used and appropriate for the study
	Metric 5: Positive Controls	N/A	All Outcomes: A positive control was not necessary for this study type
	Metric 6: Randomized Allocation of Animals	Medium	All Outcomes: The study reported the random allocation of animals into groups
Domain 3: Exposure Characterization	Metric 7: Preparation and Storage of Test Substance	High	All Outcomes: Dose preparation and storage were reported "adding a weighed amount of 1 ,2-dichlorobenzene to the appropriate volume of corn oil and mixing for 15 minutes" then dose solutions were prepared by dilution. The mixture was stable at room temp for 7 days and solutions were stored no longer than 14 days at 4 degrees C

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Health Outcome(s):	Hepatic/Liver; Cardiovascular; Immune/Hematological; Lung/Respiratory; Skin/Connective Tissue; Gastrointestinal; Renal/Kidney; Thyroid; Endocrine (Endocrine); Reproductive/Developmental; Musculoskeletal; Neurological/Behavioral; Neurological/Behavioral; Hepatic/Liver; Immune/Hematological; Reproductive/Developmental; Gastrointestinal; Thyroid; Renal/Kidney; Musculoskeletal; Lung/Respiratory; Skin/Connective Tissue; Endocrine (Endocrine);
Reported Health Effect(s):	Hepatic/Liver: Liver weight, histopathology, vlinical chemistry (Mice & rats: ALP, GGT, and glutamic pyruvic transaminase; Rats only: bilirubin, cholesterol, triglycerides, BUN, glucose, total protein); Cardiovascular: Heart weight, cholesterol, triglycerides; Immune/Hematological: Organ weight (spleen, thymus), hematology (hgb, hct, RBC, WBC, MCV, platlets, reticulocytes), Histology (thymus, spleen, bone marrow, and lymph node); histopathology (thymus (rats only) & spleen (rats and mice); Lung/Respiratory: Lung weight and histology; Skin/Connective Tissue: Skin histology; Gastrointestinal: Histology of salivary gland, esophagus, stomach, small intestine, large intestine; Renal/Kidney: clinical chemistry (BUN (rats only)), kidney weight, histology; Thyroid: Thyroid histology; Endocrine (Endocrine): Parathyroid, pituitary, pancreas, adrenals histology; Reproductive/Developmental: Organ weight (testis, ovary, uterus); Histology (testis, ovary, uterus); Musculoskeletal: Histologic examination of femur, sternebrae, vertebrae, thigh muscle; Neurological/Behavioral: Brain weight and histology; Neurological/Behavioral: Brain weight and histology; Hepatic/Liver: Liver weight, histopathology, vlinical chemistry (Mice & rats: ALP, GGT, and glutamic pyruvic transaminase; Rats only: bilirubin, cholesterol, triglycerides, BUN, glucose, total protein); Immune/Hematological: Organ weight (spleen, thymus), hematology (hgb, hct, RBC, WBC, MCV, platlets, reticulocytes), Histology (thymus, spleen, bone marrow, and lymph node); histopathology (thymus (rats only) & spleen (rats and mice); Reproductive/Developmental: Organ weight (testis, ovary, uterus); Histology (testis, ovary, uterus); Gastrointestinal: Histology of salivary gland, esophagus, stomach, small intestine, large intestine; Thyroid: Thyroid histology; Renal/Kidney: clinical chemistry (BUN (rats only)), kidney weight, histology; Musculoskeletal: Histologic examination of femur, sternebrae, vertebrae, thigh muscle; Lung/Respiratory: Lung weight and histology; Skin/Connective Tissue: Skin histology; Endocrine (Endocrine): Parathyroid, pituitary, pancreas, adrenals histology;
Duration:	Chronic (>91 days) 2 years Rat
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	1944492

Domain	Metric	Rating	Comments
Metric 8:	Consistency of Exposure Administration	High	Hepatic/Liver: Details of exposure administration were reported and consistent. gavage volume was not excessive 5ml/kg.; Cardiovascular: Details of exposure administration were reported and consistent. gavage volume was not excessive 5ml/kg.; Immune/Hematological: Details of exposure administration were reported and consistent. gavage volume was not excessive 5ml/kg.; Lung/Respiratory: Details of exposure administration were reported and consistent. gavage volume was not excessive 5ml/kg.; Skin/Connective Tissue: Details of exposure administration were reported and consistent. gavage volume was not excessive 5ml/kg.; Gastrointestinal: Details of exposure administration were reported and consistent. gavage volume was not excessive 5ml/kg.; Renal/Kidney: Details of exposure administration were reported and consistent; gavage volume was not excessive 5ml/kg.; Thyroid: Details of exposure administration were reported and consistent; gavage volume was not excessive 5ml/kg.; Endocrine (Endocrine): Details of exposure administration were reported and consistent. gavage volume was not excessive 5ml/kg.; Reproductive/Developmental: Details of exposure administration were reported and consistent. gavage volume was not excessive 5ml/kg.; Musculoskeletal: Details of exposure administration were reported and consistent. Gavage volume was not excessive 5ml/kg.; Neurological/Behavioral: Details of exposure administration were reported and consistent. gavage volume was not excessive 5ml/kg.; Neurological/Behavioral: Details of exposure administration were reported and consistent. gavage volume was not excessive 5ml/kg.; Hepatic/Liver: Details of exposure administration were reported and consistent. gavage volume was not excessive 5ml/kg.; Immune/Hematological: Details of exposure administration were reported and consistent. gavage volume was not excessive 5ml/kg.; Reproductive/Developmental: Details of exposure administration were reported and consistent. gavage volume was not excessive 5ml/kg.; Gastrointestinal: Details of exposure administration were reported and consistent; gavage volume was not excessive 5ml/kg.; Thyroid: Details of exposure administration were reported and consistent; gavage volume was not excessive 5ml/kg.; Renal/Kidney: Details of exposure administration were reported and consistent.

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Health Outcome(s):	Hepatic/Liver; Cardiovascular; Immune/Hematological; Lung/Respiratory; Skin/Connective Tissue; Gastrointestinal; Renal/Kidney; Thyroid; Endocrine (Endocrine); Reproductive/Developmental; Musculoskeletal; Neurological/Behavioral; Neurological/Behavioral; Hepatic/Liver; Immune/Hematological; Reproductive/Developmental; Gastrointestinal; Thyroid; Renal/Kidney; Musculoskeletal; Lung/Respiratory; Skin/Connective Tissue; Endocrine (Endocrine);
Reported Health Effect(s):	Hepatic/Liver: Liver weight, histopathology, vlinical chemistry (Mice & rats: ALP, GGT, and glutamic pyruvic transaminase; Rats only: bilirubin, cholesterol, triglycerides, BUN, glucose, total protein); Cardiovascular: Heart weight, cholesterol, triglycerides; Immune/Hematological: Organ weight (spleen, thymus), hematology (hgb, hct, RBC, WBC, MCV, platlets, reticulocytes), Histology (thymus, spleen, bone marrow, and lymph node); histopathology (thymus (rats only) & spleen (rats and mice); Lung/Respiratory: Lung weight and histology; Skin/Connective Tissue: Skin histology; Gastrointestinal: Histology of salivary gland, esophagus, stomach, small intestine, large intestine; Renal/Kidney: clinical chemistry (BUN (rats only)), kidney weight, histology; Thyroid: Thyroid histology; Endocrine (Endocrine): Parathyroid, pituitary, pancreas, adrenals histology; Reproductive/Developmental: Organ weight (testis, ovary, uterus); Histology (testis, ovary, uterus); Musculoskeletal: Histologic examination of femur, sternebrae, vertebrae, thigh muscle; Neurological/Behavioral: Brain weight and histology; Neurological/Behavioral: Brain weight and histology; Hepatic/Liver: Liver weight, histopathology, vlinical chemistry (Mice & rats: ALP, GGT, and glutamic pyruvic transaminase; Rats only: bilirubin, cholesterol, triglycerides, BUN, glucose, total protein); Immune/Hematological: Organ weight (spleen, thymus), hematology (hgb, hct, RBC, WBC, MCV, platlets, reticulocytes), Histology (thymus, spleen, bone marrow, and lymph node); histopathology (thymus (rats only) & spleen (rats and mice); Reproductive/Developmental: Organ weight (testis, ovary, uterus); Histology (testis, ovary, uterus); Gastrointestinal: Histology of salivary gland, esophagus, stomach, small intestine, large intestine; Thyroid: Thyroid histology; Renal/Kidney: clinical chemistry (BUN (rats only)), kidney weight, histology; Musculoskeletal: Histologic examination of femur, sternebrae, vertebrae, thigh muscle; Lung/Respiratory: Lung weight and histology; Skin/Connective Tissue: Skin histology; Endocrine (Endocrine): Parathyroid, pituitary, pancreas, adrenals histology;
Duration:	Chronic (>91 days) 2 years Rat
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	1944492

Domain	Metric	Rating	Comments
	Metric 9: Reporting of Doses/Concentrations	High	All Outcomes: Doses were reported clearly
	Metric 10: Exposure Frequency and Duration	High	All Outcomes: Exposure frequency and duration were appropriate for the study type at 5 days a week for 103 weeks
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	Medium	All Outcomes: Number of exposure groups was fewer than recommended at 2 exposure groups and one control. Spacing was appropriate and covered a range of response
	Metric 12: Exposure Route and Method	High	All Outcomes: Exposure route and method were suited to the test substance: gavage is appropriate
Domain 4: Test Animals			
	Metric 13: Test Animal Characteristics	High	All Outcomes: Species, strain, sex, and age were all reported in table 1 and starting body weight was reported in results
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: All husbandry conditions were reported in table 1: temperature, humidity, light- dark cycle, diet, water availability and were adequate and consistent across all groups
	Metric 15: Number of Animals per Group	Medium	All Outcomes: The number of animals per group was reported and appropriate for the study type: 50/group for chronic
Domain 5: Outcome Assessment			

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Health Outcome(s):	Hepatic/Liver; Cardiovascular; Immune/Hematological; Lung/Respiratory; Skin/Connective Tissue; Gastrointestinal; Renal/Kidney; Thyroid; Endocrine (Endocrine); Reproductive/Developmental; Musculoskeletal; Neurological/Behavioral; Neurological/Behavioral; Hepatic/Liver; Immune/Hematological; Reproductive/Developmental; Gastrointestinal; Thyroid; Renal/Kidney; Musculoskeletal; Lung/Respiratory; Skin/Connective Tissue; Endocrine (Endocrine);
Reported Health Effect(s):	Hepatic/Liver: Liver weight, histopathology, vlinical chemistry (Mice & rats: ALP, GGT, and glutamic pyruvic transaminase; Rats only: bilirubin, cholesterol, triglycerides, BUN, glucose, total protein); Cardiovascular: Heart weight, cholesterol, triglycerides; Immune/Hematological: Organ weight (spleen, thymus), hematology (hgb, hct, RBC, WBC, MCV, platlets, reticulocytes), Histology (thymus, spleen, bone marrow, and lymph node); histopathology (thymus (rats only) & spleen (rats and mice); Lung/Respiratory: Lung weight and histology; Skin/Connective Tissue: Skin histology; Gastrointestinal: Histology of salivary gland, esophagus, stomach, small intestine, large intestine; Renal/Kidney: clinical chemistry (BUN (rats only)), kidney weight, histology; Thyroid: Thyroid histology; Endocrine (Endocrine): Parathyroid, pituitary, pancreas, adrenals histology; Reproductive/Developmental: Organ weight (testis, ovary, uterus); Histology (testis, ovary, uterus); Musculoskeletal: Histologic examination of femur, sternebrae, vertebrae, thigh muscle; Neurological/Behavioral: Brain weight and histology; Neurological/Behavioral: Brain weight and histology; Hepatic/Liver: Liver weight, histopathology, vlinical chemistry (Mice & rats: ALP, GGT, and glutamic pyruvic transaminase; Rats only: bilirubin, cholesterol, triglycerides, BUN, glucose, total protein); Immune/Hematological: Organ weight (spleen, thymus), hematology (hgb, hct, RBC, WBC, MCV, platlets, reticulocytes), Histology (thymus, spleen, bone marrow, and lymph node); histopathology (thymus (rats only) & spleen (rats and mice); Reproductive/Developmental: Organ weight (testis, ovary, uterus); Histology (testis, ovary, uterus); Gastrointestinal: Histology of salivary gland, esophagus, stomach, small intestine, large intestine; Thyroid: Thyroid histology; Renal/Kidney: clinical chemistry (BUN (rats only)), kidney weight, histology; Musculoskeletal: Histologic examination of femur, sternebrae, vertebrae, thigh muscle; Lung/Respiratory: Lung weight and histology; Skin/Connective Tissue: Skin histology; Endocrine (Endocrine): Parathyroid, pituitary, pancreas, adrenals histology;
Duration:	Chronic (>91 days) 2 years Rat
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	1944492

Domain	Metric	Rating	Comments
Metric 16:	Outcome Assessment Methodology	Medium	Hepatic/Liver: The outcome assessment was sensitive and appropriate for the outcome of interest but was limited to gross and histopathological examination.; Cardiovascular: The outcome assessment was sensitive and appropriate for the outcome of interest, and included gross and histopathological examination.; Immune/Hematological: The outcome assessment was sensitive and appropriate for the outcome of interest but was limited to gross and histopathological examination of tissue. Hematology was not included in the 2-year study.; Lung/Respiratory: The outcome assessment was sensitive and appropriate for the outcome of interest but was limited to gross and histopathological examination.; Skin/Connective Tissue: The outcome assessment was sensitive and appropriate for the outcome of interest but was limited to gross and histopathological examination.; Gastrointestinal: the outcome assessment was sensitive and appropriate for the outcome of interest but was limited to gross and histopathological examination.; Renal/Kidney: The outcome assessment was sensitive and appropriate for the outcome of interest but was limited to gross and histopathological examination.; Thyroid: The outcome assessment was sensitive and appropriate for the outcome of interest but was limited to gross and histopathological examination of tissue. Thyroid hormones were not measured.; Endocrine (Endocrine): the outcome assessment was sensitive and appropriate for the outcome of interest but was limited to gross and histopathological examination.; Reproductive/Developmental: The outcome assessment was sensitive and appropriate for the outcome of interest but was limited to gross and histopathological examination.; Musculoskeletal: Outcome assessment was sensitive and appropriate for the outcome of interest but was limited to gross and histopathological examination.; Neurological/Behavioral: The outcome assessment was sensitive and appropriate for the outcome of interest but was limited to gross and histopathological examination.; Neurological/Behavioral: The outcome assessment was sensitive and appropriate for the outcome of interest but was limited to gross and histopathological examination of tissue.; Hepatic/Liver: The outcome assessment was sensitive and appropriate for the outcome of interest but was limited to gross and histopathological examination of tis-

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Study Citation:	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.
Health Outcome(s):	Hepatic/Liver; Cardiovascular; Immune/Hematological; Lung/Respiratory; Skin/Connective Tissue; Gastrointestinal; Renal/Kidney; Thyroid; Endocrine (Endocrine); Reproductive/Developmental; Musculoskeletal; Neurological/Behavioral; Neurological/Behavioral; Hepatic/Liver; Immune/Hematological; Reproductive/Developmental; Gastrointestinal; Thyroid; Renal/Kidney; Musculoskeletal; Lung/Respiratory; Skin/Connective Tissue; Endocrine (Endocrine);
Reported Health Effect(s):	Hepatic/Liver: Liver weight, histopathology, vlinical chemistry (Mice & rats: ALP, GGT, and glutamic pyruvic transaminase; Rats only: bilirubin, cholesterol, triglycerides, BUN, glucose, total protein); Cardiovascular: Heart weight, cholesterol, triglycerides; Immune/Hematological: Organ weight (spleen, thymus), hematology (hgb, hct, RBC, WBC, MCV, platlets, reticulocytes), Histology (thymus, spleen, bone marrow, and lymph node); histopathology (thymus (rats only) & spleen (rats and mice); Lung/Respiratory: Lung weight and histology; Skin/Connective Tissue: Skin histology; Gastrointestinal: Histology of salivary gland, esophagus, stomach, small intestine, large intestine; Renal/Kidney: clinical chemistry (BUN (rats only)), kidney weight, histology; Thyroid: Thyroid histology; Endocrine (Endocrine): Parathyroid, pituitary, pancreas, adrenals histology; Reproductive/Developmental: Organ weight (testis, ovary, uterus); Histology (testis, ovary, uterus); Musculoskeletal: Histologic examination of femur, sternebrae, vertebrae, thigh muscle; Neurological/Behavioral: Brain weight and histology; Neurological/Behavioral: Brain weight and histology; Hepatic/Liver: Liver weight, histopathology, vlinical chemistry (Mice & rats: ALP, GGT, and glutamic pyruvic transaminase; Rats only: bilirubin, cholesterol, triglycerides, BUN, glucose, total protein); Immune/Hematological: Organ weight (spleen, thymus), hematology (hgb, hct, RBC, WBC, MCV, platlets, reticulocytes), Histology (thymus, spleen, bone marrow, and lymph node); histopathology (thymus (rats only) & spleen (rats and mice); Reproductive/Developmental: Organ weight (testis, ovary, uterus); Histology (testis, ovary, uterus); Gastrointestinal: Histology of salivary gland, esophagus, stomach, small intestine, large intestine; Thyroid: Thyroid histology; Renal/Kidney: clinical chemistry (BUN (rats only)), kidney weight, histology; Musculoskeletal: Histologic examination of femur, sternebrae, vertebrae, thigh muscle; Lung/Respiratory: Lung weight and histology; Skin/Connective Tissue: Skin histology; Endocrine (Endocrine): Parathyroid, pituitary, pancreas, adrenals histology;
Duration:	Chronic (>91 days) 2 years Rat
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	1944492

Domain	Metric	Rating	Comments
Metric 17:	Consistency of Outcome Assessment	High	Hepatic/Liver: Outcome assessment was reported and was consistent across groups; Cardiovascular: Outcome assessment was reported and was consistent across groups; Immune/Hematological: Outcome assessment was reported and was consistent across groups; Lung/Respiratory: Outcome assessment was reported and was consistent across groups; Skin/Connective Tissue: Outcome assessment was reported and was consistent across groups; Gastrointestinal: Outcome assessment was reported and was consistent across groups; Renal/Kidney: Outcome assessment was reported and was consistent across groups; Thyroid: Outcome assessment was reported and was consistent across groups; Endocrine (Endocrine): Outcome assessment was reported and was consistent across groups; Reproductive/Developmental: Outcome assessment was reported and was consistent across groups; Musculoskeletal: Outcome assessment was reported and was consistent across groups; Neurological/Behavioral: Outcome assessment was reported and was consistent across groups; Neurological/Behavioral: Outcome assessment was reported and was consistent across groups; Hepatic/Liver: Outcome assessment was reported and was consistent across groups; Immune/Hematological: Outcome assessment was reported and was consistent across groups; Reproductive/Developmental: Outcome assessment was reported and was consistent across groups; Gastrointestinal: outcome assessment was reported and was consistent across groups; Thyroid: Outcome assessment was reported and was consistent across groups; Renal/Kidney: Outcome assessment was reported and was consistent across groups; Musculoskeletal: Outcome assessment was reported and was consistent across groups; Lung/Respiratory: Outcome assessment was reported and was consistent across groups; Skin/Connective Tissue: Outcome assessment was reported and was consistent across groups; Endocrine (Endocrine): Outcome assessment was reported and was consistent across groups

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Study Citation:	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.
Health Outcome(s):	Hepatic/Liver; Cardiovascular; Immune/Hematological; Lung/Respiratory; Skin/Connective Tissue; Gastrointestinal; Renal/Kidney; Thyroid; Endocrine (Endocrine); Reproductive/Developmental; Musculoskeletal; Neurological/Behavioral; Neurological/Behavioral; Hepatic/Liver; Immune/Hematological; Reproductive/Developmental; Gastrointestinal; Thyroid; Renal/Kidney; Musculoskeletal; Lung/Respiratory; Skin/Connective Tissue; Endocrine (Endocrine);
Reported Health Effect(s):	Hepatic/Liver: Liver weight, histopathology, vlinical chemistry (Mice & rats: ALP, GGT, and glutamic pyruvic transaminase; Rats only: bilirubin, cholesterol, triglycerides, BUN, glucose, total protein); Cardiovascular: Heart weight, cholesterol, triglycerides; Immune/Hematological: Organ weight (spleen, thymus), hematology (hgb, hct, RBC, WBC, MCV, platlets, reticulocytes), Histology (thymus, spleen, bone marrow, and lymph node); histopathology (thymus (rats only) & spleen (rats and mice); Lung/Respiratory: Lung weight and histology; Skin/Connective Tissue: Skin histology; Gastrointestinal: Histology of salivary gland, esophagus, stomach, small intestine, large intestine; Renal/Kidney: clinical chemistry (BUN (rats only)), kidney weight, histology; Thyroid: Thyroid histology; Endocrine (Endocrine): Parathyroid, pituitary, pancreas, adrenals histology; Reproductive/Developmental: Organ weight (testis, ovary, uterus); Histology (testis, ovary, uterus); Musculoskeletal: Histologic examination of femur, sternebrae, vertebrae, thigh muscle; Neurological/Behavioral: Brain weight and histology; Neurological/Behavioral: Brain weight and histology; Hepatic/Liver: Liver weight, histopathology, vlinical chemistry (Mice & rats: ALP, GGT, and glutamic pyruvic transaminase; Rats only: bilirubin, cholesterol, triglycerides, BUN, glucose, total protein); Immune/Hematological: Organ weight (spleen, thymus), hematology (hgb, hct, RBC, WBC, MCV, platlets, reticulocytes), Histology (thymus, spleen, bone marrow, and lymph node); histopathology (thymus (rats only) & spleen (rats and mice); Reproductive/Developmental: Organ weight (testis, ovary, uterus); Histology (testis, ovary, uterus); Gastrointestinal: Histology of salivary gland, esophagus, stomach, small intestine, large intestine; Thyroid: Thyroid histology; Renal/Kidney: clinical chemistry (BUN (rats only)), kidney weight, histology; Musculoskeletal: Histologic examination of femur, sternebrae, vertebrae, thigh muscle; Lung/Respiratory: Lung weight and histology; Skin/Connective Tissue: Skin histology; Endocrine (Endocrine): Parathyroid, pituitary, pancreas, adrenals histology;
Duration:	Chronic (>91 days) 2 years Rat
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	1944492

Domain	Metric	Rating	Comments
Metric 18:	Sampling Adequacy	High	Hepatic/Liver: Sampling was adequate; Cardiovascular: Sampling was adequate; Immune/Hematological: Sampling was adequate; Lung/Respiratory: Sampling was adequate; Skin/Connective Tissue: Sampling was adequate; Gastrointestinal: sampling was adequate; Renal/Kidney: Sampling was adequate; Thyroid: Sampling was adequate; Endocrine (Endocrine): Sampling was adequate; Reproductive/Developmental: Sampling was adequate; Musculoskeletal: Sampling was adequate; Neurological/Behavioral: Sampling was adequate; Neurological/Behavioral: Sampling was adequate; Hepatic/Liver: Sampling was adequate; Immune/Hematological: Sampling was adequate; Reproductive/Developmental: Sampling was adequate; Gastrointestinal: Sampling was adequate; Thyroid: Sampling was adequate; Renal/Kidney: Sampling was adequate; Musculoskeletal: Sampling was adequate; Lung/Respiratory: Sampling was adequate; Skin/Connective Tissue: Sampling was adequate; Endocrine (Endocrine): Sampling was adequate

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Study Citation:	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.
Health Outcome(s):	Hepatic/Liver; Cardiovascular; Immune/Hematological; Lung/Respiratory; Skin/Connective Tissue; Gastrointestinal; Renal/Kidney; Thyroid; Endocrine (Endocrine); Reproductive/Developmental; Musculoskeletal; Neurological/Behavioral; Neurological/Behavioral; Hepatic/Liver; Immune/Hematological; Reproductive/Developmental; Gastrointestinal; Thyroid; Renal/Kidney; Musculoskeletal; Lung/Respiratory; Skin/Connective Tissue; Endocrine (Endocrine);
Reported Health Effect(s):	Hepatic/Liver: Liver weight, histopathology, vlinical chemistry (Mice & rats: ALP, GGT, and glutamic pyruvic transaminase; Rats only: bilirubin, cholesterol, triglycerides, BUN, glucose, total protein); Cardiovascular: Heart weight, cholesterol, triglycerides; Immune/Hematological: Organ weight (spleen, thymus), hematology (hgb, hct, RBC, WBC, MCV, platlets, reticulocytes), Histology (thymus, spleen, bone marrow, and lymph node); histopathology (thymus (rats only) & spleen (rats and mice); Lung/Respiratory: Lung weight and histology; Skin/Connective Tissue: Skin histology; Gastrointestinal: Histology of salivary gland, esophagus, stomach, small intestine, large intestine; Renal/Kidney: clinical chemistry (BUN (rats only)), kidney weight, histology; Thyroid: Thyroid histology; Endocrine (Endocrine): Parathyroid, pituitary, pancreas, adrenals histology; Reproductive/Developmental: Organ weight (testis, ovary, uterus); Histology (testis, ovary, uterus); Musculoskeletal: Histologic examination of femur, sternebrae, vertebrae, thigh muscle; Neurological/Behavioral: Brain weight and histology; Neurological/Behavioral: Brain weight and histology; Hepatic/Liver: Liver weight, histopathology, vlinical chemistry (Mice & rats: ALP, GGT, and glutamic pyruvic transaminase; Rats only: bilirubin, cholesterol, triglycerides, BUN, glucose, total protein); Immune/Hematological: Organ weight (spleen, thymus), hematology (hgb, hct, RBC, WBC, MCV, platlets, reticulocytes), Histology (thymus, spleen, bone marrow, and lymph node); histopathology (thymus (rats only) & spleen (rats and mice); Reproductive/Developmental: Organ weight (testis, ovary, uterus); Histology (testis, ovary, uterus); Gastrointestinal: Histology of salivary gland, esophagus, stomach, small intestine, large intestine; Thyroid: Thyroid histology; Renal/Kidney: clinical chemistry (BUN (rats only)), kidney weight, histology; Musculoskeletal: Histologic examination of femur, sternebrae, vertebrae, thigh muscle; Lung/Respiratory: Lung weight and histology; Skin/Connective Tissue: Skin histology; Endocrine (Endocrine): Parathyroid, pituitary, pancreas, adrenals histology;
Duration:	Chronic (>91 days) 2 years Rat
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	1944492

Domain	Metric	Rating	Comments
Metric 19:	Blinding of Assessors	N/A	Hepatic/Liver: Study reported blinding upon re evaluation of histology; Cardiovascular: Blinding was reported for re-evaluation of histology slides; Immune/Hematological: Blinding was reported for re-evaluation of histology slides; Lung/Respiratory: Blinding was reported for re-evaluation of histology slides; Skin/Connective Tissue: Blinding was reported for re-evaluation of histology slides; Gastrointestinal: Blinding was reported for re-evaluation of histology slides; Renal/Kidney: Blinding was reported for re-evaluation of histology slides; Thyroid: Blinding was reported for re-evaluation of histology slides; Endocrine (Endocrine): Blinding was reported for re-evaluation of histology slides; Reproductive/Developmental: Blinding was reported for re-evaluation of histology slides; Musculoskeletal: Blinding was reported for re-evaluation of histology slides; Neurological/Behavioral: Blinding was reported for re-evaluation of histology slides; Neurological/Behavioral: Blinding was reported for re-evaluation of histology slides; Hepatic/Liver: Blinding was reported for re-evaluation of histology slides; Immune/Hematological: Blinding was reported for re-evaluation of histology slides; Reproductive/Developmental: Blinding was reported for re-evaluation of histology slides; Gastrointestinal: Blinding was reported for re-evaluation of histology slides; Thyroid: Blinding was reported for re-evaluation of histology slides; Renal/Kidney: Blinding was reported for re-evaluation of histology slides; Musculoskeletal: Blinding was reported for re-evaluation of histology slides; Lung/Respiratory: Blinding was reported for re-evaluation of histology slides; Skin/Connective Tissue: Blinding was reported for re-evaluation of histology slides; Endocrine (Endocrine): Blinding was reported for re-evaluation of histology slides

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Study Citation:	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.
Health Outcome(s):	Hepatic/Liver; Cardiovascular; Immune/Hematological; Lung/Respiratory; Skin/Connective Tissue; Gastrointestinal; Renal/Kidney; Thyroid; Endocrine (Endocrine); Reproductive/Developmental; Musculoskeletal; Neurological/Behavioral; Neurological/Behavioral; Hepatic/Liver; Immune/Hematological; Reproductive/Developmental; Gastrointestinal; Thyroid; Renal/Kidney; Musculoskeletal; Lung/Respiratory; Skin/Connective Tissue; Endocrine (Endocrine);
Reported Health Effect(s):	Hepatic/Liver: Liver weight, histopathology, vlinical chemistry (Mice & rats: ALP, GGT, and glutamic pyruvic transaminase; Rats only: bilirubin, cholesterol, triglycerides, BUN, glucose, total protein); Cardiovascular: Heart weight, cholesterol, triglycerides; Immune/Hematological: Organ weight (spleen, thymus), hematology (hgb, hct, RBC, WBC, MCV, platlets, reticulocytes), Histology (thymus, spleen, bone marrow, and lymph node); histopathology (thymus (rats only) & spleen (rats and mice); Lung/Respiratory: Lung weight and histology; Skin/Connective Tissue: Skin histology; Gastrointestinal: Histology of salivary gland, esophagus, stomach, small intestine, large intestine; Renal/Kidney: clinical chemistry (BUN (rats only)), kidney weight, histology; Thyroid: Thyroid histology; Endocrine (Endocrine): Parathyroid, pituitary, pancreas, adrenals histology; Reproductive/Developmental: Organ weight (testis, ovary, uterus); Histology (testis, ovary, uterus); Musculoskeletal: Histologic examination of femur, sternebrae, vertebrae, thigh muscle; Neurological/Behavioral: Brain weight and histology; Neurological/Behavioral: Brain weight and histology; Hepatic/Liver: Liver weight, histopathology, vlinical chemistry (Mice & rats: ALP, GGT, and glutamic pyruvic transaminase; Rats only: bilirubin, cholesterol, triglycerides, BUN, glucose, total protein); Immune/Hematological: Organ weight (spleen, thymus), hematology (hgb, hct, RBC, WBC, MCV, platlets, reticulocytes), Histology (thymus, spleen, bone marrow, and lymph node); histopathology (thymus (rats only) & spleen (rats and mice); Reproductive/Developmental: Organ weight (testis, ovary, uterus); Histology (testis, ovary, uterus); Gastrointestinal: Histology of salivary gland, esophagus, stomach, small intestine, large intestine; Thyroid: Thyroid histology; Renal/Kidney: clinical chemistry (BUN (rats only)), kidney weight, histology; Musculoskeletal: Histologic examination of femur, sternebrae, vertebrae, thigh muscle; Lung/Respiratory: Lung weight and histology; Skin/Connective Tissue: Skin histology; Endocrine (Endocrine): Parathyroid, pituitary, pancreas, adrenals histology;
Duration:	Chronic (>91 days) 2 years Rat
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	1944492

Domain	Metric	Rating	Comments
	Metric 20: Negative Control Response	High	All Outcomes: Control animals responded appropriately
Domain 6: Confounding / Variable Control			
	Metric 21: Confounding Variables in Test Design and Procedures	Medium	All Outcomes: Information was incompletely reported but did not identify differences among groups
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Study Citation:	NTP, (1985). Toxicology and Carcinogenesis Studies of 1,2-Dichlorobenzene (o-Dichlorobenzene) (CAS No. 95-50-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies). National Toxicology Program Technical Report Series 255:1-195.
Health Outcome(s):	Hepatic/Liver; Cardiovascular; Immune/Hematological; Lung/Respiratory; Skin/Connective Tissue; Gastrointestinal; Renal/Kidney; Thyroid; Endocrine (Endocrine); Reproductive/Developmental; Musculoskeletal; Neurological/Behavioral; Neurological/Behavioral; Hepatic/Liver; Immune/Hematological; Reproductive/Developmental; Gastrointestinal; Thyroid; Renal/Kidney; Musculoskeletal; Lung/Respiratory; Skin/Connective Tissue; Endocrine (Endocrine);
Reported Health Effect(s):	Hepatic/Liver: Liver weight, histopathology, vlinical chemistry (Mice & rats: ALP, GGT, and glutamic pyruvic transaminase; Rats only: bilirubin, cholesterol, triglycerides, BUN, glucose, total protein); Cardiovascular: Heart weight, cholesterol, triglycerides; Immune/Hematological: Organ weight (spleen, thymus), hematology (hgb, hct, RBC, WBC, MCV, platlets, reticulocytes), Histology (thymus, spleen, bone marrow, and lymph node); histopathology (thymus (rats only) & spleen (rats and mice); Lung/Respiratory: Lung weight and histology; Skin/Connective Tissue: Skin histology; Gastrointestinal: Histology of salivary gland, esophagus, stomach, small intestine, large intestine; Renal/Kidney: clinical chemistry (BUN (rats only)), kidney weight, histology; Thyroid: Thyroid histology; Endocrine (Endocrine): Parathyroid, pituitary, pancreas, adrenals histology; Reproductive/Developmental: Organ weight (testis, ovary, uterus); Histology (testis, ovary, uterus); Musculoskeletal: Histologic examination of femur, sternebrae, vertebrae, thigh muscle; Neurological/Behavioral: Brain weight and histology; Neurological/Behavioral: Brain weight and histology; Hepatic/Liver: Liver weight, histopathology, vlinical chemistry (Mice & rats: ALP, GGT, and glutamic pyruvic transaminase; Rats only: bilirubin, cholesterol, triglycerides, BUN, glucose, total protein); Immune/Hematological: Organ weight (spleen, thymus), hematology (hgb, hct, RBC, WBC, MCV, platlets, reticulocytes), Histology (thymus, spleen, bone marrow, and lymph node); histopathology (thymus (rats only) & spleen (rats and mice); Reproductive/Developmental: Organ weight (testis, ovary, uterus); Histology (testis, ovary, uterus); Gastrointestinal: Histology of salivary gland, esophagus, stomach, small intestine, large intestine; Thyroid: Thyroid histology; Renal/Kidney: clinical chemistry (BUN (rats only)), kidney weight, histology; Musculoskeletal: Histologic examination of femur, sternebrae, vertebrae, thigh muscle; Lung/Respiratory: Lung weight and histology; Skin/Connective Tissue: Skin histology; Endocrine (Endocrine): Parathyroid, pituitary, pancreas, adrenals histology;
Duration:	Chronic (>91 days) 2 years Rat
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	1944492

Domain	Metric	Rating	Comments
Metric 22:	Health Outcomes Unrelated to Exposure	Medium	Hepatic/Liver: Information provided was not sufficient to either support or dismiss the idea that there were differences unrelated to exposure; Cardiovascular: Information provided was not sufficient to either support or dismiss the idea that there were differences unrelated to exposure; Immune/Hematological: Information provided was not sufficient to either support or dismiss the idea that there were differences unrelated to exposure; Lung/Respiratory: Information provided was not sufficient to either support or dismiss the idea that there were differences unrelated to exposure; Skin/Connective Tissue: Information provided was not sufficient to either support or dismiss the idea that there were differences unrelated to exposure; Gastrointestinal: Information provided was not sufficient to either support or dismiss the idea that there were differences unrelated to exposure; Renal/Kidney: Information provided was not sufficient to either support or dismiss the idea that there were differences unrelated to exposure; Thyroid: Information provided was not sufficient to either support or dismiss the idea that there were differences unrelated to exposure; Endocrine (Endocrine): Information provided was not sufficient to either support or dismiss the idea that there were differences unrelated to exposure; Reproductive/Developmental: Information provided was not sufficient to either support or dismiss the idea that there were differences unrelated to exposure; Musculoskeletal: Information provided was not sufficient to either support or dismiss the idea that there were differences unrelated to exposure; Neurological/Behavioral: Information provided was not sufficient to either support or dismiss the idea that there were differences unrelated to exposure; Neurological/Behavioral: Information provided was not sufficient to either support or dismiss the idea that there were differences unrelated to exposure; Hepatic/Liver: Information provided was not sufficient to either support or dismiss the idea that there were differences unrelated to exposure; Immune/Hematological: Information provided was not sufficient to either support or dismiss the idea that there were differences unrelated to exposure; Reproduc-

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Health Outcome(s):	Hepatic/Liver; Cardiovascular; Immune/Hematological; Lung/Respiratory; Skin/Connective Tissue; Gastrointestinal; Renal/Kidney; Thyroid; Endocrine (Endocrine); Reproductive/Developmental; Musculoskeletal; Neurological/Behavioral; Neurological/Behavioral; Hepatic/Liver; Immune/Hematological; Reproductive/Developmental; Gastrointestinal; Thyroid; Renal/Kidney; Musculoskeletal; Lung/Respiratory; Skin/Connective Tissue; Endocrine (Endocrine);
Reported Health Effect(s):	Hepatic/Liver: Liver weight, histopathology, vlinical chemistry (Mice & rats: ALP, GGT, and glutamic pyruvic transaminase; Rats only: bilirubin, cholesterol, triglycerides, BUN, glucose, total protein); Cardiovascular: Heart weight, cholesterol, triglycerides; Immune/Hematological: Organ weight (spleen, thymus), hematology (hgb, hct, RBC, WBC, MCV, platlets, reticulocytes), Histology (thymus, spleen, bone marrow, and lymph node); histopathology (thymus (rats only) & spleen (rats and mice); Lung/Respiratory: Lung weight and histology; Skin/Connective Tissue: Skin histology; Gastrointestinal: Histology of salivary gland, esophagus, stomach, small intestine, large intestine; Renal/Kidney: clinical chemistry (BUN (rats only)), kidney weight, histology; Thyroid: Thyroid histology; Endocrine (Endocrine): Parathyroid, pituitary, pancreas, adrenals histology; Reproductive/Developmental: Organ weight (testis, ovary, uterus); Histology (testis, ovary, uterus); Musculoskeletal: Histologic examination of femur, sternebrae, vertebrae, thigh muscle; Neurological/Behavioral: Brain weight and histology; Neurological/Behavioral: Brain weight and histology; Hepatic/Liver: Liver weight, histopathology, vlinical chemistry (Mice & rats: ALP, GGT, and glutamic pyruvic transaminase; Rats only: bilirubin, cholesterol, triglycerides, BUN, glucose, total protein); Immune/Hematological: Organ weight (spleen, thymus), hematology (hgb, hct, RBC, WBC, MCV, platlets, reticulocytes), Histology (thymus, spleen, bone marrow, and lymph node); histopathology (thymus (rats only) & spleen (rats and mice); Reproductive/Developmental: Organ weight (testis, ovary, uterus); Histology (testis, ovary, uterus); Gastrointestinal: Histology of salivary gland, esophagus, stomach, small intestine, large intestine; Thyroid: Thyroid histology; Renal/Kidney: clinical chemistry (BUN (rats only)), kidney weight, histology; Musculoskeletal: Histologic examination of femur, sternebrae, vertebrae, thigh muscle; Lung/Respiratory: Lung weight and histology; Skin/Connective Tissue: Skin histology; Endocrine (Endocrine): Parathyroid, pituitary, pancreas, adrenals histology;
Duration:	Chronic (>91 days) 2 years Rat
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	1944492

Domain	Metric	Rating	Comments
	Metric 23: Data Presentation and Analysis	High	All Outcomes: Statistical methods were reported and appropriate for the data
	Metric 24: Reporting of Data	High	Hepatic/Liver: Data were reported for all outcomes by group and sex; Cardiovascular: Data were reported for all outcomes by group and sex; Immune/Hematological: Data were reported for all outcomes by group and sex; Lung/Respiratory: Data were reported for all outcomes by group and sex; Skin/Connective Tissue: Data were reported for all outcomes by group and sex; Gastrointestinal: Data were reported for all outcomes by group and sex; Renal/Kidney: Data were reported for all outcomes by group and sex; Thyroid: Data were reported for all outcomes by group and sex; Endocrine (Endocrine): Data were reported for all outcomes by group and sex; Reproductive/Developmental: Data were reported for all outcomes by group and sex; Musculoskeletal: Data were reported for all outcomes by group and sex; Neurological/Behavioral: Data were reported for all outcomes by group and sex; Neurological/Behavioral: Data were reported for all outcomes by group and sex; Hepatic/Liver: Data were reported for all outcomes by group and sex; Immune/Hematological: Data were reported for all outcomes by group and sex; Reproductive/Developmental: Data were reported by group and sex.; Gastrointestinal: Data were reported for all outcomes by group and sex; Thyroid: Data were reported for all outcomes by group and sex; Renal/Kidney: Data were reported for all outcomes by group and sex; Musculoskeletal: Data were reported for all outcomes by group and sex; Lung/Respiratory: Data were reported for all outcomes by group and sex; Skin/Connective Tissue: Data were reported for all outcomes by group and sex; Endocrine (Endocrine): Data were reported for all outcomes by group and sex

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Health Outcome(s):	Hepatic/Liver; Cardiovascular; Immune/Hematological; Lung/Respiratory; Skin/Connective Tissue; Gastrointestinal; Renal/Kidney; Thyroid; Endocrine (Endocrine); Reproductive/Developmental; Musculoskeletal; Neurological/Behavioral; Neurological/Behavioral; Hepatic/Liver; Immune/Hematological; Reproductive/Developmental; Gastrointestinal; Thyroid; Renal/Kidney; Musculoskeletal; Lung/Respiratory; Skin/Connective Tissue; Endocrine (Endocrine);
Reported Health Effect(s):	Hepatic/Liver: Liver weight, histopathology, vlinical chemistry (Mice & rats: ALP, GGT, and glutamic pyruvic transaminase; Rats only: bilirubin, cholesterol, triglycerides, BUN, glucose, total protein); Cardiovascular: Heart weight, cholesterol, triglycerides; Immune/Hematological: Organ weight (spleen, thymus), hematology (hgb, hct, RBC, WBC, MCV, platlets, reticulocytes), Histology (thymus, spleen, bone marrow, and lymph node); histopathology (thymus (rats only) & spleen (rats and mice); Lung/Respiratory: Lung weight and histology; Skin/Connective Tissue: Skin histology; Gastrointestinal: Histology of salivary gland, esophagus, stomach, small intestine, large intestine; Renal/Kidney: clinical chemistry (BUN (rats only)), kidney weight, histology; Thyroid: Thyroid histology; Endocrine (Endocrine): Parathyroid, pituitary, pancreas, adrenals histology; Reproductive/Developmental: Organ weight (testis, ovary, uterus); Histology (testis, ovary, uterus); Musculoskeletal: Histologic examination of femur, sternebrae, vertebrae, thigh muscle; Neurological/Behavioral: Brain weight and histology; Neurological/Behavioral: Brain weight and histology; Hepatic/Liver: Liver weight, histopathology, vlinical chemistry (Mice & rats: ALP, GGT, and glutamic pyruvic transaminase; Rats only: bilirubin, cholesterol, triglycerides, BUN, glucose, total protein); Immune/Hematological: Organ weight (spleen, thymus), hematology (hgb, hct, RBC, WBC, MCV, platlets, reticulocytes), Histology (thymus, spleen, bone marrow, and lymph node); histopathology (thymus (rats only) & spleen (rats and mice); Reproductive/Developmental: Organ weight (testis, ovary, uterus); Histology (testis, ovary, uterus); Gastrointestinal: Histology of salivary gland, esophagus, stomach, small intestine, large intestine; Thyroid: Thyroid histology; Renal/Kidney: clinical chemistry (BUN (rats only)), kidney weight, histology; Musculoskeletal: Histologic examination of femur, sternebrae, vertebrae, thigh muscle; Lung/Respiratory: Lung weight and histology; Skin/Connective Tissue: Skin histology; Endocrine (Endocrine): Parathyroid, pituitary, pancreas, adrenals histology;
Duration:	Chronic (>91 days) 2 years Rat
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	1944492

Domain	Metric	Rating	Comments
Additional Comments:	None		

Overall Quality Determination**High**

Study Citation:	Biodynamics, (1989). An inhalation two-generation reproduction study in rats with orthodichlorobenzene, final report [volume I - V].			
Health Outcome(s):	Mortality; Nutritional/Metabolic; Clinical signs; Reproductive/Developmental; Hepatic/Liver; Renal/Kidney; Neurological/Behavioral; Endocrine;			
Reported Health Effect(s):	Mortality: missing health effects; Nutritional/Metabolic: Body weight and food consumption; Clinical signs: missing health effects; Reproductive/Developmental: Reproductive and developmental parametersLiters examined (pup counts, sexing, pup weights dead/stillborn pups), gross examinationTestes weight, histology on testes, epididymides, seminal vesicles, prostate, vagina, uterus and ovaries; Hepatic/Liver: Liver weight and histology; Renal/Kidney: Kidney weights and histology; Neurological/Behavioral: Brain weight; Endocrine: Histology on pituitary gland;			
Duration:	Reproductive/Developmental 2-generation reproductive/developmental study			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	6331050			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance	Metric 1:	Test Substance Identity	Medium	All Outcomes: Test substance was identified as orthodichlorobenzene (CasRN or nomenclature were not reported).
	Metric 2:	Test Substance Source	High	All Outcomes: The test substance was obtained from Monsanto Company (Sauget, IL) Lot number was provided.
	Metric 3:	Test Substance Purity	High	All Outcomes: Test substance purity was reported to be >99.2%.
Domain 2: Test Design	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Control group animals were exposed to air only in the inhalation chamber.
	Metric 5:	Positive Controls	N/A	All Outcomes: Not applicable for this study.
	Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: Animals were randomly allocated to groups using a computerized sorting procedure.
Domain 3: Exposure Characterization	Metric 7:	Preparation and Storage of Test Substance	High	All Outcomes: Preparation and storage of test substance was adequately reported.
	Metric 8:	Consistency of Exposure Administration	High	All Outcomes: Test substance was administered consistently across study groups
	Metric 9:	Reporting of Doses/Concentrations	High	All Outcomes: Target, analytical and nominal concentrations were all reported without ambiguity.
	Metric 10:	Exposure Frequency and Duration	High	All Outcomes: The exposure frequency and duration were appropriate (6 hours/day).
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: The number of exposure groups and concentration studied were appropriate.
	Metric 12:	Exposure Route and Method	Medium	All Outcomes: A whole-body inhalation chamber was used; the number of air changes was reported to be 2.6-2.8 /minute.
Domain 4: Test Animals	Metric 13:	Test Animal Characteristics	High	All Outcomes: Test animal characteristics were reported without ambiguity.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: Husbandry conditions were sufficiently reported.
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: The number of animals/group was appropriate.

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Study Citation:	Biodynamics, (1989). An inhalation two-generation reproduction study in rats with orthodichlorobenzene, final report [volume I - V].			
Health Outcome(s):	Mortality; Nutritional/Metabolic; Clinical signs; Reproductive/Developmental; Hepatic/Liver; Renal/Kidney; Neurological/Behavioral; Endocrine;			
Reported Health Effect(s):	Mortality: missing health effects; Nutritional/Metabolic: Body weight and food consumption; Clinical signs: missing health effects; Reproductive/Developmental: Reproductive and developmental parametersLiters examined (pup counts, sexing, pup weights dead/stillborn pups), gross examinationTestes weight, histology on testes, epididymides, seminal vesicles, prostate, vagina, uterus and ovaries; Hepatic/Liver: Liver weight and histology; Renal/Kidney: Kidney weights and histology; Neurological/Behavioral: Brain weight; Endocrine: Histology on pituitary gland;			
Duration:	Reproductive/Developmental 2-generation reproductive/developmental study			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	6331050			
Domain	Metric	Rating	Comments	
Domain 5: Outcome Assessment				
Metric 16:	Outcome Assessment Methodology	High	All Outcomes: The outcome assessment methodology was appropriate to address the intended outcomes.	
Metric 17:	Consistency of Outcome Assessment	High	All Outcomes: Details regarding execution of study protocol were sufficient.	
Metric 18:	Sampling Adequacy	High	All Outcomes: Sampling was adequate for outcomes of interest.	
Metric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding was not necessary for outcomes of interest.	
Metric 20:	Negative Control Response	High	All Outcomes: The negative control response was appropriate.	
Domain 6: Confounding / Variable Control				
Metric 21:	Confounding Variables in Test Design and Procedures	Low	All Outcomes: Respiratory rate was not reported and is necessary given that the test substance is a respiratory irritant.	
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.	
Metric 23:	Data Presentation and Analysis	High	All Outcomes: Statistical analysis was appropriate.	
Metric 24:	Reporting of Data	Missing Conf	All Outcomes: Data were fully reported.	
Additional Comments:	None			

Overall Quality Determination**High**

*** 'Missing Conf' indicates that the metric is Acceptable, but the confidence rating is missing. This evaluation needs to be QC'd.

Study Citation:	Dow Chemical, (1982). Orthodichlorobenzene - inhalation teratology study in rats and rabbits with cover letter.			
Health Outcome(s):	Hepatic/Liver; Renal/Kidney; Reproductive/Developmental; Mortality; Nutritional/Metabolic;			
Reported Health Effect(s):	Hepatic/Liver: Maternal liver weights; Renal/Kidney: Maternal kidney weights; Reproductive/Developmental: Fetal developmentnumber and position of fetuses in utero; number of live/dead fetuses; number and position of resorption; number of corpora lutea; sex, body weight and crown-rump length of each fetus and any gross external alterations; Mortality: missing health effects; Nutritional/Metabolic: Body weight; food and water consumption;			
Duration:	Reproductive/Developmental 10-13 days during gestation			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	5305322			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
Metric 1:	Test Substance Identity	Medium	All Outcomes: Test substance was identified as orthodichlorobenzene (CASRN or nomenclature were not reported).	
Metric 2:	Test Substance Source	High	All Outcomes: The test substance was obtained from Standard Chlorine of Delaware, Inc. Lot number was provided.	
Metric 3:	Test Substance Purity	High	All Outcomes: Test substance was reported to be 98.81% pure. Purity was tested before the study began.	
Domain 2: Test Design				
Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Control group animals were exposed to air only in the inhalation chamber.	
Metric 5:	Positive Controls	N/A	All Outcomes: Not applicable for this study.	
Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: Animals were randomly allocated to groups using computer-generated tables of random numbers.	
Domain 3: Exposure Characterization				
Metric 7:	Preparation and Storage of Test Substance	High	All Outcomes: Preparation and storage of test substance was adequately reported.	
Metric 8:	Consistency of Exposure Administration	High	All Outcomes: Test substance was administered consistently across study groups.	
Metric 9:	Reporting of Doses/Concentrations	High	All Outcomes: Target, analytical and nominal concentrations were all reported without ambiguity.	
Metric 10:	Exposure Frequency and Duration	High	All Outcomes: The exposure frequency and duration were appropriate (6 hours/day)	
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: The number of exposure groups and concentration studied were appropriate and justified based on previous reports.	
Metric 12:	Exposure Route and Method	Medium	All Outcomes: Reviewer’s commentsA whole-body inhalation chamber was used; they number of air changes was not reported.	
Domain 4: Test Animals				
Metric 13:	Test Animal Characteristics	Medium	All Outcomes: Age of the animals was not reported.	
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: Husbandry conditions were sufficiently reported.	
Metric 15:	Number of Animals per Group	Medium	All Outcomes: The number of animals/group was appropriate.	
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Study Citation:	Dow Chemical, (1982). Orthodichlorobenzene - inhalation teratology study in rats and rabbits with cover letter.
Health Outcome(s):	Hepatic/Liver; Renal/Kidney; Reproductive/Developmental; Mortality; Nutritional/Metabolic;
Reported Health Effect(s):	Hepatic/Liver: Maternal liver weights; Renal/Kidney: Maternal kidney weights; Reproductive/Developmental: Fetal development number and position of fetuses in utero; number of live/dead fetuses; number and position of resorption; number of corpora lutea; sex, body weight and crown-rump length of each fetus and any gross external alterations; Mortality: missing health effects; Nutritional/Metabolic: Body weight; food and water consumption;
Duration:	Reproductive/Developmental 10-13 days during gestation
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	5305322

Domain	Metric	Rating	Comments
Domain 5: Outcome Assessment			
Metric 16:	Outcome Assessment Methodology	High	All Outcomes: The outcome assessment methodology was appropriate to address the intended outcomes.
Metric 17:	Consistency of Outcome Assessment	High	All Outcomes: Details regarding execution of study protocol were sufficient.
Metric 18:	Sampling Adequacy	High	All Outcomes: Sampling was adequate for outcomes of interest.
Metric 19:	Blinding of Assessors	N/A	All Outcomes: Blinding was not necessary for outcomes of interest.
Metric 20:	Negative Control Response	High	All Outcomes: The negative control response was appropriate.

Domain 6: Confounding / Variable Control			
Metric 21:	Confounding Variables in Test Design and Procedures	Low	All Outcomes: Respiratory rate was not reported and is necessary given that the test substance is a respiratory irritant.
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.
Metric 23:	Data Presentation and Analysis	High	All Outcomes: Statistical analysis was appropriate.
Metric 24:	Reporting of Data	High	All Outcomes: Data were adequately reported.

Additional Comments: None

Overall Quality Determination**High**

*** 'Missing Conf' indicates that the metric is Acceptable, but the confidence rating is missing. This evaluation needs to be QC'd.

Study Citation:	Dow Chemical, (1982). Orthodichlorobenzene - inhalation teratology study in rats and rabbits with cover letter.			
Health Outcome(s):	Clinical signs (Clinical signs)			
Reported Health Effect(s):	Clinical signs (Clinical signs): Clinical signs of toxicity			
Duration:	Reproductive/Developmental 10-13 days during gestation			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	5305322			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
Metric 1:	Test Substance Identity	Medium	Test substance was identified as orthodichlorobenzene (CASRN or nomenclature were not reported).	
Metric 2:	Test Substance Source	High	The test substance was obtained from Standard Chlorine of Delaware, Inc. Lot number was provided.	
Metric 3:	Test Substance Purity	High	Test substance was reported to be 98.81% pure. Purity was tested before the study began.	
Domain 2: Test Design				
Metric 4:	Negative and Vehicle Controls	High	Control group animals were exposed to air only in the inhalation chamber.	
Metric 5:	Positive Controls	N/A	Not applicable for this study.	
Metric 6:	Randomized Allocation of Animals	Medium	Animals were randomly allocated to groups using computer-generated tables of random numbers.	
Domain 3: Exposure Characterization				
Metric 7:	Preparation and Storage of Test Substance	High	Preparation and storage of test substance was adequately reported.	
Metric 8:	Consistency of Exposure Administration	High	Test substance was administered consistently across study groups.	
Metric 9:	Reporting of Doses/Concentrations	High	Target, analytical and nominal concentrations were all reported without ambiguity.	
Metric 10:	Exposure Frequency and Duration	High	The exposure frequency and duration were appropriate (6 hours/day)	
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The number of exposure groups and concentration studied were appropriate and justified based on previous reports.	
Metric 12:	Exposure Route and Method	Medium	Reviewer's commentsA whole-body inhalation chamber was used; they number of air changes was not reported.	
Domain 4: Test Animals				
Metric 13:	Test Animal Characteristics	Medium	Age of the animals was not reported.	
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	Husbandry conditions were sufficiently reported.	
Metric 15:	Number of Animals per Group	Medium	The number of animals/group was appropriate.	
Domain 5: Outcome Assessment				
Metric 16:	Outcome Assessment Methodology	High	The outcome assessment methodology was appropriate to address the intended outcomes.	
Metric 17:	Consistency of Outcome Assessment	High	Details regarding execution of study protocol were sufficient.	
Metric 18:	Sampling Adequacy	High	Sampling was adequate for outcomes of interest.	
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Study Citation:	Dow Chemical, (1982). Orthodichlorobenzene - inhalation teratology study in rats and rabbits with cover letter.			
Health Outcome(s):	Clinical signs (Clinical signs)			
Reported Health Effect(s):	Clinical signs (Clinical signs): Clinical signs of toxicity			
Duration:	Reproductive/Developmental 10-13 days during gestation			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	5305322			
Domain	Metric		Rating	Comments
	Metric 19:	Blinding of Assessors	N/A	Blinding was not necessary for outcomes of interest.
	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	Low	Respiratory rate was not reported and is necessary given that the test substance is a respiratory irritant.
	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 appropriate.
	Metric 24:	Reporting of Data	Low	Data on clinical signs were not adequately reported (incidence data not shown).
Additional Comments: None				
Overall Quality Determination			High	

Study Citation:	Hayes, W. C., Hanley, T. R., Jr, Gushow, T. S., Johnson, K. A., John, J. A. (1985). Teratogenic potential of inhaled dichlorobenzenes in rats and rabbits. Toxicological Sciences 5(1):190-202.			
Health Outcome(s):	Nutritional/Metabolic; Nutritional/Metabolic; Hepatic/Liver; Renal/Kidney; Renal/Kidney; Renal/Kidney; Reproductive/Developmental; Reproduc-			
Reported Health Effect(s):	Nutritional/Metabolic: Maternal Body weight, food and water consumption; Nutritional/Metabolic: Maternal Body weight, food and water consumption; Hepatic/Liver: Maternal Liver weights; Renal/Kidney: Maternal Kidney weight; Renal/Kidney: Maternal Kidney weight; Renal/Kidney: Maternal Kidney weight; Reproductive/Developmental: Number of and position of fetuses in utero; number of live and dead fetuses; number and position of resorption sites; number of corpora lutea; sex and pup body weight; crown-rump length; gross external examinations, soft tissue and skeletal examinations.; Repro-			
Duration:	Reproductive/Developmental GD 6-15			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	503			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1:	Test Substance Identity	High	All Outcomes: The test substance was clearly identified by name, including the specific form.
	Metric 2:	Test Substance Source	High	All Outcomes: A commercial source was provided long with the test substance lot number.
	Metric 3:	Test Substance Purity	High	All Outcomes: The test substance was analyzed for purity by GC prior to the start of the study and reported to be 98.81% pure
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Control animals were exposed to air-only under the same conditions as exposure groups.
	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 randomized using computer-generated tables of random numbers
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and Storage of Test Substance	High	All Outcomes: The methods and equipment used for vapor generation were clearly described and appropriate.
	Metric 8:	Consistency of Exposure Administration	High	All Outcomes: Exposures were consistent across all groups.
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Study Citation:	Hayes, W. C., Hanley, T. R., Jr, Gushow, T. S., Johnson, K. A., John, J. A. (1985). Teratogenic potential of inhaled dichlorobenzenes in rats and rabbits. Toxicological Sciences 5(1):190-202.
Health Outcome(s):	Nutritional/Metabolic; Nutritional/Metabolic; Hepatic/Liver; Renal/Kidney; Renal/Kidney; Renal/Kidney; Reproductive/Developmental; Reproductive/Developmental;
Reported Health Effect(s):	Nutritional/Metabolic: Maternal Body weight, food and water consumption; Nutritional/Metabolic: Maternal Body weight, food and water consumption; Hepatic/Liver: Maternal Liver weights; Renal/Kidney: Maternal Kidney weight; Renal/Kidney: Maternal Kidney weight; Renal/Kidney: Maternal Kidney weight; Reproductive/Developmental: Number of and position of fetuses in utero; number of live and dead fetuses; number and position of resorption sites; number of corpora lutea; sex and pup body weight; crown-rump length; gross external examinations, soft tissue and skeletal examinations.; Reproductive/Developmental: Number of and position of fetuses in utero; number of live and dead fetuses; number and position of resorption sites; number of corpora lutea; sex and pup body weight; crown-rump length; gross external examinations, soft tissue and skeletal examinations.;
Duration:	Reproductive/Developmental GD 6-15
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	503

Domain	Metric	Rating	Comments
	Metric 9: Reporting of Doses/Concentrations	High	Nutritional/Metabolic: Exposure concentrations were clearly reported and were selected based on preliminary probe studies. Analytical measurements were taken, but the data were not provided. The measured mean daily TWA concentrations were within 1% of the intended chamber concentrations.; Nutritional/Metabolic: Exposure concentrations were clearly reported and were selected based on preliminary probe studies. Analytical measurements were taken, but the data were not provided. The study authors indicated that measured mean daily TWA concentrations were within 1% of the intended chamber concentrations.; Hepatic/Liver: Exposure concentrations were clearly reported and were selected based on preliminary probe studies. Analytical measurements were taken, but the data were not provided. The study authors indicated that measured mean daily TWA concentrations were within 1% of the intended chamber concentrations.; Renal/Kidney: Exposure concentrations were clearly reported and were selected based on preliminary probe studies. Analytical measurements were taken, but the data were not provided. The study authors indicated that measured mean daily TWA concentrations were within 1% of the intended chamber concentrations.; Renal/Kidney: Exposure concentrations were clearly reported and were selected based on preliminary probe studies. Analytical measurements were taken, but the data were not provided. The study authors indicated that measured mean daily TWA concentrations were within 1% of the intended chamber concentrations.; Reproductive/Developmental: Exposure concentrations were clearly reported and were selected based on preliminary probe studies. Analytical measurements were taken, but the data were not provided. The study authors indicated that measured mean daily TWA concentrations were within 1% of the intended chamber concentrations.;
	Metric 10: Exposure Frequency and Duration	Low	All Outcomes: The purpose of the study was to evaluate teratogenic effects of exposure, however, animals were only exposed during the window of organogenesis. Therefore, the study may not be acceptable for assessment of implantation effects and skeletal developmental effects. It is however, acceptable for other developmental effects.

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Study Citation:	Hayes, W. C., Hanley, T. R., Jr, Gushow, T. S., Johnson, K. A., John, J. A. (1985). Teratogenic potential of inhaled dichlorobenzenes in rats and rabbits. Toxicological Sciences 5(1):190-202.			
Health Outcome(s):	Nutritional/Metabolic; Nutritional/Metabolic; Hepatic/Liver; Renal/Kidney; Renal/Kidney; Renal/Kidney; Reproductive/Developmental; Reproductive/Developmental;			
Reported Health Effect(s):	Nutritional/Metabolic: Maternal Body weight, food and water consumption; Nutritional/Metabolic: Maternal Body weight, food and water consumption; Hepatic/Liver: Maternal Liver weights; Renal/Kidney: Maternal Kidney weight; Renal/Kidney: Maternal Kidney weight; Renal/Kidney: Maternal Kidney weight; Reproductive/Developmental: Number of and position of fetuses in utero; number of live and dead fetuses; number and position of resorption sites; number of corpora lutea; sex and pup body weight; crown-rump length; gross external examinations, soft tissue and skeletal examinations.; Reproductive/Developmental: Number of and position of fetuses in utero; number of live and dead fetuses; number and position of resorption sites; number of corpora lutea; sex and pup body weight; crown-rump length; gross external examinations, soft tissue and skeletal examinations.;			
Duration:	Reproductive/Developmental GD 6-15			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	503			
Domain	Metric	Rating	Comments	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: The study includes three exposure groups in addition to controls.	
	Metric 12: Exposure Route and Method	Medium	All Outcomes: Animals were exposed, whole body, in a dynamic air chamber to vapor analyte. Based on reported airflow of ~800 L air/min and chamber volume of 4.3 m3, this reviewer calculated 11 air changes per hr	
Domain 4: Test Animals				
	Metric 13: Test Animal Characteristics	Medium	All Outcomes: Strain, species, sex and starting body weights were reported. Age was not exactly specified, but females were adults (sexually mature). The source of animals was not indicated, but the species/strains were appropriate for the study.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: Cages, room temperature, humidity, and photocycle were reported and appropriate. Food and water were available ad libitum except during exposure periods.	
	Metric 15: Number of Animals per Group	Medium	All Outcomes: The number of animals was appropriate giving greater than pregnant females per group.	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	High	All Outcomes: Outcome assessment methodology was clearly reported and appropriate	
	Metric 17: Consistency of Outcome Assessment	High	All Outcomes: The outcome was consistently assessed across study groups.	
	Metric 18: Sampling Adequacy	High	All Outcomes: Adequate sampling was used for the outcome of interest	
	Metric 19: Blinding of Assessors	N/A	Nutritional/Metabolic: Not a subjective outcome; Nutritional/Metabolic: Not a subjective outcome; Hepatic/Liver: Not a subjective outcome; Renal/Kidney: Not a subjective outcome; Renal/Kidney: Not a subjective outcome; Renal/Kidney: Not a subjective outcome; Reproductive/Developmental: This outcome includes both subjective (skeletal and visceral examinations) and non-subjective endpoints; however, blinding is not necessary for initial examinations.; Reproductive/Developmental: This outcome includes both subjective (skeletal and visceral examinations) and non-subjective endpoints; however, blinding is not necessary for initial examinations.	
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Study Citation:	Hayes, W. C., Hanley, T. R., Jr, Gushow, T. S., Johnson, K. A., John, J. A. (1985). Teratogenic potential of inhaled dichlorobenzenes in rats and rabbits. Toxicological Sciences 5(1):190-202.
Health Outcome(s):	Nutritional/Metabolic; Nutritional/Metabolic; Hepatic/Liver; Renal/Kidney; Renal/Kidney; Renal/Kidney; Reproductive/Developmental; Reproductive/Developmental;
Reported Health Effect(s):	Nutritional/Metabolic: Maternal Body weight, food and water consumption; Nutritional/Metabolic: Maternal Body weight, food and water consumption; Hepatic/Liver: Maternal Liver weights; Renal/Kidney: Maternal Kidney weight; Renal/Kidney: Maternal Kidney weight; Renal/Kidney: Maternal Kidney weight; Reproductive/Developmental: Number of and position of fetuses in utero; number of live and dead fetuses; number and position of resorption sites; number of corpora lutea; sex and pup body weight; crown-rump length; gross external examinations, soft tissue and skeletal examinations.; Reproductive/Developmental: Number of and position of fetuses in utero; number of live and dead fetuses; number and position of resorption sites; number of corpora lutea; sex and pup body weight; crown-rump length; gross external examinations, soft tissue and skeletal examinations.;
Duration:	Reproductive/Developmental GD 6-15
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	503

Domain	Metric	Rating	Comments
	Metric 20: Negative Control Response	High	Nutritional/Metabolic: Negative control responses were reported and appropriate; Nutritional/Metabolic: Negative control responses were reported and appropriate; Hepatic/Liver: Negative control responses were reported and appropriate; Renal/Kidney: Negative control responses were reported and appropriate; Renal/Kidney: Negative control responses were reported and appropriate; Renal/Kidney: Negative control responses were reported and appropriate; Reproductive/Developmental: Negative control responses were reported and seem appropriate and were reported to fall within historical values.; Reproductive/Developmental: Negative control responses were reported and seem appropriate and were reported to fall within historical values.
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 (or identified only minor differences) among study groups in the above listed confounding factors.
	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 analysis was performed, appropriate, and adequately described.
	Metric 24: Reporting of Data	High	Nutritional/Metabolic: Data for all exposure groups were adequately reported including means and standard deviations.; Nutritional/Metabolic: Data for all exposure groups were adequately reported including means and standard deviations.; Hepatic/Liver: Data for all exposure groups were adequately reported including means and standard deviations.; Renal/Kidney: Data for all exposure groups were adequately reported including means and standard deviations.; Renal/Kidney: Data for all exposure groups were adequately reported including means and standard deviations.; Renal/Kidney: Data for all exposure groups were adequately reported including means and standard deviations.; Reproductive/Developmental: Data for all exposure groups were adequately reported; Reproductive/Developmental: Data for all exposure groups were adequately reported

Additional Comments: None

Overall Quality Determination**High**

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Study Citation:	Hayes, W. C., Hanley, T. R., Jr, Gushow, T. S., Johnson, K. A., John, J. A. (1985). Teratogenic potential of inhaled dichlorobenzenes in rats and rabbits. Toxicological Sciences 5(1):190-202.		
Health Outcome(s):	Nutritional/Metabolic; Nutritional/Metabolic; Hepatic/Liver; Renal/Kidney; Renal/Kidney; Renal/Kidney; Reproductive/Developmental; Reproductive/Developmental;		
Reported Health Effect(s):	Nutritional/Metabolic: Maternal Body weight, food and water consumption; Nutritional/Metabolic: Maternal Body weight, food and water consumption; Hepatic/Liver: Maternal Liver weights; Renal/Kidney: Maternal Kidney weight; Renal/Kidney: Maternal Kidney weight; Renal/Kidney: Maternal Kidney weight; Reproductive/Developmental: Number of and position of fetuses in utero; number of live and dead fetuses; number and position of resorption sites; number of corpora lutea; sex and pup body weight; crown-rump length; gross external examinations, soft tissue and skeletal examinations.; Reproductive/Developmental: Number of and position of fetuses in utero; number of live and dead fetuses; number and position of resorption sites; number of corpora lutea; sex and pup body weight; crown-rump length; gross external examinations, soft tissue and skeletal examinations.;		
Duration:	Reproductive/Developmental GD 6-15		
Chemical:	o-Dichlorobenzene- Parent compound		
HERO ID:	503		
Domain	Metric	Rating	Comments

Study Citation:	Hayes, W. C., Hanley, T. R., Jr, Gushow, T. S., Johnson, K. A., John, J. A. (1985). Teratogenic potential of inhaled dichlorobenzenes in rats and rabbits. Toxicological Sciences 5(1):190-202.			
Health Outcome(s):	Mortality; Mortality;			
Reported Health Effect(s):	Mortality: No treatment-related maternal deaths were reported in rabbits or rats. Only one rabbit in 300 ppm exposure group died due to non-treatment related effect.; Mortality: No treatment-related maternal deaths were reported in rabbits or rats. Only one rabbit in 300 ppm exposure group died due to non-treatment related effect.;			
Duration:	Reproductive/Developmental GD6-18			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	503			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
Metric 1:	Test Substance Identity	High	All Outcomes: The test substance was clearly identified by name, including the specific form.	
Metric 2:	Test Substance Source	High	All Outcomes: A commercial source was provided long with the test substance lot number.	
Metric 3:	Test Substance Purity	High	Mortality: The test substance was analyzed for purity by GC prior to the start of the study and reported to be 99.9% pure; Mortality: The test substance was analyzed for purity by GC prior to the start of the study and reported to be 98.81% pure	
Domain 2: Test Design				
Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Control animals were exposed to air-only under the same conditions as exposure groups.	
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 randomized using computer-generated tables of random numbers	
Domain 3: Exposure Characterization				
Metric 7:	Preparation and Storage of Test Substance	High	All Outcomes: The methods and equipment used for vapor generation were clearly described and appropriate.	
Metric 8:	Consistency of Exposure Administration	High	All Outcomes: Exposures were consistent across all groups.	
Metric 9:	Reporting of Doses/Concentrations	High	Mortality: Exposure concentrations were clearly reported and were selected based on preliminary probe studies. Analytical measurements were taken, but the data were not provided. The study authors indicated that measured mean daily TWA concentrations were within 3% of the intended chamber concentrations.; Mortality: Exposure concentrations were clearly reported and were selected based on preliminary probe studies. Analytical measurements were taken, but the data were not provided. The study authors indicated that measured mean daily TWA concentrations were within 1% of the intended chamber concentrations.	
Metric 10:	Exposure Frequency and Duration	Low	All Outcomes: The purpose of the study was to evaluate teratogenic effects of exposure, however, animals were only exposed during the window of organogenesis. Therefore, the study may not be acceptable for assessment of implantation effects and skeletal developmental effects. It is however, acceptable for other developmental effects.	
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: The study includes three exposure groups in addition to controls.	
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Study Citation:	Hayes, W. C., Hanley, T. R., Jr, Gushow, T. S., Johnson, K. A., John, J. A. (1985). Teratogenic potential of inhaled dichlorobenzenes in rats and rabbits. Toxicological Sciences 5(1):190-202.			
Health Outcome(s):	Mortality; Mortality;			
Reported Health Effect(s):	Mortality: No treatment-related maternal deaths were reported in rabbits or rats. Only one rabbit in 300 ppm exposure group died due to non-treatment related effect.; Mortality: No treatment-related maternal deaths were reported in rabbits or rats. Only one rabbit in 300 ppm exposure group died due to non-treatment related effect.;			
Duration:	Reproductive/Developmental GD6-18			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	503			
Domain	Metric	Rating	Comments	
	Metric 12:	Exposure Route and Method	Medium	All Outcomes: Animals were exposed, whole body, in a dynamic air chamber to vapor analyte. Based on reported airflow of ~800 L air/min and chamber volume of 4.3 m3, this reviewer calculated 11 air changes per hr
Domain 4: Test Animals	Metric 13:	Test Animal Characteristics	Medium	All Outcomes: Strain, species, sex and starting body weights were reported. Age was not exactly specified, but females were adults (sexually mature). The source of animals was not indicated, but the species/strains were appropriate for the study.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: Cages, room temperature, humidity, and photocycle were reported and appropriate. Food and water were available ad libitum except during exposure periods.
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: The number of animals was appropriate giving greater than pregnant females per group.
Domain 5: Outcome Assessment	Metric 16:	Outcome Assessment Methodology	Medium	All Outcomes: Limited details were provided for the outcome assessment methodology "Animals were observed daily throughout the exposure period and recorded"
	Metric 17:	Consistency of Outcome Assessment	Medium	All Outcomes: The frequency, timing, and types of observations were not indicated; consistency across groups was not specified.
	Metric 18:	Sampling Adequacy	Low	All Outcomes: The number of animals sampled/group is not reported; however, it is assumed that all animals were observed for clinical signs.
	Metric 19:	Blinding of Assessors	N/A	All Outcomes: Not necessary for the outcome of interest.
	Metric 20:	Negative Control Response	High	All Outcomes: No deaths were observed in the control group
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 (or identified only minor differences) among study groups in the above listed confounding factors.
	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	All Outcomes: Statistical analyses were adequately described and applied when appropriate
	Metric 24:	Reporting of Data	High	All Outcomes: Incidences were adequately reported.
Additional Comments:	None			

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Study Citation:	Hayes, W. C., Hanley, T. R., Jr, Gushow, T. S., Johnson, K. A., John, J. A. (1985). Teratogenic potential of inhaled dichlorobenzenes in rats and rabbits. Toxicological Sciences 5(1):190-202.
Health Outcome(s):	Mortality; Mortality;
Reported Health Effect(s):	Mortality: No treatment-related maternal deaths were reported in rabbits or rats. Only one rabbit in 300 ppm exposure group died due to non-treatment related effect.; Mortality: No treatment-related maternal deaths were reported in rabbits or rats. Only one rabbit in 300 ppm exposure group died due to non-treatment related effect.;
Duration:	Reproductive/Developmental GD6-18
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	503

Domain	Metric	Rating	Comments
Overall Quality Determination		High	

Study Citation:	Hayes, W. C., Hanley, T. R., Jr, Gushow, T. S., Johnson, K. A., John, J. A. (1985). Teratogenic potential of inhaled dichlorobenzenes in rats and rabbits. Toxicological Sciences 5(1):190-202.			
Health Outcome(s):	Neurological/Behavioral (clinical signs observations); Neurological/Behavioral (clinical signs);			
Reported Health Effect(s):	Neurological/Behavioral (clinical signs observations): Cage-side observations/clinical signs; Neurological/Behavioral (clinical signs): Cage-side observations/clinical signs;			
Duration:	Reproductive/Developmental GD 6-15			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	503			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
Metric 1:	Test Substance Identity	High	All Outcomes: The test substance was clearly identified by name, including the specific form.	
Metric 2:	Test Substance Source	High	All Outcomes: A commercial source was provided long with the test substance lot number.	
Metric 3:	Test Substance Purity	High	All Outcomes: The test substance was analyzed for purity by GC prior to the start of the study and reported to be 98.81% pure	
Domain 2: Test Design				
Metric 4:	Negative and Vehicle Controls	High	All Outcomes: Control animals were exposed to air-only under the same conditions as exposure groups.	
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 randomized using computer-generated tables of random numbers	
Domain 3: Exposure Characterization				
Metric 7:	Preparation and Storage of Test Substance	High	All Outcomes: The methods and equipment used for vapor generation were clearly described and appropriate.	
Metric 8:	Consistency of Exposure Administration	High	All Outcomes: Exposures were consistent across all groups.	
Metric 9:	Reporting of Doses/Concentrations	High	Neurological/Behavioral (clinical signs observations): Exposure concentrations were clearly reported and were selected based on preliminary probe studies. Analytical measurements were taken, but the data were not provided. The measured mean daily TWA concentrations were within 1% of the intended chamber concentrations.; Neurological/Behavioral (clinical signs): Exposure concentrations were clearly reported and were selected based on preliminary probe studies. Analytical measurements were taken, but the data were not provided. The mean daily TWA concentrations were within 1% of the intended chamber concentrations.	
Metric 10:	Exposure Frequency and Duration	Low	All Outcomes: The purpose of the study was to evaluate teratogenic effects of exposure, however, animals were only exposed during the window of organogenesis. Therefore, the study may not be acceptable for assessment of implantation effects and skeletal developmental effects. It is however, acceptable for other developmental effects.	
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: The study includes three exposure groups in addition to controls.	

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Study Citation:	Hayes, W. C., Hanley, T. R., Jr, Gushow, T. S., Johnson, K. A., John, J. A. (1985). Teratogenic potential of inhaled dichlorobenzenes in rats and rabbits. Toxicological Sciences 5(1):190-202.			
Health Outcome(s):	Neurological/Behavioral (clinical signs observations); Neurological/Behavioral (clinical signs);			
Reported Health Effect(s):	Neurological/Behavioral (clinical signs observations): Cage-side observations/clinical signs; Neurological/Behavioral (clinical signs): Cage-side observations/clinical signs;			
Duration:	Reproductive/Developmental GD 6-15			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	503			
Domain		Metric	Rating	Comments
	Metric 12:	Exposure Route and Method	Medium	Neurological/Behavioral (clinical signs observations): Animals were exposed, whole body, in a dynamic air chamber to vapor analyte. Based on reported airflow of ~800 L air/min and chamber volume of 4.3 m3, this reviewer calculated 11 air changes per hr.; Neurological/Behavioral (clinical signs): Animals were exposed, whole body, in a dynamic air chamber to vapor analyte. Based on reported airflow of ~800 L air/min and chamber volume of 4.3 m3, this reviewer calculated 11 air changes per hr
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	Medium	All Outcomes: Strain, species, sex and starting body weights were reported. Age was not exactly specified, but females were adults (sexually mature). The source of animals was not indicated, but the species/strains were appropriate for the study.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: Cages, room temperature, humidity, and photocycle were reported and appropriate. Food and water were available ad libitum except during exposure periods.
	Metric 15:	Number of Animals per Group	Medium	All Outcomes: The number of animals was appropriate giving greater than pregnant females per group.
Domain 5: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	Medium	All Outcomes: Limited details were provided for the outcome assessment methodology "Animals were observed daily throughout the exposure period and recorded"
	Metric 17:	Consistency of Outcome Assessment	Medium	All Outcomes: The frequency, timing, and types of observations were not indicated; consistency across groups was not specified.
	Metric 18:	Sampling Adequacy	Low	All Outcomes: The number of animals sampled/group is not reported; however, it is assumed that all animals were observed for clinical signs.
	Metric 19:	Blinding of Assessors	Low	All Outcomes: The study did not report whether assessors were blinded to treatment group for subjective outcomes (observations of clinical signs)
	Metric 20:	Negative Control Response	High	Neurological/Behavioral (clinical signs observations): The biological responses for the negative controls were adequate.; Neurological/Behavioral (clinical signs): 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 (or identified only minor differences) among study groups in the above listed confounding factors.
	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.
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Study Citation:	Hayes, W. C., Hanley, T. R., Jr, Gushow, T. S., Johnson, K. A., John, J. A. (1985). Teratogenic potential of inhaled dichlorobenzenes in rats and rabbits. Toxicological Sciences 5(1):190-202.			
Health Outcome(s):	Neurological/Behavioral (clinical signs observations); Neurological/Behavioral (clinical signs);			
Reported Health Effect(s):	Neurological/Behavioral (clinical signs observations): Cage-side observations/clinical signs; Neurological/Behavioral (clinical signs): Cage-side observations/clinical signs;			
Duration:	Reproductive/Developmental GD 6-15			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	503			
Domain	Metric	Rating	Comments	
	Metric 23: Data Presentation and Analysis	N/A	Neurological/Behavioral (clinical signs observations): Statistical methods were not needed, because of low incidence of observed adverse clinical signs of toxicity.; Neurological/Behavioral (clinical signs): Statistical methods were not needed, under assumption that there were no clinical signs of toxicity to report in rabbits. Study protocol indicates that animals were observed daily throughout the experimental period for indications of toxicity from the test material and adverse effects from exposure were recorded.	
	Metric 24: Reporting of Data	Low	Neurological/Behavioral (clinical signs observations): The incidences for a single observation (urine soaking of the perineal area) were reported for the high exposure group only. No incidences for controls were reported, and there was no statement indicating that the control incidence may be zero; therefore, the (statistical) significance of the finding cannot be determined. Other changes in gross appearance or demeanor were reported to be not related to exposure concentration, but the data were not provided for independent review.It can be assumed that there were no other clinical signs of toxicity to report given that the study protocol indicates that animals were observed daily throughout the experimental period for indications of toxicity from the test material and adverse effects from exposure were recorded.; Neurological/Behavioral (clinical signs): No adverse clinical signs results were described, under assumption by reader that there were no deviations. For instance, all other maternal observations were summarized and tabulated and protocol indicates that animals were observed daily throughout the experimental period for indications of toxicity from the test material and adverse effects from exposure were recorded.	
Additional Comments: None				

Overall Quality Determination**Uninformative**

Study Citation:	Hoglen, N. C., Younis, H. S., Hartley, D. P., Gunawardhana, L., Lantz, R. C., Sipes, I. G. (1998). 1,2-dichlorobenzene-induced lipid peroxidation in male Fischer 344 rats is Kupffer cell dependent. Toxicological Sciences 46(2):376-385.			
Health Outcome(s):	Hepatic/Liver			
Reported Health Effect(s):	Hepatic/Liver: Formation of lipid peroxidation markers (4-HNE protein adducts) and conjugated diene formation.			
Duration:	Mechanistic-Other single ip injection			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	3058574			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
Metric 1:	Test Substance Identity	Medium	Test substance was identified by nomenclature as 1,2-dichlorobenzene (1,2-DCB).	
Metric 2:	Test Substance Source	Low	The source of the chemical was reported to be Aldrich Chemical Company but the chemical batch/lot number were not provided and the chemical identify was not ana-	
Metric 3:	Test Substance Purity	Low	lytically verified by the performing lab.	
The purity and/or grade of test substance was not reported.				
Domain 2: Test Design				
Metric 4:	Negative and Vehicle Controls	High	Authors indicate that an appropriate negative control (vehicle = corn oil) was used.	
Metric 5:	Positive Controls	N/A	Positive control was not indicated by the study.	
Metric 6:	Randomized Allocation of Animals	Low	The study did not report how animals were allocated to study groups.	
Domain 3: Exposure Characterization				
Metric 7:	Preparation and Storage of Test Substance	Medium	Authors do not provide details on how the test substance was prepared or stored. How-	
Metric 8:	Consistency of Exposure Administration	Low	ever, this is a short-term study using a single injection exposure, therefore storage is unlikely to affect results.	
Metric 9:	Reporting of Doses/Concentrations	High	Some details of exposure administration (including timing and volume of injection) are insufficiently reported.	
Metric 10:	Exposure Frequency and Duration	High	Administered dose was clearly stated as 3.6 mmol/kg.	
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	N/A	A single injection exposure is appropriate for the mechanistic endpoints evaluated in this study.	
Metric 12:	Exposure Route and Method	High	This mechanistic study was not designed to provide dose-response information. The dose was selected based on previous studies that determined 1,2-DCB to cause moderate hepatocellular necrosis after 24 h of exposure.	
I.p. injection is a suitable administration method for volatile substances.				
Domain 4: Test Animals				
Metric 13:	Test Animal Characteristics	Medium	Animal species, strain, sex, source, and starting body weight were reported, but the life-	
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	Medium	stage was not reported. This is unlikely to have a substantial impact on results.	
The rats were housed in an AAALAC-approved animal facility and all were exposed to hanging wire cages and a 12h light/dark cycle. The animals received the same food (Teklad 4%) and water ad libitum. The study does not report how many animals were in each cage or temperature/humidity conditions.				

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Study Citation:	Hoglen, N. C., Younis, H. S., Hartley, D. P., Gunawardhana, L., Lantz, R. C., Sipes, I. G. (1998). 1,2-dichlorobenzene-induced lipid peroxidation in male Fischer 344 rats is Kupffer cell dependent. Toxicological Sciences 46(2):376-385.			
Health Outcome(s):	Hepatic/Liver			
Reported Health Effect(s):	Hepatic/Liver: Formation of lipid peroxidation markers (4-HNE protein adducts) and conjugated diene formation.			
Duration:	Mechanistic-Other single ip injection			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	3058574			
Domain	Metric	Rating	Comments	
	Metric 15:	Number of Animals per Group	Low	The study reports a variable number of rats per timepoint (4-8), but numbers were sufficient for statistical analysis.
Domain 5: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	High	The methods were appropriate.
	Metric 17:	Consistency of Outcome Assessment	High	Outcome assessment protocol details were reported and there is no indication of differences in outcome evaluation across treatment 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	Outcomes assessed were not subjective, so blinding was not necessary.
	Metric 20:	Negative Control Response	High	No unusual responses were identified in negative control group.
Domain 6: Confounding / Variable Control				
	Metric 21:	Confounding Variables in Test Design and Procedures	Medium	While the information provided in the study did not indicate confounding, limited details were provided on potential sources of confounding.
	Metric 22:	Health Outcomes Unrelated to Exposure	Medium	There was no information 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. The number of rats in each group ranged between 4 and 8, but there was no clarity as to why the numbers varied or if there was animal loss before duration was completed.
	Metric 23:	Data Presentation and Analysis	High	Results are written as the mean ± the standard error of the mean (SE). Statistical comparisons are either a one or two-way analysis of variance, followed by Newman-Keuls post hoc test.
	Metric 24:	Reporting of Data	Medium	Endpoints for conjugated diene formation in liver and serum and ALT activities mostly included. No data were reported for 48hr conjugated diene formation in liver or 3hr conjugated diene formation in serum.

Additional Comments: None

Overall Quality Determination**Medium**

Study Citation:	HealthCare., Bayer (2009). o-Dichlorobenzol: Local lymph node assay in mice (LLNA/IMDS).		
Health Outcome(s):	Nutritional/Metabolic; Sensitization;		
Reported Health Effect(s):	Nutritional/Metabolic: Body weight; Sensitization: Skin sensitization; modified LLNA (lymph node weight and cell count), ear thickness, ear weight;		
Duration:	Other (specify) 3-day skin sensitization		
Chemical:	o-Dichlorobenzene- Parent compound		
HERO ID:	13006582		
Domain	Metric	Rating	Comments
Domain 1: Test Substance			
Metric 1:	Test Substance Identity	High	All Outcomes: The test substance was identified as 1,2-dichlorobenzene (CASRN 95-50-1). The study also referred to the test substance as o-Dichlorobenzene.
Metric 2:	Test Substance Source	High	All Outcomes: The source and batch/lot number were provided. The test substance was not analytically verified by the performing laboratory.
Metric 3:	Test Substance Purity	High	All Outcomes: The test substance purity was reported to be 99.9%.
Domain 2: Test Design			
Metric 4:	Negative and Vehicle Controls	High	All Outcomes: An appropriate negative control group was included (vehicle; acetone/olive oil [4:1]).
Metric 5:	Positive Controls	Medium	All Outcomes: Positive controls were not concurrently run, but the laboratory has experience with this assay and checks the reliability of the assay at regular intervals.
Metric 6:	Randomized Allocation of Animals	Low	All Outcomes: The study does not report how animals were allocated to study groups.
Domain 3: Exposure Characterization			
Metric 7:	Preparation and Storage of Test Substance	Medium	All Outcomes: The storage of the test substance was reported. The test item was formulated once (on the first day of exposure). Details were not provided. The study authors state the formulations were “visually described as solutions”. The stability of a 1% and 50% solution was analytically verified after 2 hours and 4 days.
Metric 8:	Consistency of Exposure Administration	High	All Outcomes: Details of exposure administration were reported. Animals were exposed consistently across study groups.
Metric 9:	Reporting of Doses/Concentrations	Medium	All Outcomes: Nominal doses were reported (2, 10, 50% solution). The volume applied and animal body weights were reported.
Metric 10:	Exposure Frequency and Duration	Medium	All Outcomes: Exposure frequency and duration were slightly modified from OECD 429 guidelines. The test substance was applied for 3 consecutive days, on the 4-day the animals were sacrificed, and ear thickness and lymph nodes were assessed. Guidelines expose animals for 3 consecutive days and assess proliferation (via 3H-thymidine) on day 6. The study authors justify the modification from the guidance.
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: Three concentrations plus a control were studied. A positive response was obtained from the highest dose.
Metric 12:	Exposure Route and Method	Medium	All Outcomes: The exposure route and method were appropriate. 25ul of the test solution was applied to the ear.
Domain 4: Test Animals			
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Study Citation:	HealthCare., Bayer (2009). o-Dichlorobenzol: Local lymph node assay in mice (LLNA/IMDS).			
Health Outcome(s):	Nutritional/Metabolic; Sensitization;			
Reported Health Effect(s):	Nutritional/Metabolic: Body weight; Sensitization: Skin sensitization; modified LLNA (lymph node weight and cell count), ear thickness, ear weight;			
Duration:	Other (specify) 3-day skin sensitization			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	13006582			
Domain	Metric	Rating	Comments	
	Metric 13: Test Animal Characteristics	High	All Outcomes: The test species, strain, age, sex, initial body weight and source were reported, and the test model was adequate.	
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	High	All Outcomes: All animal husbandry conditions (temperature, humidity, light cycle, food and water availability) were reported and consistent across groups. The number of animals per cage was specified.	
	Metric 15: Number of Animals per Group	Medium	All Outcomes: The number of animals per group was reported and appropriate for the study type (6/group); OECD 429 recommends at least 4/group.	
Domain 5: Outcome Assessment				
	Metric 16: Outcome Assessment Methodology	High	All Outcomes: Outcome assessment methods were adequately described and were sensitive to the outcomes of interest.	
	Metric 17: Consistency of Outcome Assessment	High	All Outcomes: Outcomes were consistently assessed across groups.	
	Metric 18: Sampling Adequacy	High	All Outcomes: Sampling was adequate for the outcomes of interest; all animals were accounted for.	
	Metric 19: Blinding of Assessors	N/A	All Outcomes: Blinding was not reported; however, blinding is not required for the outcomes of interest.	
	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: The study does not report any information on skin irritation at the application site. Clinical signs 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 analysis was described and appropriate.	
	Metric 24: Reporting of Data	High	All Outcomes: Data are fully reported with mean +/- SD and/or individual animal data.	
Additional Comments:	None			

Overall Quality Determination**High**

Study Citation:	Hollingsworth, R. L., Rowe, V. K., Oyen, F., Torkelson, T. R., Adams, E. M. (1958). Toxicity of o-dichlorobenzene: Studies on animals and industrial experience. AMA Archives of Industrial Health 17(3):180-187.			
Health Outcome(s):	all studies (Eye irritation: eye irritation.)			
Reported Health Effect(s):	all studies (Eye irritation: eye irritation.): Acute inhalation - Lethality experiments: Mortality; "gross response" (drowsiness, unsteadiness, eye irritation, difficulty breathing, anaesthesia); weight loss.Acute inhalation - Organ injury experiments: Organ weights (liver, kidney), gross and microscopic examinations (liver and kidney).Inhalation Chronic experiments: Mortality, observations of gross appearance and behavior, growth/body weights, organ weights (lungs, heart, liver, kidney, spleen, testes), hematology (rabbits and monkeys), urine tests (blood, sugar, albumin, sediment in females), serum BUN (female guinea pig and rabbits), gross and microscopic examinations. Acute oral: mortality, body weight gain.Oral chronic: mortality, body weights, organ weights (heart, liver, kidney, spleen), gross and microscopic examinations.Eye irritation: eye irritation.			
Duration:	Other (specify) Eye irritation			
Chemical:	o-Dichlorobenzene- Parent compound			
HERO ID:	2962108			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1: Test Substance Identity	High	The test substance was identified by name as o-dichlorobenzene. Physical chemical properties were provided. A CASRN was not reported.	
	Metric 2: Test Substance Source	Low	The original source was not described; the test substance was a re-distillation of a commercial product and was not analytically verified by the performing laboratory.	
	Metric 3: Test Substance Purity	High	The purity was ≥99% based on physical properties	
Domain 2: Test Design				
	Metric 4: Negative and Vehicle Controls	Low	Typically, one eye is left unexposed, acting as a negative control. This study exposed both eyes. The test substance was applied neat.	
	Metric 5: Positive Controls	N/A	Positive controls are not required for the study type	
	Metric 6: Randomized Allocation of Animals	Low	The study did not report how animals were allocated into study groups.	
Domain 3: Exposure Characterization				
	Metric 7: Preparation and Storage of Test Substance	Medium	Storage of the test substance was not reported. No preparation was required. The test substance was delivered undiluted.	
	Metric 8: Consistency of Exposure Administration	Low	Each animal received "two drops" of the test substance into the eye. It is unclear if the volume/size of the drops was consistent. Placement in the eye (e.g., into the conjunctival sac) was not specified.	
	Metric 9: Reporting of Doses/Concentrations	Low	The dose volume was not reported; typically, 0.1 mL is used.	
	Metric 10: Exposure Frequency and Duration	High	Animals received a single instillation, which is consistent with the study type.	
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	High	The study included a single (neat) exposure group. This is an appropriate initial dose level for the study type.	
	Metric 12: Exposure Route and Method	Low	The study indicated that the test substance was "introduced into both eyes;" the specific method and location (e.g., instillation into the conjunctival sac) were not described. One eye was washed after 30 seconds for about 2 minutes; the other eye remained unwashed. OECD guidelines specify that eyes should not be washed for at least 24 hrs.	
Domain 4: Test Animals				
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Study Citation:	Hollingsworth, R. L., Rowe, V. K., Oyen, F., Torkelson, T. R., Adams, E. M. (1958). Toxicity of o-dichlorobenzene: Studies on animals and industrial experience. AMA Archives of Industrial Health 17(3):180-187.
Health Outcome(s):	all studies (Eye irritation: eye irritation.)
Reported Health Effect(s):	all studies (Eye irritation: eye irritation.): Acute inhalation - Lethality experiments: Mortality; "gross response" (drowsiness, unsteadiness, eye irritation, difficulty breathing, anaesthesia); weight loss.Acute inhalation - Organ injury experiments: Organ weights (liver, kidney), gross and microscopic examinations (liver and kidney).Inhalation Chronic experiments: Mortality, observations of gross appearance and behavior, growth/body weights, organ weights (lungs, heart, liver, kidney, spleen, testes), hematology (rabbits and monkeys), urine tests (blood, sugar, albumin, sediment in females), serum BUN (female guinea pig and rabbits), gross and microscopic examinations. Acute oral: mortality, body weight gain.Oral chronic: mortality, body weights, organ weights (heart, liver, kidney, spleen), gross and microscopic examinations.Eye irritation: eye irritation.
Duration:	Other (specify) Eye irritation
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	2962108

Domain	Metric	Rating	Comments
	Metric 13: Test Animal Characteristics	Low	Details were provided in a citation (Spencer et al. 1951). The animals (rabbits) were from in-house colonies.Strains, sex, initial body weights, and age were not reported, but the animal model is appropriate for the study type. Prior to the start of the study, rabbits' eyes were examined using fluorescein to ensure they were normal.
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Low	Husbandry conditions were not sufficiently reported.
	Metric 15: Number of Animals per Group	Medium	The study used two animals. This is appropriate for the study type.
Domain 5: Outcome Assessment			
	Metric 16: Outcome Assessment Methodology	Low	Eyes were examined immediately after washing and then at 2, 24, 48, and 168 hours. Current guidelines also specify examinations at 72 hrs. Examinations were done before and after staining with a 5% solution of fluorescein in water. Scoring criteria (e.g., Draize) were not specified.
	Metric 17: Consistency of Outcome Assessment	High	The protocol description suggests that animals were examined consistently.
	Metric 18: Sampling Adequacy	High	Based on the information provided, both animals were examined.
	Metric 19: Blinding of Assessors	Low	Blinding is not mentioned in OECD TG 405; however, it is mentioned that the grading of ocular responses is necessarily subjective and that persons conducting the examinations should be adequately trained. Blinding or qualifications were not mentioned in the study report.
	Metric 20: Negative Control Response	N/A	Controls were not included.
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 (or identified only minor differences) among study groups in the above listed confounding factors.
	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	Typically, an irritation score is calculated based on the grade assigned to several end-points in individual animals, but statistical analysis is not required.

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Study Citation:	Hollingsworth, R. L., Rowe, V. K., Oyen, F., Torkelson, T. R., Adams, E. M. (1958). Toxicity of o-dichlorobenzene: Studies on animals and industrial experience. AMA Archives of Industrial Health 17(3):180-187.
Health Outcome(s):	all studies (Eye irritation: eye irritation.)
Reported Health Effect(s):	all studies (Eye irritation: eye irritation.): Acute inhalation - Lethality experiments: Mortality; "gross response" (drowsiness, unsteadiness, eye irritation, difficulty breathing, anaesthesia); weight loss.Acute inhalation - Organ injury experiments: Organ weights (liver, kidney), gross and microscopic examinations (liver and kidney).Inhalation Chronic experiments: Mortality, observations of gross appearance and behavior, growth/body weights, organ weights (lungs, heart, liver, kidney, spleen, testes), hematology (rabbits and monkeys), urine tests (blood, sugar, albumin, sediment in females), serum BUN (female guinea pig and rabbits), gross and microscopic examinations. Acute oral: mortality, body weight gain.Oral chronic: mortality, body weights, organ weights (heart, liver, kidney, spleen), gross and microscopic examinations.Eye irritation: eye irritation.
Duration:	Other (specify) Eye irritation
Chemical:	o-Dichlorobenzene- Parent compound
HERO ID:	2962108

Domain	Metric	Rating	Comments
Metric 24:	Reporting of Data	Low	Irritation scores were not reported. Responses for each group were qualitatively described in detail, including the timing and description of a response, if any, and time to reversal. Based on the descriptions, the test substance was an eye irritant, but without irritation scores, it cannot be determined whether it meets GHS classification.

Additional Comments: None

Overall Quality Determination**Low**

Study Citation:	Mohtashamipur, E., Triebel, R., Straeter, H., Norpoth, K. (1987). The bone marrow clastogenicity of eight halogenated benzenes in male NMRI mice. <i>Mutagenesis</i> 2(2):111-113.
Health Outcome(s):	Mortality
Reported Health Effect(s):	Mortality: LD50 values
Duration:	Acute (less than or equal to 24 hr) 1 or 2 doses within 24 hrs
Chemical:	o-Dichlorobenzene- Isomer: m-dichlorobenzene
HERO ID:	201693

Domain	Metric	Rating	Comments
Domain 1: Test Substance			
	Metric 1: Test Substance Identity	High	Test substance is clearly identified by name (isoform specified)
	Metric 2: Test Substance Source	Low	The test substance was commercially obtained. A batch or lot number were not provided.
	Metric 3: Test Substance Purity	High	Synthetic grade, purity 99%
Domain 2: Test Design			
	Metric 4: Negative and Vehicle Controls	N/A	Negative controls are not required for acute toxicity studies
	Metric 5: Positive Controls	N/A	Not required for study type
	Metric 6: Randomized Allocation of Animals	Low	Allocation of animals was not specified
Domain 3: Exposure Characterization			
	Metric 7: Preparation and Storage of Test Substance	Medium	There are limited details on preparation and storage of the test substance, but these are unlikely to have a substantial impact on results.
	Metric 8: Consistency of Exposure Administration	Low	Details of exposure administration were not reported (cited to other publications). These publications were not available for review. Injection volumes were not reported.
	Metric 9: Reporting of Doses/Concentrations	Low	Doses were not reported. It is unclear if the LD50 value reported was one of the dose groups, or if it was a calculated LD50 value. However, the main purpose of the acute study was to determine the LD50 value, and that is provided.
	Metric 10: Exposure Frequency and Duration	High	Single dose acute toxicity study
	Metric 11: Number of Exposure Groups and Dose/Concentration Spacing	N/A	Not applicable to an acute toxicity study
	Metric 12: Exposure Route and Method	High	Animals were dosed i.p., this is a PECO relevant route of exposure
Domain 4: Test Animals			
	Metric 13: Test Animal Characteristics	Medium	Animal species, strain, sex, age, and source were provided. Initial body weights were not reported.
	Metric 14: Adequacy and Consistency of Animal Husbandry Conditions	Low	All animal husbandry conditions were not reported. It was only specified that animals were housed 5/cage with free access to food and water; no other details were provided. This is unlikely to have a major impact on an acute study.
	Metric 15: Number of Animals per Group	Low	It was reported that 25-30 mice were used, but it is unclear if these mice were split between chemicals tested, or if that was the number per group.

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Study Citation:	Mohtashamipur, E., Triebel, R., Straeter, H., Norpoth, K. (1987). The bone marrow clastogenicity of eight halogenated benzenes in male NMRI mice. <i>Mutagenesis</i> 2(2):111-113.
Health Outcome(s):	Mortality
Reported Health Effect(s):	Mortality: LD50 values
Duration:	Acute (less than or equal to 24 hr) 1 or 2 doses within 24 hrs
Chemical:	o-Dichlorobenzene- Isomer: m-dichlorobenzene
HERO ID:	201693

Domain	Metric	Rating	Comments
Domain 5: Outcome Assessment			
	Metric 16: Outcome Assessment Methodology	Low	The outcome assessment methodology was not reported (e.g., how long animals were monitored for mortality post-dosing).
	Metric 17: Consistency of Outcome Assessment	Low	Details regarding the execution of the study protocol for outcome assessment (e.g., timing of assessment across groups) were not reported, and these deficiencies are likely to have a substantial impact on results.
	Metric 18: Sampling Adequacy	Low	Details regarding sampling of outcomes were not reported
	Metric 19: Blinding of Assessors	N/A	not necessary for this outcome of interest
	Metric 20: Negative Control Response	N/A	Not applicable for the 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 (or identified only minor differences) among study groups in the above listed confounding factors.
	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	not necessary for the outcome of interest
	Metric 24: Reporting of Data	Medium	LD50 values were reported, but it is not specified how many mortalities were observed.
Additional Comments: The form 3's for the mortality outcome are identical for all three isomers.			

Overall Quality Determination**Medium**

Study Citation:	Umemura, T., Saito, M., Takagi, A., Kurokawa, Y. (1996). Isomer-specific acute toxicity and cell proliferation in livers of B6C3F1 mice exposed to dichlorobenzene. Toxicology and Applied Pharmacology 137(2):268-274.			
Health Outcome(s):	Hepatic/Liver			
Reported Health Effect(s):	Hepatic/Liver: DCB induced hepatocyte cell proliferation and ALT activity in spite of the lack of manifest hepatotoxicity.			
Duration:	Short-term (>1-30 days) 1-7 Day Hepatic toxicity study			
Chemical:	o-Dichlorobenzene- Isomer: m-dichlorobenzene			
HERO ID:	4912371			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1:	Test Substance Identity	Medium	Document identifies test substances used in study. But no casrns were provided
	Metric 2:	Test Substance Source	High	The manufacturer source of the test substances was stated in material and methods.
	Metric 3:	Test Substance Purity	High	Test substance purity is >98% as stated in materials and methods.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	Each endpoint has a control group in this study. Corn oil is given as negative control
	Metric 5:	Positive Controls	N/A	Positive controls were not needed in this study.
	Metric 6:	Randomized Allocation of Animals	Low	No mention of randomization of animals.
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and Storage of Test Substance	Medium	Each test substance was dissolved in corn oil at a concentration of 5% (w/v).
	Metric 8:	Consistency of Exposure	High	Administration was consistent across each endpoint measured.
	Metric 9:	Administration Reporting of Doses/Concentrations	High	Doses and concentrations were labelled on graphs and stated in text clearly.
	Metric 10:	Exposure Frequency and Duration	High	One time dosing and endpoints measured over the course of the week.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The number of dose groups and dose spacing were justified and toxicity was seen with these doses.
	Metric 12:	Exposure Route and Method	High	Exposure route and methods were appropriate for this study.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	High	There was sufficient information on the test animals including where they came from, age, etc.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	Appropriate animal husbandry conditions were stated in materials and methods.
	Metric 15:	Number of Animals per Group	Medium	5 animals was sufficient for statistical analysis for this short-term study.
Domain 5: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	High	Assessment methodology was sensitive and appropriate for the outcomes of interest.
	Metric 17:	Consistency of Outcome Assessment	High	Outcome of this study was consistent across groups and experiments.
	Metric 18:	Sampling Adequacy	High	Sampling in this study was adequate.
	Metric 19:	Blinding of Assessors	N/A	Blinding of assessors was not required for this study as there was histopathology.

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Study Citation:	Umemura, T., Saito, M., Takagi, A., Kurokawa, Y. (1996). Isomer-specific acute toxicity and cell proliferation in livers of B6C3F1 mice exposed to dichlorobenzene. Toxicology and Applied Pharmacology 137(2):268-274.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	Hepatic/Liver: DCB induced hepatocyte cell proliferation and ALT activity in spite of the lack of manifest hepatotoxicity.
Duration:	Short-term (>1-30 days) 1-7 Day Hepatic toxicity study
Chemical:	o-Dichlorobenzene- Isomer: m-dichlorobenzene
HERO ID:	4912371

Domain	Metric	Rating	Comments
	Metric 20: Negative Control Response	High	Negative control response is appropriate in this study.

Domain 6: Confounding / Variable Control

Metric 21:	Confounding Variables in Test Design and Procedures	High	No confounding variables in this study.
Metric 22:	Health Outcomes Unrelated to Exposure	High	No deleterious effects in the control groups.
Metric 23:	Data Presentation and Analysis	High	Statistical analysis was explained properly and is appropriate for this study.
Metric 24:	Reporting of Data	High	Reporting of data was sufficient and all information was given.

Additional Comments: None

Overall Quality Determination**High**

Study Citation:	Umemura, T., Saito, M., Takagi, A., Kurokawa, Y. (1996). Isomer-specific acute toxicity and cell proliferation in livers of B6C3F1 mice exposed to dichlorobenzene. Toxicology and Applied Pharmacology 137(2):268-274.			
Health Outcome(s):	Hepatic/Liver			
Reported Health Effect(s):	Hepatic/Liver: DCB induced hepatocyte cell proliferation and ALT activity in spite of the lack of manifest hepatotoxicity.			
Duration:	Short-term (>1-30 days) 1-7 Day Hepatic toxicity study			
Chemical:	o-Dichlorobenzene- Isomer: o-dichlorobenzene			
HERO ID:	4912371			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
	Metric 1:	Test Substance Identity	Medium	Document identifies test substances used in study. But no casrns were provided
	Metric 2:	Test Substance Source	High	The manufacturer source of the test substances was stated in material and methods.
	Metric 3:	Test Substance Purity	High	Test substance purity is >98% as stated in materials and methods.
Domain 2: Test Design				
	Metric 4:	Negative and Vehicle Controls	High	Each endpoint has a control group in this study. Corn oil is given as negative control
	Metric 5:	Positive Controls	N/A	Positive controls were not needed in this study.
	Metric 6:	Randomized Allocation of Animals	Low	No mention of randomization of animals.
Domain 3: Exposure Characterization				
	Metric 7:	Preparation and Storage of Test Substance	Medium	Each test substance was dissolved in corn oil at a concentration of 5% (w/v).
	Metric 8:	Consistency of Exposure Administration	High	Administration was consistent across each endpoint measured.
	Metric 9:	Reporting of Doses/Concentrations	High	Doses and concentrations were labelled on graphs and stated in text clearly.
	Metric 10:	Exposure Frequency and Duration	High	One time dosing and endpoints measured over the course of the week.
	Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	The number of dose groups and dose spacing were justified and toxicity was seen with these doses.
	Metric 12:	Exposure Route and Method	High	Exposure route and methods were appropriate for this study.
Domain 4: Test Animals				
	Metric 13:	Test Animal Characteristics	High	There was sufficient information on the test animals including where they came from, age, etc.
	Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	Appropriate animal husbandry conditions were stated in materials and methods.
	Metric 15:	Number of Animals per Group	Medium	5 animals was sufficient for statistical analysis for this short-term study.
Domain 5: Outcome Assessment				
	Metric 16:	Outcome Assessment Methodology	High	Assessment methodology was sensitive and appropriate for the outcomes of interest.
	Metric 17:	Consistency of Outcome Assessment	High	Outcome of this study was consistent across groups and experiments.
	Metric 18:	Sampling Adequacy	High	Sampling in this study was adequate.
	Metric 19:	Blinding of Assessors	N/A	Blinding of assessors was not required for this study as there was histopathology.

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Study Citation:	Umemura, T., Saito, M., Takagi, A., Kurokawa, Y. (1996). Isomer-specific acute toxicity and cell proliferation in livers of B6C3F1 mice exposed to dichlorobenzene. Toxicology and Applied Pharmacology 137(2):268-274.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	Hepatic/Liver: DCB induced hepatocyte cell proliferation and ALT activity in spite of the lack of manifest hepatotoxicity.
Duration:	Short-term (>1-30 days) 1-7 Day Hepatic toxicity study
Chemical:	o-Dichlorobenzene- Isomer: o-dichlorobenzene
HERO ID:	4912371

Domain	Metric	Rating	Comments
	Metric 20: Negative Control Response	High	Negative control response is appropriate in this study.

Domain 6: Confounding / Variable Control

Metric 21:	Confounding Variables in Test Design and Procedures	High	No confounding variables in this study.
Metric 22:	Health Outcomes Unrelated to Exposure	High	No deleterious effects in the control groups.
Metric 23:	Data Presentation and Analysis	High	Statistical analysis was explained properly and is appropriate for this study.
Metric 24:	Reporting of Data	High	Reporting of data was sufficient and all information was given.

Additional Comments: None

Overall Quality Determination**High**

Study Citation:	Allis, J. W., Simmons, J. E., House, D. E., Robinson, B. L., Berman, E. (1992). The differential hepatotoxicity and cytochrome P450 responses of Fischer-344 rats to the three isomers of dichlorobenzene. Journal of Biochemical Toxicology 7(4):257-264.			
Health Outcome(s):	Hepatic/Liver			
Reported Health Effect(s):	Hepatic/Liver: Increased serum AST and ALT levels, and centrilobular hepatic necrosis.			
Duration:	Acute (less than or equal to 24 hr) 24 hours			
Chemical:	o-Dichlorobenzene- Isomer: ortho-DCB			
HERO ID:	4930708			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
Metric 1:	Test Substance Identity	High	Missing Comment	
Metric 2:	Test Substance Source	High	Missing Comment	
Metric 3:	Test Substance Purity	Low	No information on purity of test substances.	
Domain 2: Test Design				
Metric 4:	Negative and Vehicle Controls	High	Missing Comment	
Metric 5:	Positive Controls	N/A	No need for positive controls in this study.	
Metric 6:	Randomized Allocation of Animals	Low	No randomized allocation of animals stated in study.	
Domain 3: Exposure Characterization				
Metric 7:	Preparation and Storage of Test Substance	High	Missing Comment	
Metric 8:	Consistency of Exposure Administration	High	Missing Comment	
Metric 9:	Reporting of Doses/Concentrations	High	Missing Comment	
Metric 10:	Exposure Frequency and Duration	High	Missing Comment	
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	Missing Comment	
Metric 12:	Exposure Route and Method	High	Missing Comment	
Domain 4: Test Animals				
Metric 13:	Test Animal Characteristics	High	Missing Comment	
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	Missing Comment	
Metric 15:	Number of Animals per Group	Low	Number of animals per dose is only 1, but sufficient for statistics.	
Domain 5: Outcome Assessment				
Metric 16:	Outcome Assessment Methodology	High	Missing Comment	
Metric 17:	Consistency of Outcome Assessment	High	Missing Comment	
Metric 18:	Sampling Adequacy	High	Missing Comment	
Metric 19:	Blinding of Assessors	N/A	Blinding of assessors is not necessary since it is only one animal per dose.	
Metric 20:	Negative Control Response	High	Missing Comment	

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Study Citation:	Allis, J. W., Simmons, J. E., House, D. E., Robinson, B. L., Berman, E. (1992). The differential hepatotoxicity and cytochrome P450 responses of Fischer-344 rats to the three isomers of dichlorobenzene. Journal of Biochemical Toxicology 7(4):257-264.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	Hepatic/Liver: Increased serum AST and ALT levels, and centrilobular hepatic necrosis.
Duration:	Acute (less than or equal to 24 hr) 24 hours
Chemical:	o-Dichlorobenzene- Isomer: ortho-DCB
HERO ID:	4930708

Domain	Metric	Rating	Comments
Domain 6: Confounding / Variable Control			
	Metric 21: Confounding Variables in Test Design and Procedures	High	Missing Comment
	Metric 22: Health Outcomes Unrelated to Exposure	High	Missing Comment
	Metric 23: Data Presentation and Analysis	High	Missing Comment
	Metric 24: Reporting of Data	High	Missing Comment

Additional Comments: None

Overall Quality Determination**High**

Study Citation:	Stine, E. R., Gunawardhana, L., Sipes, I. G. (1991). The acute hepatotoxicity of the isomers of dichlorobenzene in Fischer-344 and Sprague-Dawley rats: Isomer-specific and strain-specific differential toxicity. Toxicology and Applied Pharmacology 109(3):472-481.		
Health Outcome(s):	Hepatic/Liver		
Reported Health Effect(s):	Hepatic/Liver: Hepatotoxicity		
Duration:	Acute (less than or equal to 24 hr) Acute (single exposure) toxicity study		
Chemical:	o-Dichlorobenzene- Isomer: MISSING ISOMER NEED TO FIX		
HERO ID:	4933243		
Domain	Metric	Rating	Comments
Domain 1: Test Substance			
Metric 1:	Test Substance Identity	Medium	Missing Comment
Metric 2:	Test Substance Source	High	Missing Comment
Metric 3:	Test Substance Purity	High	Missing Comment
Domain 2: Test Design			
Metric 4:	Negative and Vehicle Controls	High	Missing Comment
Metric 5:	Positive Controls	N/A	Missing Comment
Metric 6:	Randomized Allocation of Animals	Medium	Missing Comment
Domain 3: Exposure Characterization			
Metric 7:	Preparation and Storage of Test Substance	High	Missing Comment
Metric 8:	Consistency of Exposure Administration	Medium	Missing Comment
Metric 9:	Reporting of Doses/Concentrations	High	Missing Comment
Metric 10:	Exposure Frequency and Duration	High	Missing Comment
Metric 11:	Number of Exposure Groups and Dose/Concentration Spacing	High	Missing Comment
Metric 12:	Exposure Route and Method	High	Missing Comment
Domain 4: Test Animals			
Metric 13:	Test Animal Characteristics	High	Missing Comment
Metric 14:	Adequacy and Consistency of Animal Husbandry Conditions	High	Missing Comment
Metric 15:	Number of Animals per Group	Medium	Missing Comment
Domain 5: Outcome Assessment			
Metric 16:	Outcome Assessment Methodology	High	Missing Comment
Metric 17:	Consistency of Outcome Assessment	High	Missing Comment
Metric 18:	Sampling Adequacy	Medium	Missing Comment
Metric 19:	Blinding of Assessors	Low	Missing Comment
Metric 20:	Negative Control Response	High	Missing Comment

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Study Citation:	Stine, E. R., Gunawardhana, L., Sipes, I. G. (1991). The acute hepatotoxicity of the isomers of dichlorobenzene in Fischer-344 and Sprague-Dawley rats: Isomer-specific and strain-specific differential toxicity. Toxicology and Applied Pharmacology 109(3):472-481.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	Hepatic/Liver: Hepatotoxicity
Duration:	Acute (less than or equal to 24 hr) Acute (single exposure) toxicity study
Chemical:	o-Dichlorobenzene- Isomer: MISSING ISOMER NEED TO FIX
HERO ID:	4933243

Domain	Metric	Rating	Comments
Domain 6: Confounding / Variable Control			
Metric 21:	Confounding Variables in Test Design and Procedures	High	Missing Comment
Metric 22:	Health Outcomes Unrelated to Exposure	High	Missing Comment
Metric 23:	Data Presentation and Analysis	High	Missing Comment
Metric 24:	Reporting of Data	High	Missing Comment

Additional Comments: None

Overall Quality Determination**High**

Study Citation:	Biodynamics, (1987). Primary dermal irritation study in rabbits (4- and 24-hour exposure) of dichlorobenzene waste.			
Health Outcome(s):	Irritation; Irritation;			
Reported Health Effect(s):	Irritation: Dermal irritation, edema, erythema, necrosis, and eschar.; Irritation: Dermal irritation, edema, erythema, necrosis, and eschar.;			
Duration:	Acute (less than or equal to 24 hr) 4h			
Chemical:	o-Dichlorobenzene- Mixture: Dichlorobenzene Waste			
HERO ID:	5278523			
Domain	Metric	Rating	Comments	
Domain 1: Test Substance				
Metric 1:	Test Substance Identity	Low	All Outcomes: Test Substance was identified along with Lot# and origin. But no CASRN was provided, neither the ratio of mixtures	
Metric 2:	Test Substance Source	High	All Outcomes: Source of test substance was identified.	
Metric 3:	Test Substance Purity	Low	All Outcomes: Purity of test substance was not reported. Its a waste and the ratio of the mixtures were not given	
Domain 2: Test Design				
Metric 4:	Negative and Vehicle Controls	N/A	All Outcomes: Skin irritation study does not need a control.	
Metric 5:	Positive Controls	N/A	All Outcomes: No positive controls needed for this study.	
Metric 6:	Randomized Allocation of Animals	Medium	All Outcomes: Animals were randomly placed in cages	
Domain 3: Exposure Characterization				
Metric 7:	Preparation and Storage of Test Substance	Medium	All Outcomes: Storage of substance was not identified. It came as a mixture. Black tars- The test substance storage is not important as the test substance is directly applied to the skin.	
Metric 8:	Consistency of Exposure	High	All Outcomes: All animals received the same exposure, just different time points.	
Metric 9:	Administration	High	All Outcomes: This study reported how much they used on the animals.	
Metric 10:	Reporting of Doses/Concentrations	High	All Outcomes: All rabbits were administered the same dose and each group were measured at their specific time points.	
Metric 11:	Exposure Frequency and Duration	High	All Outcomes: The number of exposure groups was explained in the study.	
Metric 12:	Number of Exposure Groups and Dose/Concentration Spacing	High	All Outcomes: Justification of exposure route was explained in this study.	
Domain 4: Test Animals				
Metric 13:	Exposure Route and Method	High	All Outcomes: Animal characteristics were noted in this study (breed, sex, age).	
Metric 14:	Test Animal Characteristics	High	All Outcomes: Animal husbandry was adequately explained in this study.	
Metric 15:	Adequacy and Consistency of Animal Husbandry Conditions	N/A	All Outcomes: This was an acute study finding out any toxic effects on the skin.	
Domain 5: Outcome Assessment				
Metric 16:	Number of Animals per Group	High	All Outcomes: The intended outcome of interest and the assessment methodology was sensitive and appropriate for the study.	
	Outcome Assessment Methodology	High	All Outcomes: The intended outcome of interest and the assessment methodology was sensitive and appropriate for the study.	

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Study Citation:	Biodynamics, (1987). Primary dermal irritation study in rabbits (4- and 24-hour exposure) of dichlorobenzene waste.			
Health Outcome(s):	Irritation; Irritation;			
Reported Health Effect(s):	Irritation: Dermal irritation, edema, erythema, necrosis, and eschar.; Irritation: Dermal irritation, edema, erythema, necrosis, and eschar.;			
Duration:	Acute (less than or equal to 24 hr) 4h			
Chemical:	o-Dichlorobenzene- Mixture: Dichlorobenzene Waste			
HERO ID:	5278523			
Domain	Metric	Rating	Comments	
	Metric 17: Consistency of Outcome Assessment	High	All Outcomes: The outcome of this study was consistent.	
	Metric 18: Sampling Adequacy	High	All Outcomes: For this type of study, the number of animals per group was sufficient for this type of study.	
	Metric 19: Blinding of Assessors	N/A	All Outcomes: Assessors did not need to be blinded for this study.	
	Metric 20: Negative Control Response	N/A	All Outcomes: There was no control, given this is a skin irritation study.	
Domain 6: Confounding / Variable Control				
	Metric 21: Confounding Variables in Test Design and Procedures	High	All Outcomes: The study reported all information to determine whether confounding bias may exist.	
	Metric 22: Health Outcomes Unrelated to Exposure	High	All Outcomes: No adverse health outcomes reported following study.	
	Metric 23: Data Presentation and Analysis	Low	All Outcomes: This was a qualitative study; however, there were no reports of using statistics.	
	Metric 24: Reporting of Data	High	All Outcomes: Data for all outcomes was presented.	
Additional Comments:	None			
Overall Quality Determination		High		