

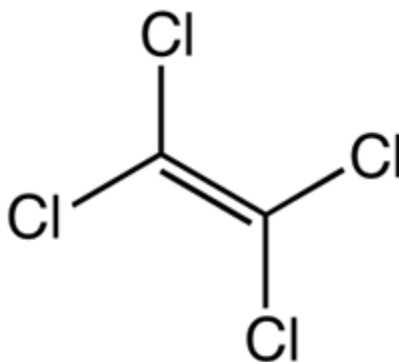


Final Risk Evaluation for Perchloroethylene

Systematic Review Supplemental File:

Data Extraction for Human Health Hazard Studies

CASRN: 127-18-4



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1 Data extraction of studies considered for dose-response assessment

The tables below present data summaries of animal and epidemiological studies considered for dose-response assessment, as described in Section 3.2.5 of the Risk Evaluation. Studies that were excluded due to an Unacceptable or Low data quality score are not included. The presented effect doses/concentrations are values reported by the study authors and do not necessarily represent the PODs used for risk estimation.

Table 1.1. Summary of the epidemiologic database considered for dose-response assessment

Target Organ/ System	Outcome/ Endpoint	Study Population	Exposure	Results	Reference	Data Quality Evaluation
Neurological/ Behavior	Sensory nervous system function, visual and auditory evoked potentials	22 healthy male volunteers with a mean age of 26.5 years, ranging 23 to 35 years of age, participated in a study conducted in former Federal Republic of Germany	Exposure in inhalation chamber to 10 ppm and 50 ppm perchloroethylene, maintained during a period of 4d for 4h daily	Statistically significant mild change in visual function (visually evoked potentials) but no change in transmission of auditory impulse (brainstem auditory evoked potentials)	(Altmann et al., 1990)	Medium
Renal	Urinary TP, Alb, B2M, RBP, TRF, IgG, THG, GAGs, BB50, HF5, BBA, PGE2, TXB, PGF1alpha, PGF2alpha, IAP, TNAP, NAG, and FNU;; serum creatinine, AGBM, B2M, LAM	50 workers in dry-cleaning shops (9 men and 41 women, 17-65 years old) and 50 blood donors (9 men and 41 women, 17-63 years old), Europe (country not specified), date not provided	Blood and air Perc in dry-cleaning workers exposed for 10 years	Significant increase in frequency of abnormal levels in Perc-exposed subjects for urinary albumin, Beta-2-microglobulins, retinol-binding proteins, transferrin, immunoglobulin G, Tamm-Horsfall glycoproteins, glycosaminoglycans, brush-border antigens, and for serum laminin fragments.	(Mutti et al. 1992)	Medium

Target Organ/ System	Outcome/ Endpoint	Study Population	Exposure	Results	Reference	Data Quality Evaluation
Neurological/ Behavior	Pattern memory (Number correct)	'Dry Cleaner Study Population' (n=65). men and women; Detroit , USA	Perchloroethylene. Cumulative lifetime exposure levels based on complete work histories, hobbies, and industrial hygiene evaluations of subjects in participating shops:. Categories: low (n=24, average 3.4 years at shop), moderate (n=18,average 8.1 years at shop), and high (n=23, average 20.2 years at shop).	Significant decrease (6.7%) was observed in the adjusted mean performance on the pattern memory (number correct) between the low and high Perc exposure categories.	(Echeverria et al. 1995)	Medium
Neurological/ Behavior	Color confusion index (CCI)	35 exposed dry-cleaners and ironers (33 females, 2 males) in Modena, Italy; 35 unexposed controls	Perchloroethylene (Perc) occupational, 8 hr time- weighted average (TWA) mean airborne concentrations: all workers (6.23 ppm), dry- cleaners (7.27 ppm), ironers (4.80 ppm)	A statistically significant increase in mean color confusion index was observed for Perc exposed workers and in dry- cleaners specifically, compared to unexposed controls Non-significant differences were observed in the mean color confusion index for Perc- exposed ironers compared to unexposed controls. A statistically significant correlation was observed between perc exposure and color confusion index among exposed workers.	(Cavalleri et al 1994)	Medium

<p>Hematological and Immune</p>	<p>Multiple hematological and immune measures</p>	<p>40 exposed male dry- cleaning employees (20 with smoking history; 20 non-smokers); 40 controls from same city (20 smokers; 20 non-smokers); Tanta city, Egypt</p>	<p>Perchloroethylene vapor concentration measured with Kitagawa detection tubes (5 determinations/workshop)</p>	<p>Increased IgE, total WBC, total lymphocytic counts, T lymphocytes (CD4+, CD8+), natural killer (CD3+ CD16CD56+) cells, B (CD19+) lymphocytes</p> <p>No difference in eosinophils, monocytes, platelets, CD3+ lymphocyte subpopulations, interferon-gamma</p>	<p>(Emara et al., 2010)</p>	<p>High</p>
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Table 1.2 Summary of the animal toxicological database considered for dose-response assessment

Target Organ/System	Study Type	Species/ Strain/ Sex (Number/ group)	Exposure Route	Doses/ Concentrations	Duration	Cancer Incidence	Effect	Reference	Data Quality Evaluation
Cancer	Chronic	Rat, Fischer, M/ F (n= 100/ group)	Inhalation, vapor, whole body	0, 339, 1356, or 4069 mg/ m ³ (0, 50, 200, or 600 ppm)	6 hours/ day, 5 days/ week for 104 weeks	600 ppm: 1/ 50 (F) and none in males	Renal cell carcinoma	(JISA, 1993)	High
Cancer	Chronic	Rat, Fischer, M/ F (n= 100/ group)	Inhalation, vapor, whole body	0, 339, 1356, or 4069 mg/ m ³ (0, 50, 200, or 600 ppm)	6 hours/ day, 5 days/ week for 104 weeks	control: 1/ 50, 50 ppm: 2/ 50, 200 ppm: 1/ 50, 600 ppm: 2/ 50 (M), only one control female	Renal cell adenoma	(JISA, 1993)	High
Cancer	Chronic	Mouse, Crj: BDF1, M/ F (n = 100/ group)	Inhalation, vapor, whole body	0, 68, 339, or 1696 mg/ m ³ (0, 10, 50, or 250 ppm)	6 hours/ day, 5 days/ week for 104 weeks	50 ppm: 1/ 50 (M) and none in exposed female mice	Renal cell adenoma	(JISA, 1993)	High
Cancer	Chronic	Mouse, Crj: BDF1, M/ F (n = 100/ group)	Inhalation, vapor, whole body	0, 68, 339, or 1696 mg/ m ³ (0, 10, 50, or 250 ppm)	6 hours/ day, 5 days/ week for 104 weeks	50 ppm: 1/ 50 (M) and none in exposed female mice	Renal cell carcinoma	(JISA, 1993)	High

Target Organ/System	Study Type	Species/ Strain/ Sex (Number/ group)	Exposure Route	Doses/ Concentrations	Duration	Cancer Incidence	Effect	Reference	Data Quality Evaluation
Cancer	Chronic	Rat, F344/ N, M/ F (n=100/ group)	Inhalation, vapor, whole body	0, 1356, or 2713 mg/ m3 (0, 200 or 400 ppm)	103 weeks	control: 0/ 49; low dose: 3/ 49; high dose:5/ 50 (M) and in one high-dose female rat	Tubal cell hyperplasia	(NTP, 1986)	High
Cancer	Chronic	Rat, F344/ N, M/ F (n=100/ group)	Inhalation, vapor, whole body	0, 678, or 1356 mg/ m3(0, 100 or 200 ppm)	103 weeks	control: 1/ 49; low dose: 3/ 49; high dose: 4/ 50 (M)	Renal tubule adenomas and adenocarcinomas	(NTP, 1986)	High
Cancer	Chronic	Mouse, B6C3F1, M/ F (n=98-100/ group)	Inhalation, vapor, whole body	mg/ m3 (0, 100 or 200 ppm)	103 weeks	1 low-dose male mouse	Renal tubule adenocarcinoma	(NTP, 1986)	High
Hepatic	Chronic	Rat, F344/ DuCrj, M/ F (n=100/ group)	Inhalation, vapor, whole body	0, 339, 1356, or 4069 mg/ m3 (0, 50, 200 or 600 ppm)	6 hours/ day, 5 days/ week for 104 weeks (sacrificed at 110 weeks)	LOAEL= 1356 mg/ m3 (M), spongiosis LOAEL = 4069 mg/ m3 (M), hyperplasia	Spongiosis hepatitis and hyperplasia	(JISA, 1993)	High
Hepatic	Chronic	Mouse, Crj/ BDF1, M/ F (n=100/ group)	Inhalation, vapor, whole body	0, 68, 339, or 1696 mg/ m3 mg/ m3 (0, 10, 50 or 250 ppm)	6 hours/ day, 5 days/ week for 104 weeks (sacrificed at 110 weeks)	LOAEL= 339 mg/ m3 (M) LOAEL = 1696 mg/ m3 (F)	Focal necrosis liver degeneration	(JISA, 1993)	High
Renal	Chronic	Rat, F344/ DuCrj , M/ F (n=100/ group)	Inhalation, vapor, whole body	0, 339, 1356, or 4069 mg/ m3 (0, 50, 200 or 600 ppm)	6 hours/ day, 5 days/ week for 104 weeks	LOAEL= 1356 mg/ m3 (M/ F), increased relative kidney	Increased relative kidney weights and karyomegaly in the proximal; atypical	(JISA, 1993)	High

Target Organ/System	Study Type	Species/ Strain/ Sex (Number/ group)	Exposure Route	Doses/ Concentrations	Duration	Cancer Incidence	Effect	Reference	Data Quality Evaluation
					(sacrificed at 110 weeks)	weights and karyomegaly in the proximal tubules LOAEL = 4069 mg/ m3 (M/ F), atypical tubular dilation LOAEL = 4069 mg/ m3 (M), exacerbation of chronic renal disease	tubular dilation; exacerbation of chronic renal disease		

Target Organ/System	Study Type	Species/ Strain/ Sex (Number/ group)	Exposure Route	Doses/ Concentrations	Duration	Cancer Incidence	Effect	Reference	Data Quality Evaluation
Renal	Chronic	Mouse, Crj/ BDF1, M/ F (n=100/ group)	Inhalation, vapor, whole body	0, 68, 166, Or 1696 mg/ m3 (0, 10, 50 or 250 ppm)	6 hours/ day, 5 days/ week for 104 weeks (sacrificed at 110 weeks)	LOAEL= 1696 mg/ m3 (M/ F), relative kidney weight, karyomegaly in the proximal tubules, and atypical tubular dilation	Increased relative kidney weights and karyomegaly in the proximal tubules and atypical tubular dilation but was not statistically significant	(JISA, 1993)	High
Hepatic	Chronic	Mouse, B6C3F1, M/ F	Inhalation, vapor,	0, 678, 1356 mg/ m3	6 hours/ day, 5 days/ week for 103 weeks	LOAEL= 678 mg/ m3 (M)	Liver degeneration	(NTP, 1986)	High

Target Organ/System	Study Type	Species/ Strain/ Sex (Number/ group)	Exposure Route	Doses/ Concentrations	Duration	Cancer Incidence	Effect	Reference	Data Quality Evaluation
		(n=98-100/ group)	whole body	(0, 100 or 200 ppm)		LOAEL = 1356 mg/ m3 (F)	and necrosis in		
Hepatic	Subchronic	Mouse, Swiss-Cox, M (n=12-15/ group all doses except two highest doses: 4-6/ group)	Oral, gavage	0, 20, 100, 200, 500, 1000, 1500 or 2000 mg/ kg/ day	5 days/ week for 6 weeks	NOAEL= 20 mg/ kg-day (M) LOAEL= 100 mg/ kg-day (M)	Increased liver/ body weight ratio at 100 mg/ kg-day; increased triglycerides at 100 mg/ kg-day; no change at 20 mg/ kg-day	(Buben and O'Flaherty, 1985)	High
Renal	Chronic	Rat, F344/ N, M/ F (n=100/ group)	Inhalation, vapor, whole body	0, 1356, or 2713mg/ m3 (0 200, or 400ppm)	6 hours/ day, 5 days/ week for 103 weeks	LOAEL= 1356 mg/ m3 (200 ppm) (M/ F)	Karyomegaly and cytomegaly of the proximal tubules in all exposed rats	(NTP, 1986)	High
Renal	Chronic	Mouse, B6C3F1, M/ F (n=98-100/ group)	Inhalation, vapor, whole body	0, 678, or 1356 mg/ m3 (0, 100 or 200 ppm)	6 hours/ day, 5 days/ week for 103 weeks	LOAEL= 678 mg/ m3 (M/ F)	Karyomegaly and cytomegaly of the proximal tubules in all exposed mice; nephrosis was observed in exposed females, casts increased in all exposed males and in high-dose females	(NTP, 1986)	High

Target Organ/System	Study Type	Species/ Strain/ Sex (Number/ group)	Exposure Route	Doses/ Concentrations	Duration	Cancer Incidence	Effect	Reference	Data Quality Evaluation
Developmental	Developmental	Rat, Sprague Dawley, F (n=22/ group)	Inhalation, vapor, whole body	Actual concentration s: 0, 448, 1689, or 4069 mg/ m3 (0, 66, 249 or 600 ppm) Target concentration s: 0, 509, 1696, or 4069 mg/ m3 (0, 75, 250 or 600 ppm)	6 hours/ day, 7 days/ week on GDs 0-19	Maternal LOAEL = 4069 mg/ m3 (from summary table 4-38) Fetal LOAEL = 1696 mg/ m3 (from summary table 4-38)	Maternal toxicity (slight, but statistically significant, decreased body weight gain; decreased gravid uterine weight); fetal body weight and placental weight decrements, increased delays in thoracic vertebral ossification	(Carney et al., 2006)	High

Target Organ/System	Study Type	Species/ Strain/ Sex (Number/ group)	Exposure Route	Doses/ Concentrations	Duration	Cancer Incidence	Effect	Reference	Data Quality Evaluation
Reproductive	Reproductive	Rat, Sprague Dawley, M/ F (two-generation study) (n=48/ group)	Inhalation, vapor, whole body	0, 678, 2035, or 6782 mg/ m ³ (0, 100, 300 or 1000 ppm)	F0: 6 hours/ day, 5 days/ week for 11 weeks pre-mating; 6 hours/ day, 7 days/ week for up to 21 days during mating period; 6 hours/ day, 5 days/ week postmating until termination for males and 6 hours/ day, 5 days/ week for females postmating through GD 20 (28 litters/ dose)	NOAEL = 678 mg/ m ³ for parental systematic toxicity (increased death of mothers) LOAEL = 678 mg/ m ³ for F1A pups	Increased death of F1A and F2A and F2B pups; decreased body weight	(Tinston, 1994)	High
Developmental Effects (Neurotoxicity)	Developmental	Rat, Sprague Dawley (n = 13-21/ group)	Inhalation, vapor, whole body	0, 678, or 6104 mg/ m ³ (0, 100 or 900 ppm)	7 hours/ day on GDs 7-13 or 14-21 (GDs 13-21 litters/ dose, male and female offspring assessed)	NOAEL= 678 mg/ m ³ LOAEL= 6104 mg/ m ³	Decreased weight gain; behavioral changes, more extensive for late pregnancy exposure; decreased brain acetylcholine	(Nelson et al., 1979)	Medium

Target Organ/System	Study Type	Species/ Strain/ Sex (Number/ group)	Exposure Route	Doses/ Concentrations	Duration	Cancer Incidence	Effect	Reference	Data Quality Evaluation
Developmental	Developmental	Rat, Sprague Dawley (two-generation study) (n=48/ group)	Inhalation, vapor, whole body	0, 678, 2035, or 6782 mg/m ³ (0, 100, 300 or 1000 ppm)	F0: 6 hours/day, 5 days/week for 11 weeks pre-mating; 6 hours/day, 7 days/week for up to 21 days during mating period; 6 hours/day, 5 days/week post-mating until termination for males and 6 hours/day, 5 days/week for females post-mating through D 20 (28 litters/dose)	NOAEL = 300 ppm LOAEL = 1,000 ppm	CNS depression/ Behavioral effects (decreased activity, reduced response to sound) in F1 pups	(Tinston, 1994)	High

2 Data extraction of studies not considered for dose-response assessment

Table 2.1 Summary of the Epidemiological Database for Perchloroethylene not considered for dose- response

Target Organ/ System	Outcome/ Endpoint	Study Population	Exposure	Results	Reference	Data Quality Evaluation
Acute Toxicity/Poisoning	Clinical observations including nausea, irritation of the eyes, sinus discomfort, and blood pressure	Five researchers, 1930s, sex and age not reported	One to two hour inhalation chamber exposures at approximately 500, 1000, 1500, and 2000 ppm perchloroethylene	Subjects reported feeling nauseous and having eye irritation after a 500 ppm exposure and faintness at higher exposure levels	(Carpenter, 1937)	Low
Acute Toxicity/Poisoning	Clinical observations including nausea, dizziness, eye irritation, and sleepiness	Subject information not reported	Controlled inhalation chamber exposure to approximately 100, 200, 280, 600, and 1000 ppm perchloroethylene for an unreported duration	Mild eye irritation, sinus discomfort, and light headedness reported at lower concentrations, more severe symptoms at higher concentrations	(Rowe et al. 1952)	Low

Target Organ/ System	Outcome/ Endpoint	Study Population	Exposure	Results	Reference	Data Quality Evaluation
Acute Toxicity/Poisoning	Clinical observations including eye irritation, light headedness, and respiratory rate	21 year old male employee	Accidental occupational exposure with estimated mean perchloroethylene concentration of 393 ppm	Subject was initially unconscious, later reported eye irritation, light headedness, and faintness	(Stewart et al. 1961)	Medium
Acute Toxicity/Poisoning	Clinical observations including eye irritation, headache, nausea and dizziness	Sixteen healthy male technical employees ranging in age from 24 to 64 years; five subjects were selected for repeated exposure	7-hour inhalation chamber exposure to approximately 100 ppm perchloroethylene for 1-5 days	Subjects reported low-grade chronic sinusitis, a mild frontal headache, and mild eye and throat irritation	(Stewart et al. 1970)	Medium
Acute Toxicity/Poisoning	Headache, nausea, dizziness, chest pain, abdominal pain, irritation of eyes nose or throat	12 subjects, Wisconsin, 1975, 19-42 years of age	Perchloroethylene, controlled exposure of 0, 25, 100 ppm for 5.5 hrs	No significant associations between perchloroethylene exposure and clinical observations	(Stewart et al. 1977)	Medium

Target Organ/ System	Outcome/ Endpoint	Study Population	Exposure	Results	Reference	Data Quality Evaluation
Cancer	Cancer diagnosis: liver, kidney, bladder, pancreas, lung, cervix, ovary, Hodgkin's disease, non- Hodgkin's lymphoma, and multiple myeloma	Adults working in the Netherlands during the 1970 census, including 23,714 women and 5,619 men working as launderers and dry cleaners	Occupation in dry cleaning or laundering industry served as surrogate for Perc exposure	Significant increase in incidence of lung, cervical, and ovarian cancer diagnosis and Hodgkin's disease (women only), all other outcomes were non-significant	(Anderson et al. 1999)	Medium
Cancer	Renal cell carcinoma diagnosis	Renal cell carcinoma cases (n= 315) and population controls (n=313), Oklahoma City, occupational history through ~1988	Primary occupation in dry cleaning industry served as surrogate for Perc exposure	Non significant association between dry cleaning occupation and renal cell carcinoma in males (negative) and females (positive)	(Asal et al. 1988)	Medium

Target Organ/ System	Outcome/ Endpoint	Study Population	Exposure	Results	Reference	Data Quality Evaluation
Cancer	Leukemia incidence	Adults, permanent residents of five Upper Cape towns, Massachusetts, in 1983-1986 (35 leukemia cases, 464 living + 723 deceased controls)	Modeled household exposure to perchloroethylene through the public water distribution system; estimated dose ranged 0.01-209.4 mg (for no latency) or 0.01-90.6 mg (for 5-year latency)	A statistically significant increase in odds of leukemia was observed for "high" exposure group vs. non-exposed to perchloroethylene, after 0-year and 5-year latency periods (non- statistically significant increase for ever exposed vs. non- exposed)	(Aschengrau et al. 1993)	Medium
Cancer	Kidney cancer, liver cancer, bladder cancer, Non-Hodgkin's lymphoma, Hodgkin's lymphoma, all cause cancer mortality, lung cancer , cervical cancer, esophageal cancer mortality	5,369 dry cleaners members of a dry cleaning union in St. Louis, men and women, follow-up 1948-1993	Dry cleaner occupation, perchloroethylene the dominant solvent	Non-significant increase in Hodgkin's lymphoma mortality for the entire follow-up period, and for the two shorter follow-up periods	(Blair et al. 2003)	Medium

Target Organ/ System	Outcome/ Endpoint	Study Population	Exposure	Results	Reference	Data Quality Evaluation
Cancer	Cause-specific mortality: kidney cancer, Hodgkin lymphoma, Leukemias, ALS	Camp Lejeune, North Carolina cohort; n=154,932 median age, start of follow-up: 20 median age, end of follow-up: 49 Camp Pendleton, California cohort n=154,969 median age, start of follow-up: 20 median age, end of follow-up: 49 exposure period: 1975-1985; mortality follow-up period: 1979-2008	Chemical name: Perchloroethylene (PCE); exposure matrix: estimated monthly average PCE concentration in Tarawa Terrace water system (1975-1985) Mean: 75.7 ug/L, Median: 84.9 ug/L, Range: 0-158.1 ug/L; estimated monthly average PCE concentration in Hadnot Point water system (1975-1985) Mean: 15.7 ug/L, Median: 15.4 ug/L, Range: 0-38.7 ug/L; Duration: On average an individual in the Camp Lejeune cohort resided at the base for 18 months.	Positive, non-significant associations observed between cumulative exposure to PCE and mortality due to kidney cancer.	(Bove et al. 2014)	High

Target Organ/ System	Outcome/ Endpoint	Study Population	Exposure	Results	Reference	Data Quality Evaluation
Cancer	Excess risk of renal cell carcinoma (RCC)	Hospital-based case control study of patients diagnosed with renal cell carcinoma (RCC) in Arnsberg, Germany between 1992 and 2000 (134 cases, 401 gender- and age-matched controls).	TCE and Perc exposure probability and duration were based on self-assessment. Analyses of industries with exposure to TCE were based on an IARC database (CAREX). A job exposure matrix (JEM) was used to assess exposure to degreasing agents (also other agents).	The ORs for RCC risk were increased for self-assessed overall exposure to TCE. RCC ORs were not significantly elevated based self-assessed overall exposure to Perc.	(Brüning et al. 2003)	High
Cancer	Diffuse large B-cell lymphoma	Georgia population (2000 census)	Geocoded toxic release sites data for Perc from 1988-1998 EPA's TRI	Significantly decreased risk for diffuse large B-cell lymphoma with increasing mean distance (per 1 mile) to Perc TRI sites.	(Bulka et al. 2016)	Medium

Target Organ/ System	Outcome/ Endpoint	Study Population	Exposure	Results	Reference	Data Quality Evaluation
Cancer	Mortality from lymphatic and haematopoietic cancer	1704 dry cleaning workers in four US cities (San Francisco/Oakland, Chicago, Detroit, and New York)	Employment in a shop using Perc, mean (sd) years of employment for exposed workers 6.2 (5.0)	<p>Significant elevated SMRs were observed for all cancers, esophageal cancer, and trachea, bronchus, and lung cancer.</p> <p>SMRs were significantly lower for liver cancer.</p> <p>No significant association was found for kidney cancer, lymphatic and haematopoietic cancer, and bladder cancer.</p>	(Calvert et al. 2010)	Medium

Target Organ/ System	Outcome/ Endpoint	Study Population	Exposure	Results	Reference	Data Quality Evaluation
Cancer	Diagnosis of cancer in oral cavity, oropharynx, hypopharynx, oral cavity, and larynx (detailed list of codes in text)	Case-control, women only, 296 cases, 775 controls, diagnosed 2001-2007, general population, 18-85 years, subset of ICARE cohort	Perc, exposure qualitatively stated, modeled as cumulative exposure index (CEI)	Statistically significant positive association between Perc and head/neck cancers in ever/never analysis; null association in continuous cumulative exposure assessment	(Carton et al. 2017)	Medium
Cancer	Cancers of the bladder, prostate, colon, stomach, rectum, kidney, pancreas, esophagus, and liver, as well as melanoma and non-Hodgkin's lymphoma.	3730 male, Canadian patients aged 35 to 70 years diagnosed 1979-1985 in 18 largest Montreal hospitals; 533 controls from electoral lists in Quebec. A second control group consisted of the population controls together with patients with cancers at sites distal to the primary cancer being assessed..	PERC exposure determined from self-reported job history categorized by chemists and industrial hygienists based on degree of confidence, frequency, and relative levels (not quantitative)	Significant increase in the OR for prostate cancer associated with Perc exposure (substantial), non-significant OR for all other cancers	(Christensen et al. 2013)	Medium

Target Organ/ System	Outcome/ Endpoint	Study Population	Exposure	Results	Reference	Data Quality Evaluation
Cancer	Renal cell carcinoma	718 cases (men) of renal cell carcinoma from the New Zealand Cancer Registry and 12,758 male controls, 1978-1986	Occupational (dry-cleaning and laundry workers exposed to perchloroethylene)	Non-significant elevation in risk of kidney cancer among dry-cleaning workers	(Delahunt et al. 1995)	Medium
Cancer	Renal cell carcinoma	White newly diagnosed cases with age- and gender- stratified random sample white controls	JEM (developed by NCI)	No significant association between Perc and RCC for the total population nor when separated by sex.	(Dosemeci et al. 1999)	Medium
Cancer	Breast cancer incidence	920 incident breast cancer cases, 1293 controls, Cape Cod, Massachusetts, 1983-1993,	Water distribution modeled exposure to Perc-lined public water distribution pipelines	Perc was not significantly associated with breast cancer, but there was a modest increase in risk in women with high perc exposure	(Gallagher 2011)	Medium

Target Organ/ System	Outcome/ Endpoint	Study Population	Exposure	Results	Reference	Data Quality Evaluation
Cancer	Bladder cancer	113,343 cases and 566,715 matched controls from the Nordic Occupational Cancer (NOCCA) project (through 2005)	Perc exposure estimated via linkage between occupational codes and Nordic Occupational Cancer (NOCCA) project job exposure matrix (JEM)	No significant trend in risk with increasing Perc exposure, significant increase in hazard ratio was only observed in the mid exposure group	(Hadkhale et al. 2017)	Medium
Cancer	Neuroblastoma	Children (75 cases, 14602 controls), ages <6 born in 1990-2007 in California within 5 km of exposure monitoring stations, cases from California Cancer Registry	Perc (0.186 ppbV) in ambient air, pollution monitoring stations used to estimate maternal exposure during pregnancy from birth certificate address	Non-significant positive association between Perc and neuroblastomas per interquartile increase in exposure at 5km radius	(Heck et al. 2013)	Medium
Cancer	Astrocytic brain cancer risk	Men in southern Louisiana, United States, exposed from 1978 - 1980; in northern New Jersey and Philadelphia, Pennsylvania, United States, exposed from 1979 - 1981 (n=620, 300 cases, 320 controls)	Perchloroethylene, low exposure (1)	Chi trend= -0.65. Exposure not significantly associate with astrocytic brain cancer	(Heineman et al. 1994)	Medium

Target Organ/ System	Outcome/ Endpoint	Study Population	Exposure	Results	Reference	Data Quality Evaluation
Cancer	Kidney cancer (total, parenchymal cancer, pelvical cancer, unspecified cancer) , lung cancer	1,644,958 economically active men in the census of year 1960 and 1,154,091 economically active women in the census of year 1970. from the Swedish family Center Database	Occupation as launderers and dry cleaners (with perc mentioned as solvent used in dry cleaning)	Non-significant elevations in excess risk of total kidney cancer and renal parenchymal cancer in men; Significant elevations of pelvical or renal unspecified cancers in men.	(Ji et al. 2005)	Medium
Cancer	Cancer mortality	Lockheed Martin aircraft manufacturing factory workers in Burbank, California (employed after January 1, 1960; followed up through December 31, 2008)	Years of exposure to Perc based on job histories and industrial hygiene surveys	No significant trend for any specific cancer or total cancer by increasing years of exposure.	(Lipworth et al. 2011)	High
Cancer	Total cancer incidence, liver , pancreas; bladder kidney, lymphomas	Men and women (n=378 cancer cases), aged 20-64, working on laundry and dry-cleaning shops in Denmark in 1970	Exposure during laundry or dry cleaning to perchloroethylene	Significant increase in pancreas cancer incidence in men and women combined	(Lyng and Thygesen 1990)	Low

Target Organ/ System	Outcome/ Endpoint	Study Population	Exposure	Results	Reference	Data Quality Evaluation
Cancer	Incident cancers of the esophagus, gastric cardia, pancreas, cervix uteri, bladder, and kidney, primary liver cancer, non-Hodgkin lymphoma	Laundry and dry cleaning workers identified from the 1970 censuses in Denmark, Norway, Sweden, and Finland (1,616 case, 2,398 controls)	Occupation (laundry and dry cleaning); mean perchloroethylene for dry cleaners 160 mg/m ³	Non-significant increased risk of kidney cancer incidence among assistants in dry cleaning shops; Non-significant decrease in risk of kidney cancer for dry cleaners. No elevations in risk of kidney cancer were observed with length of employment.	(Lyng et al. 2006)	Medium

Target Organ/ System	Outcome/ Endpoint	Study Population	Exposure	Results	Reference	Data Quality Evaluation
Cancer	Kidney/renal cancer, all cancer discharges (with and without skin cancer) ICD9 189.0 and 189.1	All residents of New York City from 1993 to 2004, at least 45 years old, who were admitted as inpatients to a state regulated hospital (N=10,916 kidney/renal cancer discharges)	Dry cleaning facilities using perchloroethylene in New York City (5 exposure levels based on the distribution of density of Perc dry cleaners per squared kilometer): 0-0.47; 0.47 - 1.90, 1.90- 1.50; 1.50-2.70; 2.70-16.43	Significant association between the density of perchloroethylene dry cleaning establishments and the rate of hospital discharges that include a diagnosis of kidney cancer among persons 45 years of age and older living in New York City	(Ma et al. 2009)	Medium
Cancer	Renal cell carcinoma diagnosis	Renal cell carcinoma cases (n= 1732) and population controls (n=2309), complete occupational history collected 1989-1991, Australia, Denmark, Germany, Sweden, USA	Renal cell carcinoma diagnosis	Significantly increased risk for renal cell carcinoma with exposure to dry cleaning solvents	(Mandel et al. 1995)	High

Target Organ/ System	Outcome/ Endpoint	Study Population	Exposure	Results	Reference	Data Quality Evaluation
Cancer	Lung cancer	Investigation of occupational exposure and environmental causes of respiratory cancers (ICARE) study subjects, population-based case-control study in France 2001-2007 (2274 men cases and 2780 men controls)	Cumulative Exposure Index (CEI) based on self-reported job histories and probability, intensity, and frequency of exposure to Perc based on jobs	Perc was not significantly associated with lung cancer in men.	(Mattei et al. 2014)	Medium
Cancer	Kidney cancer (renal cell carcinoma), renal pelvic carcinoma	489 cases of kidney cancer, 147 cases of pelvic cancer and 523 controls in New South Wales	Occupation in dry cleaning industry	Significantly elevated risk of renal pelvic carcinoma associated with working in the dry cleaning industry compared to population controls	(McCredie and Stewart 1993)	Medium
Cancer	Kidney cancer (renal cell carcinoma)	368 cases and 396 controls in Denmark, interviewed between 1989-1992	Occupational exposure in dry cleaning industry	Non-significant elevations in risk of renal cell carcinoma in men and in women employed in the dry cleaning industry 10 or more years before the interview	(Mellemggaard et al 1994)	Medium

Target Organ/ System	Outcome/ Endpoint	Study Population	Exposure	Results	Reference	Data Quality Evaluation
Cancer	All Non-Hodgkin lymphoma and by non-Hodgkin lymphoma subtype (i.e., small lymphocytic, follicular, diffuse, other),	All newly diagnosed cases of non-Hodgkin lymphomas, chronic lymphocytic leukemia (CLL) during 1991–1993 among men and women age 20 to 74 years in 11 areas in Italy	Perc exposure based on job-specific questionnaires and industrial hygiene experts for level of probability (i.e., low, medium, high) and intensity of exposure (i.e., very low, low, medium, and high) with durations of less than 15 years and 15 or more years.	Perc was not significantly associated with non-Hodgkin lymphoma either by intensity or duration of exposure.	(Miligi et al. 2006)	High
Cancer	Mycosis fungoides (MF)	100 patients with Mycosis Fungoides and 2846 controls, 35-69 years of age, from Denmark, Sweden, France, Germany, Italy, and Spain, 1995-1997	Occupational exposure to Perc assessed with job exposure matrix	A positive, non-significant association was observed between Mycosis Fungoides and male subjects with exposure to Perc \geq median of control exposure vs. unexposed male subjects	(Morales-Suárez-Varela et al. 2013)	High

Target Organ/ System	Outcome/ Endpoint	Study Population	Exposure	Results	Reference	Data Quality Evaluation
Cancer	Brain cancer: glioma and meningioma cases	489 glioma cases, 197 meningioma cases, and 799 controls from three USA hospitals in Arizona, Massachusetts and Pennsylvania	Occupational exposure to Perc via self-reported occupational history and industrial hygienist assigned level of exposure	Perc was not significantly associated with glioma or meningioma	(Neta et al. 2012)	High
Cancer	Mortality from all cancer (SMR)	1690 workers employed in facilities that used perc as their primary solvent in Oakland, Detroit, Chicago, or New York City, workers employed at least one year prior to 1960	Years of employment in a perc facility	A positive trend of increasing risk of all cancer mortality was observed with an increase in both years of exposure and latency (time since first employment in a perc facility)	(NIOSH 1985)	High
Cancer	Excess risk of renal cell carcinoma (RCC)	Multi-center population level case- control study of 935 patients diagnosed with RCC between 1991 and 1995 and 4298 controls matched by geographical region, sex and age (~1:4 ratio of cases to controls).	Exposure was categorized as medium, high or substantial based on a job exposure matrix (JEM or a job-exposure-task matrix (JETM).	Odds ratios showed low to no significant increased risk of renal cell carcinoma for Perc exposure, no dose response trends.	(Pesch et al. 2000)	Medium

Target Organ/ System	Outcome/ Endpoint	Study Population	Exposure	Results	Reference	Data Quality Evaluation
Cancer	Cancer of the liver	15 million people participating in a decennial census in Denmark, Finland, Iceland, Norway, and Sweden. Aged 30-64 in years 1960-1990.	Employment in dry cleaning and/or laundering during time period of predominant Perc use	Significantly elevated SIRs were observed in women for stomach, liver, cervical, oral cavity, and lung cancers. No association was found for kidney, bladder, and non-Hodgkin's lymphoma cancer incidence in women.	(Pukkala et al. 2009)	Medium
Cancer	Diagnosis of kidney cancer	General population case-control study of kidney cancer (1217 cases; 1235 controls). Detroit (2002 - 2007) and Chicago (2003).	Job exposure matrix was used to determine years exposed, average weekly exposure and cumulative hours exposed. to perc	Increased risk of kidney cancer for high intensity exposure group; OR 3.0 (1.3 - 7.4) for 3rd tertile (>1820 hours) vs. unexposed for cumulative hours exposed. No significant associations observed in for other levels of perc exposure.	(Purdue et al. 2016)	High

Target Organ/ System	Outcome/ Endpoint	Study Population	Exposure	Results	Reference	Data Quality Evaluation
Cancer	Mortality from multiple myeloma	Aircraft maintenance workers (n = 14,457; 10,730 men and 3725 women) at Hill Air Force Base (Utah, USA), for at least one year from 1952-1956, and followed up through 2000	Occupational exposure to Perc (yes/no) based on job- exposure matrix; no quantitative assessment available	Positive association between mortality from multiple myeloma and occupational exposure to Perc compared to no exposure (statistically significant for females, non-statistically significant for males)	(Radican et al. 2008)	Medium
Cancer	Childhood cancers, neural tube defects, oral clefts,	Children born to mothers with exposure to contaminated drinking water at Camp Lejeune : 51 cases and 526 controls	Perchloroethylene (perc) in drinking water during 1st trimester of pregnancy; modelled exposure high (≥ 44 ppb), low (< 44 ppb)	Positive, non-significant associations observed between childhood cancers and any, high or low 1st trimester exposure to perc compared to unexposed).	(Ruckart et al. 2013)	High

Target Organ/ System	Outcome/ Endpoint	Study Population	Exposure	Results	Reference	Data Quality Evaluation
Cancer	Age of diagnosis of breast cancer (male only).	Case-control, male Marines born before 1969, diagnosed 1995-2013, with identifiable tour dates/locations	Perc, residential drinking water at Camp Lejeune , cumulative exposure >159 ppb	Non-significant positive association between Perc exposure and breast cancer diagnosis and age of diagnosis	(Ruckart et al. 2015)	High
Cancer	Glioma	Non-farm workers from the Upper Midwest Health Study (798 cases and 1141 controls from Iowa, Michigan, Minnesota, and Wisconsin 1995-1997)	Perc (perchloroethylene) use (self-reported occupational history through 1992, bibliographic database of published exposure)	Perc was associated with a significant decrease in gliomas.	(Ruder et al. 2013)	High
Cancer	Total lymphoma, HL, B-NHL, T-NHL, B-NHL subentities (DLBCL, FL, CLL, multiple myeloma, marginal zone lymphoma)	710 participating cases (matched to 710 controls) with malignant lymphoma among men and women aged 18 to 80 years in 6 regions in Germany	Cumulative occupational exposure to Perc [ppm*years] based on intensity, the frequency, and duration of Perc exposure (0 to >78.8 ppm*years)	Perc was not significantly associated with malignant lymphoma or any specific type of lymphoma; however, there was an increase (non-significant) in risk of total lymphoma in the highest exposure group (>78.8 ppm*years).	(Seidler et al. 2007)	High

Target Organ/ System	Outcome/ Endpoint	Study Population	Exposure	Results	Reference	Data Quality Evaluation
Cancer	Kidney, bladder, liver, NHL, overall cancer incidence	Swedish national cohort of dry-cleaning and laundry workers (n = 10,389) assembled in 1984 followed up for new cases of cancer by matching with the Swedish cancer register from 1985 to 2006	Occupation as dry cleaners and laundry workers exposed to perchloroethylene; exposure levels in the 1970s were of the order of 100–200 mg/m ³ (15–30 ppm)	Non-significant elevated risk of Hodgkin's lymphoma, kidney and liver cancer, significantly elevated risk of Non-Hodgkin's lymphoma and lung cancer; no elevated risk of bladder cancer	(Seldén and Ahlborg 2011)	Medium
Cancer	Kidney cancer incidence	Greater Montreal metropolitan area. Case-control study of occupationally-exposed men aged 35 to 70 year old (4263 cases, 533 population controls; also hospital and cancer controls).	Any or substantial exposure	ORs were not significantly elevated for PCE exposure and kidney cancer (no quantitative data were provided).	(Siemiatycki 1991)	Medium
Cancer	Bladder and other urinary cancer mortality	National Institute for Occupational Safety and Health (NIOSH) Cohort, 34494 workers at NY microelectronics and business machine facility, 2009, 52-65yrs	Cumulative Perc exposure score based on department- exposure matrix	Perc was not significantly associated with bladder and other urinary cancers mortality.	(Silver et al. 2014)	Medium

Target Organ/ System	Outcome/ Endpoint	Study Population	Exposure	Results	Reference	Data Quality Evaluation
Cancer	Testicular cancer	National Institute for Occupational Safety and Health (NIOSH) Cohort, 34494 workers at NY microelectronics and business machine facility, 2009, 52-65yrs	Cumulative Perc exposure score based on department- exposure matrix	Perc was not significantly associated with testicular cancer incidence.	(Silver et al. 2014)	Medium
Cancer	Acute myeloid lymphoma	Cases of acute myeloid leukemia (n=14,337) diagnosed between 1961 and 2005, and controls (n=71,027) matched by age, sex, and country identified from the Nordic Occupational Cancer Study cohort	Cumulative Perc exposure estimated using job exposure matrix, Median (ppm-yr) 12.1	No significant increase in acute myeloid leukemia risk was observed with low, moderate, or high exposure to Perc, compared to referent group when hazard ratios were calculated using a 10-year lag (p- value = 0.39). Findings for analysis stratified by sex or age were not reported	(Talibov et al. 2014)	High

Target Organ/ System	Outcome/ Endpoint	Study Population	Exposure	Results	Reference	Data Quality Evaluation
Cancer	Cancer diagnosis: liver/biliary, kidney, bladder, pancreas, lung, cervix, Hodgkin's lymphoma, and non-Hodgkin's lymphoma	Adults working in the Sweden during the 1960 and 1970 census, including 31,418 women and 15,515 men working as launderers, dry cleaners, or pressers	Occupation as a dry cleaner, launderer, or presser served as surrogate for Perc exposure	Increased incidence of Hodgkin's disease (significant), lung (significant), cervix (significant), liver/biliary passages, kidney, and bladder cancer, all other outcomes were non-significant	(Travier et al 2002)	High
Cancer	Lung cancer	Lung cancer cases and randomly selected population-based controls frequency matched by sex and age in Montreal Canada	Perc exposure (any or substantial) was assessed by a team of industrial chemists and hygienists based on self-reported job histories	Increase in OR for any exposure or substantial exposure to Perc, results were only significant for any exposure in Study I and in the pooled analysis	(Vizcaya et al. 2013)	Medium
Cancer	Liver and kidney cancer, non-Hodgkin's lymphoma (NHL) and multiple myeloma (MM)	All subjects aged 30–64 years who participated in 1960 through 1990 censuses in Finland, Iceland, Norway and Sweden ; five matched control per case	Job-exposure matrix, intensity × prevalence of perchloroethylene exposure (90th percentile:: 0.05 units)	A positive, non-significant association was observed between high cumulative perchloroethylene exposure (intensity × prevalence) and kidney cancer in men and women.	(Vlaanderen et al. 2013)	High

Target Organ/ System	Outcome/ Endpoint	Study Population	Exposure	Results	Reference	Data Quality Evaluation
Cancer	Renal pelvis cancer, bladder cancer	Employed Swedish residents (1,014 and 360 renal pelvis cancers and 18,244 and 3,347 bladder cancers among men and women, respectively)	Occupation type (workers in laundry, ironing , dyeing) or industry	Non-significant excess risk of renal pelvis cancer among men working in laundry, ironing , dyeing industry.	(Wilson et al. 2008)	Medium
Cardiovascular	Major cardiac birth defects	1,090 live births in the TCE study area and 3.6 million births in the comparison group (NY State without NYC) (1978-2002) .	Maternal exposure to Perc through soil vapor intrusion (4.1-9.5 ug/m3 indoor air sampling) associated with a 1979 spill from a semiconductor manufacturing facility in Endicott, New York	Adjusted rate ratios for low birth weight (LBW), small for gestational age (SGA), term LBW, cardiac defects and conotruncal defects were significantly elevated in the Perc study area.	(Forand et al. 2012)	Medium
Cardiovascular	Blood pressure and heart rate	21 year old male employee	Accidental occupational exposure with estimated mean perchloroethylene concentration of 393 ppm	No effects observed for Cardiovascular outcomes.	(Stewart et al. 1961)	Medium

Target Organ/ System	Outcome/ Endpoint	Study Population	Exposure	Results	Reference	Data Quality Evaluation
Clinical Chemistry/Biochemical	Urinalysis	Five researchers, 1930s, sex and age not reported	One to two hour inhalation chamber exposures at approximately 500, 1000, 1500, and 2000 ppm perchloroethylene	No effects observed for Clinical Chemistry/Biochemical outcomes.	(Carpenter 1937)	Low
Clinical Chemistry/Biochemical	Clinical chemistry panel and urinalysis	21 year old male employee	Accidental occupational exposure with estimated mean perchloroethylene concentration of 393 ppm	Minor, transient elevations of alkaline phosphatase and SGP-T	(Stewart et al. 1961)	Medium
Clinical Chemistry/Biochemical	Clinical chemistry panel and urinalysis	Sixteen healthy male technical employees ranging in age from 24 to 64 years; five subjects were selected for repeated exposure	7-hour inhalation chamber exposure to approximately 100 ppm perchloroethylene for 1-5 days	No effects observed for Clinical Chemistry/Biochemical outcomes.	(Stewart et al. 1970)	Medium
Clinical Symptoms	Ears, nose, throat, ophthalmological, cutaneous, respiratory, digestive signs, neurological symptoms, Epworth test > 8, pre-narcotic syndrome	50 exposed workers from 22 dry-cleaning establishments in France, 95 matched unexposed controls	Ambient perchloroethylene levels, blood perc levels; years of employment; median value of atmospheric perc was 7 ppm (0.22–33), the median blood level of perc was 73.6 µg/l (11.8–144).	Perchloroethylene exposure was not associated with significant increase in clinical symptoms among dry-cleaning employees compared to unexposed controls.	(Lucas et al. 2015)	Medium

Target Organ/ System	Outcome/ Endpoint	Study Population	Exposure	Results	Reference	Data Quality Evaluation
Growth (early life) and Development	Childhood cancers, neural tube defects, oral clefts,	Children born during 1968–1985 to mothers exposed to contaminated drinking water at Camp Lejeune during pregnancy: 51 cases and 651 controls	Perchloroethylene (perc) in drinking water during 1st trimester of pregnancy; modelled exposure above MCL (≥ 5 ppb), below MCL (< 5 ppb)	Positive non-significant association observed between neural tube defects and exposure to perc ≤ 5 ppb compared to unexposed. Negative, non-significant association observed between neural tube defects and any exposure to perc, or exposure > 5 ppb compared to unexposed.	(Ruckart et al. 2013)	High
Hematological and Immune	Primary Sjogren syndrome	Cases (n= 175) followed up in departments of Internal Medicine of three University Hospitals and matched controls (n=350) (2010-2013)	Occupational Perc exposure based on self-reported occupational histories, expert judgement of industrial hygienists and occupational practitioners, as well as the French JEM (used more for the chlorinated solvents)	Significant increase in risk for Sjogren' syndrome with occupational Perc exposure; increase OR with high final cumulative exposure, but was not significant	(Chaigne et al 2015)	Medium

Target Organ/ System	Outcome/ Endpoint	Study Population	Exposure	Results	Reference	Data Quality Evaluation
Hematological and Immune	Systemic Sclerosis	Meta-analysis of 14 case-control studies (6 with TCE and/or PCE exposure analysis). The perc studies included 714 cases and 2479 controls. The TCE studies included 1029 cases and 2884 controls.	Proportion of subjects exposed to solvents occupationally	A positive, non-significant association was observed between risk of SSc and perc exposure	(Zhao et al. 2016)	Medium
Mortality	Mortality from all causes	5,369 dry cleaners members of a dry cleaning union in St. Louis, men and women, follow-up 1948-1993	Dry cleaner occupation, perchloroethylene the dominant solvent	Significant elevations in all-cause cancer mortality for the entire follow-up period, and for the first and second follow-up periods; and for men and women, and for blacks and whites	(Blair et al. 2003)	Medium

Neurological/Behavior	<p>Risky behavior endpoints measured/ analyzed: smoking usage as a teen, smoking usage as an adult, alcohol usage as a teen, alcohol usage as an adult, drug usage as a teen, drug usage as an adult, multiple risky behaviors as a teen, multiple risky behaviors as an adult, selected risky behaviors as a teen among subjects without prenatal exposure to smoking, selected risky behaviors (smoking, alcohol, drug usage) as an adult among subjects without prenatal exposure to smoking</p>	<p>585 exposed and 562 unexposed born 1969-1983 in Cape Cod, MA and 365 older siblings</p>	<p>EPA's water distribution system modeling software modeled cumulative prenatal and childhood Perc exposure</p>	<p>Among subjects in the ≥ 67th exposure percentile group, a higher risk of multiple risky behaviors as a teen (significant) or adult (not significant) was observed in comparison to unexposed subjects</p>	<p>(Aschengrau et al 2011)</p>	<p>Medium</p>
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Neurological/Behavior	Drinking frequently as a teenager	1378 men and women in Cape Cod, MA, 1969-1983, Mean age 29 years	Perchloroethylene, Cumulative exposure levels in drinking water prenatally and during childhood (age 5 years). Mean 142 g, median 34g, range 11mg - 4668g.	<p>A positive, significant association was observed between initiating smoking at a young age, drinking frequently as a teenager at a young age, use of more than 1 drug as teenager, use of more than 1 major drug as an adult and cumulative Perc exposure in drinking water when comparing highest tertile with lowest tertile.</p> <p>A positive, non-significant association was observed between heavy smoking at a young age, drinking heavily in the past 30 days at a young age and cumulative Perc exposure in drinking water when comparing highest tertile with lowest tertile</p>	(Aschengrau et al. 2016)	Medium
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Target Organ/ System	Outcome/ Endpoint	Study Population	Exposure	Results	Reference	Data Quality Evaluation
Neurological/Behavior	Cause-specific mortality: kidney cancer, Hodgkin lymphoma, Leukemias, ALS	Camp Lejeune, North Carolina cohort; n=154,932 median age, start of follow-up: 20 median age, end of follow-up: 49 Camp Pendleton, California cohort n=154,969 median age, start of follow-up: 20 median age, end of follow-up: 49 exposure period: 1975-1985; mortality follow-up period: 1979-2008	Chemical name: Perchloroethylene (PCE); exposure matrix: estimated monthly average PCE concentration in Tarawa Terrace water system (1975-1985) Mean: 75.7 ug/L, Median: 84.9 ug/L, Range: 0-158.1 ug/L; estimated monthly average PCE concentration in Hadnot Point water system (1975-1985) Mean: 15.7 ug/L, Median: 15.4 ug/L, Range: 0-38.7 ug/L; Duration: On average an individual in the Camp Lejeune cohort resided at the base for 18 months.	Positive, non-significant associations observed between cumulative exposure to PCE and mortality due to ALS	(Bove et al. 2014)	High

Target Organ/ System	Outcome/ Endpoint	Study Population	Exposure	Results	Reference	Data Quality Evaluation
Neurological/Behavior	Pattern memory (Number correct)	'Dry Cleaner Study Population' (n=65). men and women; Detroit , USA	Perchloroethylene. Cumulative lifetime exposure levels based on complete work histories, hobbies, and industrial hygiene evaluations of subjects in participating shops:. Categories: low (n=24, average 3.4 years at shop), moderate (n=18, average 8.1 years at shop), and high (n=23, average 20.2 years at shop).	Significant decrease (6.7%) was observed in the adjusted mean performance on the pattern memory (number correct) between the low and high Perc exposure categories.	(Echeverria et al. 1995)	Medium
Neurological/Behavior	Parkinson's Disease (PD)	99 male twin pairs 35-84 years of age from US National Academy of Sciences/National Research Council World War II Veteran Twins Registry, 1993-1995	Self-reported exposure to Perc	A positive, non-significant association was observed between Parkinson Disease and ever exposure to Perc	(Goldman et al. 2012)	High
Neurological/Behavior	Autism spectrum disorders	3,137 children in North Carolina (1,931 total, 201 cases) and West Virginia (1,246 total, 173 cases), 2000-2004, 8 years old	1996 modeled perc in ambient air, geometric mean concentration: 227.0 (NC) and 172.2 (WV) ng/m ³	A positive, non-significant association between ambient perc (80th vs. 20th percentile) and autism spectrum disorder	(Kalkbrenner et al. 2010)	High

Target Organ/ System	Outcome/ Endpoint	Study Population	Exposure	Results	Reference	Data Quality Evaluation
Neurological/Behavior	Autism Spectrum Disorder	Nurses' Health Study II children 3-18 years (US; 325 cases/22101 controls).	Perc air concentrations at mother's location at birth	Perc exposure was significantly associated with Autism Spectrum Disorder based on a significant increase in odds ratio comparing the highest to the lowest concentration quintile.	(Roberts et al. 2013)	High
Neurological/Behavior	Diseases of the nervous system mortality	National Institute for Occupational Safety and Health (NIOSH) Cohort, 34494 workers at NY microelectronics and business machine facility, 2009, 52-65yrs	Cumulative Perc exposure score based on department- exposure matrix	Perc exposure was significantly associated with increased risk of mortality from diseases of the nervous system.	(Silver et al. 2014)	Medium
Neurological/Behavior	Neurological examination including the Romberg test, Crawford manual dexterity tests, and Flannagan coordination, arithmetic, and inspection tests	Sixteen healthy male technical employees ranging in age from 24 to 64 years; five subjects were selected for repeated exposure	7-hour inhalation chamber exposure to approximately 100 ppm perchloroethylene for 1-5 days	Slightly impaired performance on the Romberg test, no other effects observed	(Stewart et al. 1970)	Medium

Target Organ/ System	Outcome/ Endpoint	Study Population	Exposure	Results	Reference	Data Quality Evaluation
Neurological/Behavior	Michigan eye-hand coordination, rotary pursuit, Flanagan coordination, saccade eye velocity, dual-attention tasks, Lorr-McNair mood evaluation test, electroencephalogram	12 subjects, Wisconsin, 1975, 19-42 years of age	Perchloroethylene, controlled exposure of 0, 25, 100 ppm for 5.5 hrs	Perchloroethylene (100 ppm) had statistically significant negative correlation with Flanagan coordination in some sessions, no other significant effects were found	(Stewart et al. 1977)	Medium
Neurological/Behavior	Failure to meet test-based standards for English language arts in 3rd grade standardized tests.	Children (n=201,559) born 1994-1998 in New York City, enrolled in 3rd grade public schools before 2008.	Perchloroethylene in ambient air estimated from EPA's National Air Toxics Assessment (NATA) from 1996 (prenatal exposure). High perchloroethylene category: median 1.13 mg/m ³ , range 0.84 - 9.2 mg/m ³ . Low perchloroethylene category: median 0.63 mg/m ³ , range 0.28 - 0.84 mg/m ³ .	A positive, not statistically significant association (borderline) was observed between English language arts test and highest quartile of Perc exposure compared to lowest 3 quartiles.	(Stingone et al. 2016)	Medium

Target Organ/ System	Outcome/ Endpoint	Study Population	Exposure	Results	Reference	Data Quality Evaluation
Neurological/Behavior	Autism spectrum disorder diagnosis with Social Communication Questionnaire score of 15+	217 cases, 224 interview controls, 4856 birth certificate controls, children born from 2005-2009 in 6 counties of Pennsylvania	Perc exposure (94-267 ng/m3) during gestation estimated with National Air Toxics Assessment 2005 model from addresses at birth	Perc showed non-significant positive association with Autism Spectrum Disorder diagnosis relative to birth certificate controls across all quartiles of exposure	(Talbot et al 2015)	Medium
Neurological/Behavior	Autism diagnosis	Children (n=619 cases) born to mothers living within 5 km of air pollutant monitoring stations in Los Angeles County during pregnancy, 1995-2006, monitored until age 6	Maternal ambient Perc exposure during entire pregnancy	A positive, significant association was observed between autistic disorder by age 6 years and maternal ambient Perc exposure	(von Ehrenstein et al. 2014)	High
Neurological/Behavior	Autism Spectrum Disorder	Children born 1994 followed for 9 years, 284 cases and 657 birth month- and sex- matched control births from the San Francisco area	1996 EPA estimated annual average concentrations of Perc on the census tract level, mean (SD) exposure for cases: 0.61 (0.33 ug/m3)	Non significant positive association observed for 3rd and 4th quartile of Perc exposure compared to those exposed to the median exposure level or less.	(Windham et al. 2006)	Medium

Target Organ/ System	Outcome/ Endpoint	Study Population	Exposure	Results	Reference	Data Quality Evaluation
Renal	Chronic renal disease (chronic and unspecified nephritis, renal failure, and other renal sclerosis) mortality	National Institute for Occupational Safety and Health (NIOSH) Cohort, 34494 workers at NY microelectronics and business machine facility, 2009, 52-65yrs	Cumulative Perc exposure score based on department- exposure matrix	Perc was not significantly associated with mortality from chronic renal diseases.	(Silver et al. 2014)	Medium
Reproductive	Polycystic ovary syndrome, endometriosis, infertility (i.e., trouble getting pregnant), and miscarriage	828 women, Cape Cod, MA, 1969-1983, 24-38 years	Early life Perc exposure with water modeling software (mean cumulative exposure 121.7 g)	Perc was not significantly associated with polycystic ovary syndrome, endometriosis, trouble getting pregnant, or miscarriage.	(Mahalingaiah et al. 2016)	High
Reproductive	Mean birth weight difference (g)	11,896 singleton births, Camp Lejeune, North Carolina	Perchloroethylene, median (of exposed average monthly concentrations during pregnancy) 35.8 ppb	Significant negative associations between exposure to perc and mean birth weight (quartiles compared to unexposed): Q2 - 28.5 g (-55.1, -1.9); non-significant associations for Q1 4.4 g (-17.4, 26.1), Q3 3.8 g (-28.3, 36.0), and Q4 8.2 g (-29.5, 46.0)	(Ruckart et al. 2014)	High

Target Organ/ System	Outcome/ Endpoint	Study Population	Exposure	Results	Reference	Data Quality Evaluation
Respiratory	Mortality from nonmalignant respiratory disease	Aircraft maintenance workers (n = 14,457; 10,730 men and 3725 women) at Hill Air Force Base (Utah, USA), for at least one year from 1952-1956, and followed up through 2000	Occupational exposure to Perc (yes/no) based on job- exposure matrix; no quantitative assessment available	Positive, statistically significant, association between mortality from nonmalignant respiratory disease in males and occupational exposure to Perc compared to no exposure (negative, non- statistically significant association for females)	(Radican et al. 2008)	Medium

Table 2.2 Summary of the Animal Toxicological Database for Perchloroethylene not considered for dose-response

Target Organ/System	Study Type	Species/ Strain/ Sex (Number/ group)	Exposure Route	Doses/ Concentrations	Duration	NOAEL/ LOAEL/ LC50 (mg/m ³ or mg/kg-day) (Sex)	Effect	Reference	Data Quality Evaluation
Body Weight	Short-term (1-30 days)	Rat Sprague-Dawley - [rat] Female (8)	Inhalation	0 , 686 , 2058 , 6860 mg/ m ³ (0 , 100 , 300 , 1000 ppm)	6 hours/ day 5 days/ week for 4 weeks (20 exposure days)	Not Reported	Decreased body weight	Boverhof et al (2013)	High
Body Weight	Reproductive	Rat Other Both (24/ sex/ group in F0 parents)	Inhalation	0 , 686 , 2058 , 6860 mg/ m ³ (0 , 100 , 300 , 1000 ppm)	6 hours/ day 5 days / week in multi-generation study (including prior to mating through 2 nd generation)	Not Reported	No body weight decrease greater than 10% from control; liver weights increased at 1000 ppm in F0 males and F1 females but no histopathology changes seen.	Halogenated Solvents (1995)	Medium
Body Weight	Chronic (> 90 days)	Rat Osborne-Mendel - [rat] Male (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 471 , 941 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	Decreased survival, decreased body weight gain, toxic nephropathy, hunched appearance	National Institute of Health (1977)	Medium
Body Weight	Chronic (> 90 days)	Rat Osborne-Mendel - [rat] Female (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 474 , 949 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	Decreased survival, decreased body weight gain, toxic nephropathy, hunched appearance	National Institute of Health (1977)	Medium

Target Organ/ System	Study Type	Species/ Strain/ Sex (Number/ group)	Exposure Route	Doses/ Concentrations	Duration	NOAEL/ LOAEL/ LC50 (mg/ m3 or mg/ kg-day) (Sex)	Effect	Reference	Data Quality Evaluation
Body Weight	Chronic (> 90 days)	Mouse B6C3F1 - [mouse] Male (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 536 , 1072 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	Decreased survival, decreased body weight gain, hunched appearance, hepatocellular carcinoma, toxic nephropathy	National Institute of Health (1977)	Medium
Body Weight	Chronic (> 90 days)	Mouse B6C3F1 - [mouse] Female (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 386 , 772 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	Decreased survival, decreased body weight gain, hunched appearance, hepatocellular carcinoma, toxic nephropathy	National Institute of Health (1977)	Medium
Cancer	Chronic (> 90 days)	Rat Osborne- Mendel - [rat] Male (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 471 , 941 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	No effects were observed on incidences of neoplastic or non- neoplastic lesions based on necropsy and histopathology examination for these organs/ systems.	National Institute of Health (1977)	Medium

Target Organ/ System	Study Type	Species/ Strain/ Sex (Number/ group)	Exposure Route	Doses/ Concentrations	Duration	NOAEL/ LOAEL/ LC50 (mg/ m3 or mg/ kg-day) (Sex)	Effect	Reference	Data Quality Evaluation
Cancer	Chronic (> 90 days)	Mouse B6C3F1 - [mouse] Male (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 536 , 1072 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	Decreased survival, decreased body weight gain, hunched appearance, hepatocellular carcinoma, toxic nephropathy	National Institute of Health (1977)	Medium
Cancer	Chronic (> 90 days)	Mouse B6C3F1 - [mouse] Female (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 386 , 772 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	Decreased survival, decreased body weight gain, hunched appearance, hepatocellular carcinoma, toxic nephropathy	National Institute of Health (1977)	Medium
Cancer	Chronic (> 90 days)	Rat Osborne- Mendel - [rat] Female (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 474 , 949 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	No effects were observed on incidences of neoplastic or non- neoplastic lesions based on necropsy and histopathology examination for these organs/ systems.	National Institute of Health (1977)	Medium
Cardiovascular	Chronic (> 90 days)	Rat Osborne- Mendel - [rat] Male (50	Oral	0 , 471 , 941 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	No effects were observed on incidences	National Institute of Health (1977)	Medium

Target Organ/ System	Study Type	Species/ Strain/ Sex (Number/ group)	Exposure Route	Doses/ Concentrations	Duration	NOAEL/ LOAEL/ LC50 (mg/ m3 or mg/ kg-day) (Sex)	Effect	Reference	Data Quality Evaluation
		(treated), 20 (untreated and vehicle controls)					of neoplastic or non- neoplastic lesions based on necropsy and histopathology examination for these organs/ systems.		
Cardiovascular	Chronic (> 90 days)	Rat Osborne- Mendel - [rat] Female (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 474 , 949 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	No effects were observed on incidences of neoplastic or non- neoplastic lesions based on necropsy and histopathology examination for these organs/ systems.	National Institute of Health (1977)	Medium
Cardiovascular	Chronic (> 90 days)	Mouse B6C3F1 - [mouse] Male (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 536 , 1072 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	No effects were observed on incidences of neoplastic or non- neoplastic lesions based on necropsy and histopathology examination for these organs/ systems.	National Institute of Health (1977)	Medium

Target Organ/ System	Study Type	Species/ Strain/ Sex (Number/ group)	Exposure Route	Doses/ Concentrations	Duration	NOAEL/ LOAEL/ LC50 (mg/ m3 or mg/ kg-day) (Sex)	Effect	Reference	Data Quality Evaluation
Cardiovascular	Chronic (> 90 days)	Mouse B6C3F1 - [mouse] Female (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 386 , 772 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	No effects were observed on incidences of neoplastic or non-neoplastic lesions based on necropsy and histopathology examination for these organs/systems.	National Institute of Health (1977)	Medium
Endocrine	Chronic (> 90 days)	Rat Osborne- Mendel - [rat] Male (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 471 , 941 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	No effects were observed on incidences of neoplastic or non- neoplastic lesions based on necropsy and histopathology examination for these organs/ systems.	National Institute of Health (1977)	Medium
Endocrine	Chronic (> 90 days)	Rat Osborne- Mendel - [rat] Female (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 474 , 949 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	No effects were observed on incidences of neoplastic or non- neoplastic lesions based on necropsy and histopathology examination for these organs/ systems.	National Institute of Health (1977)	Medium

Target Organ/ System	Study Type	Species/ Strain/ Sex (Number/ group)	Exposure Route	Doses/ Concentrations	Duration	NOAEL/ LOAEL/ LC50 (mg/ m3 or mg/ kg-day) (Sex)	Effect	Reference	Data Quality Evaluation
Endocrine	Chronic (> 90 days)	Mouse B6C3F1 - [mouse] Male (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 536 , 1072 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	No effects were observed on incidences of neoplastic or non- neoplastic lesions based on necropsy and histopathology examination for these organs/ systems.	National Institute of Health (1977)	Medium
Endocrine	Chronic (> 90 days)	Mouse B6C3F1 - [mouse] Female (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 386 , 772 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	No effects were observed on incidences of neoplastic or non- neoplastic lesions based on necropsy and histopathology examination for these organs/ systems.	National Institute of Health (1977)	Medium

Target Organ/ System	Study Type	Species/ Strain/ Sex (Number/ group)	Exposure Route	Doses/ Concentrations	Duration	NOAEL/ LOAEL/ LC50 (mg/ m3 or mg/ kg-day) (Sex)	Effect	Reference	Data Quality Evaluation
Gastrointestinal	Chronic (> 90 days)	Rat Osborne- Mendel - [rat] Male (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 471 , 941 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	No effects were observed on incidences of neoplastic or non- neoplastic lesions based on necropsy and histopathology examination for these organs/ systems.	National Institute of Health (1977)	Medium
Gastrointestinal	Chronic (> 90 days)	Rat Osborne- Mendel - [rat] Female (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 474 , 949 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	No effects were observed on incidences of neoplastic or non- neoplastic lesions based on necropsy and histopathology examination for these organs/ systems.	National Institute of Health (1977)	Medium
Gastrointestinal	Chronic (> 90 days)	Mouse B6C3F1 - [mouse] Male (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 536 , 1072 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	No effects were observed on incidences of neoplastic or non- neoplastic lesions based on necropsy and histopathology examination for these organs/ systems	National Institute of Health (1977)	Medium

Target Organ/ System	Study Type	Species/ Strain/ Sex (Number/ group)	Exposure Route	Doses/ Concentrations	Duration	NOAEL/ LOAEL/ LC50 (mg/ m3 or mg/ kg-day) (Sex)	Effect	Reference	Data Quality Evaluation
Gastrointestinal	Chronic (> 90 days)	Mouse B6C3F1 - [mouse] Female (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 386 , 772 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	No effects were observed on incidences of neoplastic or non- neoplastic lesions based on necropsy and histopathology examination for these organs/ systems.	National Institute of Health (1977)	Medium
Growth (early life) and Development	Reproductive	Rat Other Both (24/ sex/ group in F0 parents)	Inhalation	0 , 686 , 2058 , 6860 mg/ m ³ (0 , 100 , 300 , 1000 ppm)	6 hours/ day in multi-generation study (including prior to mating through 2 nd generation)	Not Reported	Decreased F1 male and female pup weights from PNDs 5 to 29	Halogenated Solvents (1995)	Medium
Hematological and Immune	Short-term (1- 30 days)	Rat Sprague- Dawley - [rat] Female (8)	Inhalation	0 , 686 , 2058 , 6860 mg/ m ³ (0 , 100 , 300 , 1000 ppm)	6 hours/ day 5 days/ week for 4 weeks (20 exposure days)	Not Reported	No effects on survival, hematology, antibody responses to sheep red blood cells, bronchoalveol ar lavage parameters, spleen, thymus, or kidney	Boverhof et al (2013)	High

Target Organ/ System ¹	Study Type	Species/ Strain/ Sex (Number/ group) ²	Exposure Route	Doses/ Concentrations ³	Duration ⁴	NOAEL/ LOAEL/ LC50 ⁵ (mg/ m3 or mg/ kg-day) (Sex)	Effect ⁶	Reference ⁷	Data Quality Evaluation ⁸
							weights, or spleen, thymus, lung, nasal, trachea, or bone marrow histopathology.		
Hematological and Immune	Chronic (> 90 days)	Rat Osborne-Mendel - [rat] Male (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 471 , 941 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	No effects were observed on incidences of neoplastic or non-neoplastic lesions based on necropsy and histopathology examination for these organs/ systems.	National Institute of Health (1977)	Medium
Hematological and Immune	Chronic (> 90 days)	Rat Osborne-Mendel - [rat] Female (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 474 , 949 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	No effects were observed on incidences of neoplastic or non-neoplastic lesions based on necropsy and histopathology examination for these organs/ systems.	National Institute of Health (1977)	Medium

Target Organ/ System	Study Type	Species/ Strain/ Sex (Number/ group)	Exposure Route	Doses/ Concentrations	Duration	NOAEL/ LOAEL/ LC50 (mg/m ³ or mg/ kg-day) (Sex)	Effect	Reference	Data Quality Evaluation
Hematologica l and Immune	Chronic (> 90 days)	Mouse B6C3F1 - [mouse] Male (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 536 , 1072 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	No effects were observed on incidences of neoplastic or non-neoplastic lesions based on necropsy and histopathology examination for these organs/ systems.	National Institute of Health (1977)	Medium
Hematologica l and Immune	Chronic (> 90 days)	Mouse B6C3F1 - [mouse] Female (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 386 , 772 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	No effects were observed on incidences of neoplastic or non-neoplastic lesions based on necropsy and histopathology examination for these organs/ systems.	National Institute of Health (1977)	Medium
Hematologica l and Immune	Subchronic (> 30-90 days) and Chronic (> 90 days)	Mouse (MRL/MpL); female [susceptible to autoimmune diseases]	Oral	0, 0.5 mg/mL	12, 18, and 24 weeks	Not Reported	Increased serum anti-nuclear, anti-dsDNA and anti-scleroderma 70 antibodies; increased malondialdehyde (MDA)-protein adducts and their antibodies; Splenocytes stimulated with MDS-mouse serum albumin resulted in increased Th17 cell proliferation and increased IL-17 production;	Wang et al (2017)	

Target Organ/ System	Study Type	Species/ Strain/ Sex (Number/ group)	Exposure Route	Doses/ Concentrations	Duration	NOAEL/ LOAEL/ LC50 (mg/m ³ or mg/ kg-day) (Sex)	Effect	Reference	Data Quality Evaluation
							decreased antioxidants GSH and SOD		
Hepatic	Short-term (1- 30 days)	Rat Sprague- Dawley - [rat] Female (8)	Inhalation	0 , 686 , 2058 , 6860 mg/ m ³ (0 , 100 , 300 , 1000 ppm)	6 hours/ day 5 days/ week for 4 weeks (20 exposure days)	Not Reported	Increased liver weight	Boverhof et al (2013)	High
Hepatic	Reproductive	Rat Other Both (24/ sex/ group in F0 parents)	Inhalation	0 , 686 , 2058 , 6860 mg/ m ³ (0 , 100 , 300 , 1000 ppm)	6 hours/ day in multi-generation study (including prior to mating through 2 nd generation)	Not Reported	No body weight decrease greater than 10% from control; liver weights increased at 1000 ppm in F0 males and F1 females but no histopathology changes seen.	Halogenated Solvents (1995)	Medium
Hepatic	Chronic (> 90 days)	Rat Osborne- Mendel - [rat] Male (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 471 , 941 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	No effects were observed on incidences of neoplastic or non- neoplastic lesions based on necropsy and histopathology examination for these organs/ systems.	National Institute of Health (1977)	Medium
Hepatic	Chronic (> 90 days)	Mouse B6C3F1 - [mouse] Male (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 536 , 1072 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	Decreased survival, decreased body weight gain, hunched appearance, hepatocellular carcinoma, toxic nephropathy	National Institute of Health (1977)	Medium

Target Organ/ System	Study Type	Species/ Strain/ Sex (Number/ group)	Exposure Route	Doses/ Concentrations	Duration	NOAEL/ LOAEL/ LC50 (mg/m ³ or mg/ kg-day) (Sex)	Effect	Reference	Data Quality Evaluation
Hepatic	Chronic (> 90 days)	Mouse B6C3F1 - [mouse] Female (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 386 , 772 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	Decreased survival, decreased body weight gain, hunched appearance, hepatocellular carcinoma, toxic nephropathy	National Institute of Health (1977)	Medium
Hepatic	Chronic (> 90 days)	Rat Osborne-Mendel - [rat] Female (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 474 , 949 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	No effects were observed on incidences of neoplastic or non-neoplastic lesions based on necropsy and histopathology examination for these organs/ systems.	National Institute of Health (1977)	Medium
Mortality	Acute (< 24hr)	Fischer 344-[rat] Both (6)	Oral	0 , 1300 , 2500 , 3200 , 4000 , 5000 mg/ kg-bw/ day	1 day	Not Reported	Not reported	Dow Chemical (1983)	Low
Mortality	Short-term (1-30 days)	Rat Sprague-Dawley - [rat] Female (8)	Inhalation	0 , 686 , 2058 , 6860 mg/ m ³ (0 , 100 , 300 , 1000 ppm)	6 hours/ day 5 days/ week for 4 weeks (20 exposure days)	Not Reported	No effects on survival, hematology, antibody responses to sheep red blood cells, bronchoalveolar lavage parameters, spleen, thymus, or kidney weights, or spleen, thymus, lung, nasal, trachea, or bone marrow histopathology	Boverhof et al (2013)	High

Target Organ/ System	Study Type	Species/ Strain/ Sex (Number/ group)	Exposure Route	Doses/ Concentrations	Duration	NOAEL/ LOAEL/ LC50 (mg/m ³ or mg/ kg-day) (Sex)	Effect	Reference	Data Quality Evaluation
Mortality	Chronic (> 90 days)	Rat Osborne- Mendel - [rat] Male (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 471 , 941 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	Decreased survival, decreased body weight gain, toxic nephropathy, hunched appearance	National Institute of Health (1977)	Medium
Mortality	Chronic (> 90 days)	Rat Osborne- Mendel - [rat] Female (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 474 , 949 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	Decreased survival, decreased body weight gain, toxic nephropathy, hunched appearance	National Institute of Health (1977)	Medium
Mortality	Chronic (> 90 days)	Mouse B6C3F1 - [mouse] Male (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 536 , 1072 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	Decreased survival, decreased body weight gain, hunched appearance, hepatocellular carcinoma, toxic nephropathy	National Institute of Health (1977)	Medium
Mortality	Chronic (> 90 days)	Mouse B6C3F1 - [mouse] Female (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 386 , 772 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	Decreased survival, decreased body weight gain, hunched appearance, hepatocellular carcinoma, toxic nephropathy	National Institute of Health (1977)	Medium

Target Organ/ System	Study Type	Species/ Strain/ Sex (Number/ group)	Exposure Route	Doses/ Concentrations	Duration	NOAEL/ LOAEL/ LC50 (mg/m ³ or mg/ kg-day) (Sex)	Effect	Reference	Data Quality Evaluation
Neurological/ Behavior	Reproductive	Rat Other Both (24/ sex/ group in F0 parents)	Inhalation	0 , 686 , 2058 , 6860 mg/ m ³ (0 , 100 , 300 , 1000 ppm)	6 hours/ day in multi-generation study (including prior to mating through 2 nd generation)	Not Reported	Neurological: clinical signs (decreased activity and response to sound). Renal: Increased kidney weight; increased incidence of minimal chronic progressive glomerulo- nephropathy; increased pleomorphism within the proximal tubular nuclei. Effects seen in F0 and F1 parents.	Halogenated Solvents (1995)	Medium
Neurological/ Behavior	Chronic (> 90 days)	Rat Osborne- Mendel - [rat] Male (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 471 , 941 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	decreased survival, decreased body weight gain, toxic nephropathy, hunched appearance	National Institute of Health (1977)	Medium
Neurological/ Behavior	Chronic (> 90 days)	Rat Osborne- Mendel - [rat] Female (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 474 , 949 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	decreased survival, decreased body weight gain, toxic nephropathy, hunched appearance	National Institute of Health (1977)	Medium

Target Organ/ System	Study Type	Species/ Strain/ Sex (Number/ group)	Exposure Route	Doses/ Concentrations	Duration	NOAEL/ LOAEL/ LC50 (mg/m ³ or mg/ kg-day) (Sex)	Effect	Reference	Data Quality Evaluation
Neurological/ Behavior	Chronic (> 90 days)	Mouse B6C3F1 - [mouse] Male (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 536 , 1072 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	Decreased survival, decreased body weight gain, hunched appearance, hepatocellular carcinoma, toxic nephropathy	National Institute of Health (1977)	Medium
Neurological/ Behavior	Chronic (> 90 days)	Mouse B6C3F1 - [mouse] Female (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 386 , 772 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	Decreased survival, decreased body weight gain, hunched appearance, hepatocellular carcinoma, toxic nephropathy	National Institute of Health (1977)	Medium
Renal	Reproductive	Rat Other Both (24/ sex/ group in F0 parents)	Inhalation	0 , 686 , 2058 , 6860 mg/ m ³ (0 , 100 , 300 , 1000 ppm)	6 hours/ day in multi-generation study (including prior to mating through 2 nd generation)	Not Reported	Neurological: clinical signs (decreased activity and response to sound). Renal: Increased kidney weight; increased incidence of minimal chronic progressive glomerulo- nephropathy; increased pleomorphism within the proximal tubular nuclei. Effects seen in F0 and F1 parents.	Halogenated Solvents (1995)	Medium

Target Organ/ System	Study Type	Species/ Strain/ Sex (Number/ group)	Exposure Route	Doses/ Concentrations	Duration	NOAEL/ LOAEL/ LC50 (mg/ m3 or mg/ kg-day) (Sex)	Effect	Reference	Data Quality Evaluation
Renal	Chronic (> 90 days)	Rat Osborne- Mendel - [rat] Male (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 471 , 941 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	Decreased survival, decreased body weight gain, toxic nephropathy, hunched appearance	National Institute of Health (1977)	Medium
Renal	Chronic (> 90 days)	Rat Osborne- Mendel - [rat] Female (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 474 , 949 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	Decreased survival, decreased body weight gain, toxic nephropathy, hunched appearance	National Institute of Health (1977)	Medium
Renal	Chronic (> 90 days)	Mouse B6C3F1 - [mouse] Male (50 (treated),	Oral	0 , 536 , 1072 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	Decreased survival, decreased body weight gain, hunched appearance, hepatocellular carcinoma, toxic nephropathy	National Institute of Health (1977)	Medium

Target Organ/ System	Study Type	Species/ Strain/ Sex (Number/ group)	Exposure Route	Doses/ Concentrations	Duration	NOAEL/ LOAEL/ LC50 ⁵ⁱ (mg/ m3 or mg/ kg-day) (Sex)	Effect	Reference	Data Quality Evaluation
Renal	Chronic (> 90 days)	Mouse B6C3F1 - [mouse] Female (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 386 , 772 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	decreased survival, decreased body weight gain, hunched appearance, hepatocellular carcinoma, toxic nephropathy	National Institute of Health (1977)	Medium
Reproductive / Develop- mental	Reproductive	Rat Other Both (24/ sex/ group in F0 parents)	Inhalation	0 , 686 , 2058 , 6860 mg/ m ³ (0 , 100 , 300 , 1000 ppm)	6 hours/ day in multi-generation study (including prior to mating through 2 nd generation)	NOAEL = 2058 mg/ m ³	At the 1000 ppm, there were reductions in percentage of pups born alive (F1, F2a, and F2b litters) and decreased pup survival PND 1-5 (F1 ,F2a, and F2c litters) and PND 5-22 (F1 and F2a). Decreased testes weights observed at 300 and 1000 ppm of F1 parents, but there was no associated histopathology, no male- dependent effects on fertility, and no change in testes weights in F0 males.	Halogenated Solvents (1995)	Medium

Target Organ/ System	Study Type	Species/ Strain/ Sex (Number/ group)	Exposure Route	Doses/ Concentrations	Duration	NOAEL/ LOAEL/ LC50 (mg/ m3 or mg/ kg-day) (Sex)	Effect	Reference	Data Quality Evaluation
Reproductive / Develop- mental	Chronic (> 90 days)	Rat Osborne- Mendel - [rat] Male (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 471 , 941 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	No effects were observed on incidences of neoplastic or non- neoplastic lesions based on necropsy and histopathology examination for these organs/ systems.	National Institute of Health (1977)	Medium
Reproductive / Develop- mental	Chronic (> 90 days)	Rat Osborne- Mendel - [rat] Female (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 474 , 949 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	No effects were observed on incidences of neoplastic or non- neoplastic lesions based on necropsy and histopathology examination for these organs/ systems.	National Institute of Health (1977)	Medium
Reproductive / Develop- mental	Chronic (> 90 days)	Mouse B6C3F1 - [mouse] Male (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 536 , 1072 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	No effects were observed on incidences of neoplastic or non- neoplastic lesions based on necropsy and histopathology examination for these organs/ systems.	National Institute of Health (1977)	Medium

Target Organ/ System	Study Type	Species/ Strain/ Sex (Number/ group)	Exposure Route	Doses/ Concentrations	Duration	NOAEL/ LOAEL/ LC50 (mg/ m3 or mg/ kg-day) (Sex)	Effect	Reference	Data Quality Evaluation
Reproductive / Develop- mental	Chronic (> 90 days)	Mouse B6C3F1 - [mouse] Female (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 386 , 772 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	No effects were observed on incidences of neoplastic or non- neoplastic lesions based on necropsy and histopathology examination for these organs/ systems.	National Institute of Health (1977)	Medium
Respiratory	Short-term (1- 30 days)	Rat Sprague- Dawley - [rat] Female (8)	Inhalation	0 , 686 , 2058 , 6860 mg/ m ³ (0 , 100 , 300 , 1000 ppm)	6 hours/ day 5 days/ week for 4 weeks (20 exposure days)	Not Reported	No effects on survival, hematology, antibody responses to sheep red blood cells, bronchoalveolar lavage parameters, spleen, thymus, or kidney weights, or spleen, thymus, lung, nasal, trachea, or bone marrow histopathology	Boverhof et al (2013)	High

Target Organ/ System	Study Type	Species/ Strain/ Sex (Number/ group)	Exposure Route	Doses/ Concentrations	Duration	NOAEL/ LOAEL/ LC50 (mg/ m3 or mg/ kg-day) (Sex)	Effect	Reference	Data Quality Evaluation
Respiratory	Chronic (> 90 days)	Rat Osborne- Mendel - [rat] Male (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 471 , 941 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	No effects were observed on incidences of neoplastic or non- neoplastic lesions based on necropsy and histopathology examination for these organs/ systems.	National Institute of Health (1977)	Medium
Respiratory	Chronic (> 90 days)	Rat Osborne- Mendel - [rat] Female (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 474 , 949 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	No effects were observed on incidences of neoplastic or non- neoplastic lesions based on necropsy and histopathology examination for these organ systems	National Institute of Health (1977)	Medium
Respiratory	Chronic (> 90 days)	Mouse B6C3F1 - [mouse] Male (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 536 , 1072 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	No effects were observed on incidences of neoplastic or non- neoplastic lesions based on necropsy and histopathology examination for these organs/ systems.	National Institute of Health (1977)	Medium

Target Organ/ System ¹	Study Type	Species/ Strain/ Sex (Number/ group) ²	Exposure Route	Doses/ Concentrations ³	Duration ⁴	NOAEL/ LOAEL/ LC50 (mg/ m3 or mg/ kg-day) (Sex)	Effect ⁶	Reference ⁷	Data Quality Evaluation ⁸
Respiratory	Chronic (> 90 days)	Mouse B6C3F1 - [mouse] Female (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 386 , 772 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	No effects were observed on incidences of neoplastic or non- neoplastic lesions based on necropsy and histopathology examination for these organs/ systems.	National Institute of Health (1977)	Medium
Skin and Connective Tissue	Chronic (> 90 days)	Rat Osborne- Mendel - [rat] Male (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 471 , 941 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	No effects were observed on incidences of neoplastic or non- neoplastic lesions based on necropsy and histopathology examination for these organs/ systems.	National Institute of Health (1977)	Medium
Skin and Connective Tissue	Chronic (> 90 days)	Rat Osborne- Mendel - [rat] Female (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 474 , 949 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	No effects were observed on incidences of neoplastic or non- neoplastic lesions based on necropsy and histopathology examination for these organs/ systems.	National Institute of Health (1977)	Medium

Target Organ/ System	Study Type	Species/ Strain/ Sex (Number/ group)	Exposure Route	Doses/ Concentrations	Duration	NOAEL/ LOAEL/ LC50 (mg/ m3 or mg/ kg-day) (Sex)	Effect	Reference	Data Quality Evaluation
Skin and Connective Tissue	Chronic (> 90 days)	Rat Osborne- Mendel - [rat] Female (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 474 , 949 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	No effects were observed on incidences of neoplastic or non- neoplastic lesions based on necropsy and histopathology examination for these organs/ systems.	National Institute of Health (1977)	Medium
Skin and Connective Tissue	Chronic (> 90 days)	Mouse B6C3F1 - [mouse] Male (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 536 , 1072 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	No effects were observed on incidences of neoplastic or non- neoplastic lesions based on necropsy and histopathology examination for these organs/ systems.	National Institute of Health (1977)	Medium
Skin and Connective Tissue	Chronic (> 90 days)	Mouse B6C3F1 - [mouse] Female (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 386 , 772 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	No effects were observed on incidences of neoplastic or non- neoplastic lesions based on necropsy and histopathology examination for these organs/ systems.	National Institute of Health (1977)	Medium

Target Organ/ System	Study Type	Species/ Strain/ Sex (Number/ group)	Exposure Route	Doses/ Concentrations	Duration	NOAEL/ LOAEL/ LC50 (mg/ m3 or mg/ kg-day) (Sex)	Effect	Reference	Data Quality Evaluation
Thyroid	Chronic (> 90 days)	Rat Osborne- Mendel - [rat] Male (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 471 , 941 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	No effects were observed on incidences of neoplastic or non- neoplastic lesions based on necropsy and histopathology examination for these organs/ systems.	National Institute of Health (1977)	Medium
Thyroid	Chronic (> 90 days)	Rat Osborne- Mendel - [rat] Female (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 474 , 949 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	No effects were observed on incidences of neoplastic or non- neoplastic lesions based on necropsy and histopathology examination for these organs/ systems.	National Institute of Health (1977)	Medium
Thyroid	Chronic (> 90 days)	Mouse B6C3F1 - [mouse] Male (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 536 , 1072 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	No effects were observed on incidences of neoplastic or non- neoplastic lesions based on necropsy and histopathology examination for these organs/ systems.	National Institute of Health (1977)	Medium

Target Organ/ System	Study Type	Species/ Strain/ Sex (Number/ group)	Exposure Route	Doses/ Concentrations	Duration	NOAEL/ LOAEL/ LC50 (mg/ m3 or mg/ kg-day) (Sex)	Effect	Reference	Data Quality Evaluation
Thyroid	Chronic (> 90 days)	Mouse B6C3F1 - [mouse] Female (50 (treated), 20 (untreated and vehicle controls))	Oral	0 , 386 , 772 mg/ kg-bw/ day	5 days/ week for 78 weeks	Not Reported	No effects were observed on incidences of neoplastic or non- neoplastic lesions based on necropsy and histopathology examination for these organs/ systems.	National Institute of Health (1977)	Medium
Developmental Effects (Neurotoxicity)	Developmental	Mouse, NMRI, M, n = 36-48/ group	Oral, gavage	0, 5, or 320 mg/ kg- day	PNDs 10-16, for exposure days and PND 60 was last day of study	LOAEL = 5 mg/ kg-day	Spontaneous activity (locomotion, rearing, and total activity	(Fredriksson et al., 1993)	Medium

* Unacceptable studies not included in table