United States
Environmental Protection Agency

Office of Chemical Safety and
Pollution Prevention

Risk Evaluation for Trichloroethylene

Systematic Review Supplemental File:

Data Extraction for Human Health Hazard Studies

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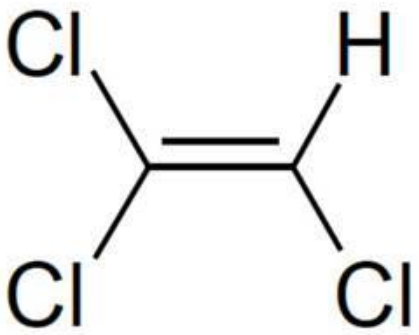

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Note: The tables below present data summaries of animal and epidemiological studies considered for dose-response assessment, as described in Section 3.2.5 of the Risk Evaluation. Studies that were excluded due to an Unacceptable or Low data quality 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.

1 Summary of Animal Studies Considered for Dose-Response Assessment of TCE

Target Organ/ System	Study Type	Species/ Strain/Sex (Number/ group)[1]	Exposure Route	Doses/ Concentrations[2]	Duration[3]	Effect Dose/ Concentration[4] (mg/m3 or mg/kg-day) (Sex)	Effect[5]	Reference[6]	Data Quality Evaluation[7]
Mortality	Develop-mental	Rat, F344, F (n=8-12 dams/group)	Oral, gavage (corn oil)	0, 10.1, 32, 101, 320, 475, 633, 844 or 1125 mg/kg-day	Gestation days 6-15	NOAEL= 844 mg/kg-day[8]	Dam mortality	(Narotsky et al., 1995)	High
Mortality	Chronic	Rat, ACI, M/F (n=100/group)	Oral, gavage (corn oil)	0, 500 or 1000 mg/kg-day	5 days/week for 103 weeks	LOAEL= 500 mg/kg-day (M) NOAEL= 500 mg/kg-day (F)[9]	Mortality	(NTP, 1988)	Medium
Mortality	Chronic	Rat, August, M/F (n=100/group)	Oral, gavage (corn oil)	0, 500 or 1000 mg/kg-day	5 days/week for 103 weeks	NOAEL= 1000 mg/kg-day (M/F)[9]	Mortality	(NTP, 1988)	Medium
Mortality	Chronic	Rat, Marshall, M/F (n=100/group)	Oral, gavage (corn oil)	0, 500 or 1000 mg/kg-day	5 days/week for 103 weeks	LOAEL= 500 mg/kg-day (M/F)[9]	Mortality	(NTP, 1988)	Medium
Mortality	Chronic	Rat, Osborne-Mendel, M/F (n=100/group)	Oral, gavage (corn oil)	0, 500 or 1000 mg/kg-day	5 days/week for 103 weeks	NOAELs= 1000 mg/kg-day (M) and 500 mg/kg-day (F)[9]	Mortality	(NTP, 1988)	Medium

Target Organ/ System	Study Type	Species/ Strain/Sex (Number/ group)[1]	Exposure Route	Doses/ Concentrations[2]	Duration[3]	Effect Dose/ Concentration[4] (mg/m3 or mg/kg-day) (Sex)	Effect[5]	Reference[6]	Data Quality Evaluation[7]
Mortality	Acute	Mouse, CD-1, Female (38+)	Inhalation	0, 5, 10, 25, 50, 100 or 200 ppm	3 hour	NOAEC = 25 ppm	Dose-responsive statistically significant increase in mortality following respiratory infection beginning at 50 ppm	(Selgrade and Gilmour, 2010)	High
Body Weight	Develop-mental	Rat, F344, F (n=8-12 dams/group)	Oral, gavage (corn oil)	0, 10.1, 32, 101, 320, 475, 633, 844 or 1125 mg/kg-day	Gestation days 6-15	NOAEL= 320 mg/kg-day (F)[8]	Significant decrease in dam body weight gain GD 6-20	(Narotsky et al., 1995)	High
Body Weight	Short-term	Rat, F344, M/F (n=40/group [20 pairs/group], 80 controls	Oral, diet	Doses in mg/kg-day were not available (0, 0.60, 1.20, 2.40, 3.61 or 4.82%, micro-encapsulated)	14 days	NOAEL= 0.60% (M/F)[9]	Significant decrease in body weight gain	(George et al., 1986)	High

Target Organ/ System	Study Type	Species/ Strain/Sex (Number/ group)[1]	Exposure Route	Doses/ Concentrations[2]	Duration[3]	Effect Dose/ Concentration[4] (mg/m3 or mg/kg-day) (Sex)	Effect[5]	Reference[6]	Data Quality Evaluation[7]
Body Weight	Repro-ductive	Rat, F344, M/F (n=16/group)	Oral, diet	0, 72, 186 or 389 mg/kg-day (estimated) (0, 0.15, 0.30 or 0.60%, micro-encapsulated)	Breeders were exposed continuously to TCE in the feed; sexes were housed separately for 1 week premating, then males and females from the same dose group were randomly paired and cohabited for 13-14 weeks; pregnant females were exposed throughout gestation	LOAEL= 72 mg/kg-day (estimated) (0.15%) (M/F)[8]	Significant decrease in terminal body weight in both sexes; significant decrease in postpartum dam body weight at all doses in F0 and F1 rats	(George et al., 1986)	High

Target Organ/ System	Study Type	Species/ Strain/Sex (Number/ group)[1]	Exposure Route	Doses/ Concentrations[2]	Duration[3]	Effect Dose/ Concentration[4] (mg/m3 or mg/kg-day) (Sex)	Effect[5]	Reference[6]	Data Quality Evaluation[7]
Cardio-vascular	Re-productive	Rat, Sprague Dawley, F (n=116 females allocated to 11 groups)	Oral, drinking water	Data for estimation of doses in mg/kg-day were not available (0, 1.5 or 1100 ppm)	2 months before mating and/or during gestation	Maternal NOAEL= 1100 ppm in water (F) Developmental LOAEL= 1.5 ppm in water[8]	Statistically significant increase in heart defects in fetuses, primarily atrial septal defects, found at both dose levels in groups exposed prior to pregnancy and during pregnancy	(Dawson et al., 1993)	Medium
Cardio-vascular	Develop-mental	Rat, Sprague-Dawley, F (n=55 controls and 9-13/dosed group)	Oral, drinking water	0, 0.00045, 0.048, 0.218, or 129 mg/kg-d (0, 0.0025, 0.25, 1.5 or 1100 ppm)	Throughout pregnancy (22 days)	NOAEL= 0.048 mg/kg-d (F)[8]	Statistically significant increase in percentage of abnormal hearts and the percentage of litters with abnormal hearts at 0.048 mg/kg-d (250 ppb) and higher	(Johnson et al., 2003)	Medium
Immune	Short-term	Rat, Sprague Dawley, F (n=16/group)	Inhalation, vapor, whole body	0, 543, 1629 or 5430 mg/m3 (0, 100, 300 or 1000 ppm)	6 hours/day, 5 days/week for 4 weeks	NOAEL= 1629 mg/m3 (F)[8]	Immuno-suppression (decreased plaque-forming cell assay response)	(Woolhiser et al., 2006)	High

Target Organ/ System	Study Type	Species/ Strain/Sex (Number/ group)[1]	Exposure Route	Doses/ Concentrations[2]	Duration[3]	Effect Dose/ Concentration[4] (mg/m3 or mg/kg-day) (Sex)	Effect[5]	Reference[6]	Data Quality Evaluation[7]
Immune	Subchronic	Mouse, MRL-lpr/lpr (autoimmune prone strain), M (n=5/group)	Inhalation, vapor, whole body	0, 2715, 5430 or 10,859 mg/m3 (0, 500, 1000 or 2000 ppm)	4 hours/day, 6 days/week for 8 weeks	LOAEL= 2715 mg/m3 (M)[8]	Auto-immunity (changes in immune-reactive organs)	(Kaneko et al., 2000)	Medium
Immune	Short-term	Mouse, CD-1, M (n=9-12/group)	Oral, gavage in 10% emulphor	0, 24 or 240 mg/kg-day	Daily for 14 days	LOAEL= 24 mg/kg-day (M)[8]	Statistically significant decrease in cell-mediated immune response to SRBC	(Sanders et al., 1982)	High
Immune	Chronic	Mouse, NZB x NZW, F (n=10/group)	Oral, drinking water	0, 0.35 or 3.5 mg/kg-day (0, 1.4 or 14 ppm)	27 weeks	LOAEL= 0.35 mg/kg-day (F)[8]	Auto-immunity (increased anti-dsDNA antibodies at 19 and 32-34 weeks	(Keil et al., 2009)	High
Immune	Chronic	Mouse, B6C3F1, F (n=10/group)	Oral, drinking water	0, 0.35 or 3.5 mg/kg-day (0, 1.4 or 14 ppm)	30 weeks	LOAEL= 0.35 mg/kg-day (F)[8]	Auto-immunity (increased dsDNA and ssDNA antibodies and decrease in thymus weight.	(Keil et al., 2009)	High

Target Organ/ System	Study Type	Species/ Strain/Sex (Number/ group)[1]	Exposure Route	Doses/ Concentrations[2]	Duration[3]	Effect Dose/ Concentration[4] (mg/m3 or mg/kg-day) (Sex)	Effect[5]	Reference[6]	Data Quality Evaluation[7]
Immune	Chronic	Mouse, CD-1, M/F (n=14-50/group)	Oral, drinking water with 1% emulphor	0, 18, 217, 393 or 660 mg/kg-day (0, 0.1, 1.0, 2.5 or 5 mg/mL)	4-6 months	LOAEL= 18 mg/kg-day (F)[8]	Immuno-suppression in females (decreased cell-mediated immunity and bone marrow stem cell colonization in females)	(Sanders et al., 1982)	High
Immune	Acute	Mouse, CD-1, Female (4-5)	Inhalation	0, 50, 100 or 200 ppm	3 hour	LOAEC = 50 ppm (24hr); NOAEC = 50 ppm (72hr)	Following respiratory bacterial infection, reduced clearance from lung, increased percent of mice infected, and reduced amount of phagocytosis	(Selgrade and Gilmour, 2010)	High
Hepatic	Short-term	Rat, Sprague Dawley, F (n=16/group)	Inhalation, vapor, whole body	0, 553, 1629 or 5429 mg/m3 (0, 100, 300 or 1000 ppm)	6 hours/day, 5 days/week for 4 weeks	NOAEL= 1629 mg/m3 (F)[9] BMDL= 137 mg/m3 (25.2 ppm) (F)[8]	Increased liver/body weight ratio	(Woolhiser et al., 2006)	Medium
Hepatic	Short-term/Subchronic	Mouse, NMRI, M/F (n=10-20/group)	Inhalation, (not stated if vapor or aerosol), whole body	0, 201, 407, 814, 1222, 1629, 2443, 4886, 9773 or 19,546 mg/m3 (0, 37, 75, 150, 225, 300, 450, 900, 1800 or 3600 ppm)	Continuous and intermittent exposures, variable time periods of 1-24 hours/day for 30 days	LOAEL= 201 mg/m3 (M/F)[9]	Increased liver weight	(Kjellstrand et al., 1983)	Medium

Target Organ/ System	Study Type	Species/ Strain/Sex (Number/ group)[1]	Exposure Route	Doses/ Concentrations[2]	Duration[3]	Effect Dose/ Concentration[4] (mg/m3 or mg/kg-day) (Sex)	Effect[5]	Reference[6]	Data Quality Evaluation[7]
Hepatic	Subchronic	Mouse, MRL-lpr/lpr, M (n=5/group)	Inhalation, vapor, whole body	0, 2715, 5430 or 10,859 mg/m3 (0, 500, 1000 or 2000 ppm)	4 hours/day, 6 days/week for 8 weeks	LOAEL= 2715 mg/m3 (M)[8]	Liver inflammation including sporadic necrosis in the hepatic lobule	(Kaneko et al., 2000)	Medium
Hepatic	Subchronic	Mouse, Swiss-Cox, M (n=12-15/group)	Oral, gavage (corn oil)	0, 100, 200, 400, 800, 1600, 2400 or 3200 mg/kg-day	5 days/week for 6 weeks	LOAEL= 100 mg/kg-day[9]	Increased liver/body weight ratio	(Buben and O'Flaherty, 1985)	High
Neuro-logical	Subchronic	Rat, Wistar, M (n=5/group)	Inhalation, vapor, whole body	0, 271, 543 or 1629 mg/m3 (0, 50, 100 and 300 ppm)	8 hours/day, 5 days/week for 6 weeks	LOAEL= 271 mg/m3 (M)[8]	Significant decreases in wakefulness at all concentrations	(Arito et al., 1994)	Medium
Neuro-logical	Develop-mental	Rat, F344, F (n=8-12 dams/group)	Oral, gavage (corn oil)	0, 10.1, 32, 101, 320, 475, 633, 844 or 1125 mg/kg-day	Gestation days 6-15	NOAEL= 475 mg/kg-day (F)[8]	Transient ataxia in dams, usually within 4 hours of dosing	(Narotsky et al., 1995)	High

Target Organ/ System	Study Type	Species/ Strain/Sex (Number/ group)[1]	Exposure Route	Doses/ Concentrations[2]	Duration[3]	Effect Dose/ Concentration[4] (mg/m3 or mg/kg-day) (Sex)	Effect[5]	Reference[6]	Data Quality Evaluation[7]
Neuro-logical	Short-term/ Subchronic	Rat, Sprague Dawley, (M weanlings) (n=12/group)	Oral, drinking water	(Control) 0 mg/kg-day for 8 weeks; (Group 1) 47 mg/kg-day for 4 weeks + 0 mg/kg-day for 4 weeks; (Group 2) 47 mg/kg-day for 4 weeks + 0 mg/kg-day for 2 weeks + 24 mg/kg-day for 2 weeks	Various (see Doses/Con-centrations column)	LOAEL= 47 mg/kg-day (M weanlings)[8]	Cognitive effects (Demyelination of hippocampus in all TCE-treated groups)	(Isaacson et al., 1990)	Medium

Target Organ/ System	Study Type	Species/ Strain/Sex (Number/ group)[1]	Exposure Route	Doses/ Concentrations[2]	Duration[3]	Effect Dose/ Concentration[4] (mg/m3 or mg/kg-day) (Sex)	Effect[5]	Reference[6]	Data Quality Evaluation[7]
Neuro-logical	Repro-ductive	Rat, F344, M/F (n=40/group [20 pairs/group], 80 controls	Oral, diet	0, 72, 186 or 389 mg/kg-day, estimated (0, 0.15, 0.30 or 0.60%, micro-encapsulated)	Breeders were exposed continuously to TCE in the feed; sexes were housed separately for 1 week premating, then males and females from the same dose group were randomly paired and cohabited for 13-14 weeks; pregnant females were exposed throughout gestation	72 mg/kg-day (estimated) (M/F pups)[8]	Open field testing in pups: a statistically significant dose-related trend toward increased time required for male and female pups to cross the first grid in the test device	(George et al., 1986)	High
Neuro-logical	Develop-mental	Mouse, NMRI, M (n=12 male pups from 3-4 different litters/group of non-dosed dams)	Oral, gavage (fat emulsions prepared from egg lecithin and peanut oil)	0, 50 or 290 mg/kg-day	Postnatal days 10-16	LOAEL= 50 mg/kg-day (M pups)[8]	Decreased rearing activity on postnatal day 60 (M pups)	(Fredriksson et al., 1993)	Medium

Target Organ/ System	Study Type	Species/ Strain/Sex (Number/ group)[1]	Exposure Route	Doses/ Concentrations[2]	Duration[3]	Effect Dose/ Concentration[4] (mg/m3 or mg/kg-day) (Sex)	Effect[5]	Reference[6]	Data Quality Evaluation[7]
Ocular	Develop-mental	Rat, F344, F (n=8-12 dams/group)	Oral, gavage (corn oil)	0, 10.1, 32, 101, 320, 475, 633, 844 or 1125 mg/kg-day	Gestation days 6-15	NOAEL= 32 mg/kg-day for dose-related increase (M/F pups combined)[8]; NOAEL= 844 mg/kg-d for statistically significant increase (M/F pups combined)[8] BMDL= 60 mg/kg-day[8]	Increased percentage of pups with eye defects	(Narotsky et al., 1995)	High
Renal	Short-term	Rat, Sprague Dawley, F (n=16/group)	Inhalation, vapor, whole body	0, 553, 1629 or 5429 mg/m3 (0, 100, 300 or 1000 ppm)	6 hours/day, 5 days/week for 4 weeks	NOAEL= 1629 mg/m3 (F)[9]	Increased kidney weight/body weight ratio	(Woolhiser et al., 2006)	Medium
Renal	Chronic	Rat, Sprague Dawley, M/F (n=135 M controls, 145 F controls, 260/exposed group)	Inhalation, (not clear if vapor or aerosol), whole body	0, 543, 1629 or 3258 mg/m3 (0, 100, 300 or 600 ppm)	7 hours/day, 5 days/week for 104 weeks	NOAEL= 3258 mg/m3 (F) NOAEL= 543 mg/m3 (M)[9]	Increased renal megalo-nucleo-cytosis in males at mid and high concentration	(Maltoni et al., 1986)	High
Renal	Chronic	Rat, Sprague Dawley, M/F (n=60/group)	Oral, gavage (olive oil)	0, 50 or 250 mg/kg-day	4-5 days/week for 52 weeks	NOAEL= 250 mg/kg-day (F) NOAEL= 50 mg/kg-day (M)[9]	Increased renal megalo-nucleo-cytosis in high-dose males	(Maltoni et al., 1986)	High

Target Organ/ System	Study Type	Species/ Strain/Sex (Number/ group)[1]	Exposure Route	Doses/ Concentrations[2]	Duration[3]	Effect Dose/ Concentration[4] (mg/m3 or mg/kg-day) (Sex)	Effect[5]	Reference[6]	Data Quality Evaluation[7]
Renal	Chronic	Rat, ACI, August Marshall and Osborne-Mendel, M/F (n=100/group/ rat strain)	Oral, gavage (corn oil)	0, 500 or 1000 mg/kg-day	5 days/week for 103 weeks	LOAEL= 500 mg/kg-day (M/F of all rat strains)[9] BMDL10= 9.45 mg/kg-day (F, most sensitive strain [Marshall])[8]	Kidney cytomegaly and toxic nephropathy in rats of all exposed groups	(NTP, 1988)	Medium

Target Organ/ System	Study Type	Species/ Strain/Sex (Number/ group)[1]	Exposure Route	Doses/ Concentrations[2]	Duration[3]	Effect Dose/ Concentration[4] (mg/m3 or mg/kg-day) (Sex)	Effect[5]	Reference[6]	Data Quality Evaluation[7]
Renal	Subchronic/ Chronic	Mouse, NMRI, M/F (n=10-20/group)	Inhalation, (not stated if vapor or aerosol), whole body	0, 201, 407, 814, 1222, 1629, 2443, 4886, 9773 or 19,546 mg/m3 (0, 37, 75, 150, 225, 300, 450, 900, 1800 or 3600 ppm)	Continuous and intermittent exposures of 1-24 hours/day for 30 or 120 days	NOAELs (30-day exposure)= 201 mg/m3 (M) and 407 mg/m3 (F)[9]	Increased kidney weight	(Kjellstrand et al., 1983)	Medium
Renal	Chronic	Mouse, B6C3F1, M/F (n=180/group)	Inhalation, (not clear if vapor or aerosol), whole body,	0, 543, 1629 or 3258 mg/m3 (0, 100, 300 or 600 ppm)	7 hours/day, 5 days/week for 78 weeks	NOAEL= 3258 mg/m3 (M/F)[9]	Renal megalo-nucleocytosis was not present in control or treated mice of either sex	(Maltoni et al., 1986)	Medium
Repro-ductive	Short-term/ Subchronic	Rat, Wistar, M (n=12-13/group)	Inhalation, (unclear if vapor or aerosol), whole body	0 or 2041 mg/m3 (0 or 376 ppm)	4 hours/day, 5 days/week for 2-10 weeks exposure; 2-8 weeks unexposed	LOAEL= 2041 mg/m3 (M)[8]	Sperm abnormalities, alterations in testes histology (smaller, necrotic spermatogenic tubules), and increased pre- and/or postimplanation loss in groups with 2 or 10 weeks exposure or 5 weeks exposure with 2 weeks recovery	(Kumar et al., 2000)	Medium

Target Organ/ System	Study Type	Species/ Strain/Sex (Number/ group)[1]	Exposure Route	Doses/ Concentrations[2]	Duration[3]	Effect Dose/ Concentration[4] (mg/m3 or mg/kg-day) (Sex)	Effect[5]	Reference[6]	Data Quality Evaluation[7]
Repro-ductive	Subchronic/ Chronic	Rat, Wistar, M (n=6/group)	Inhalation, (unclear if vapor or aerosol), whole body	0 or 2041 mg/m3 (0 or 376 ppm)	4 hours/day, 5 days/week for 12 or 24 weeks	LOAEL= 2041 mg/m3 (M)[8]	Decreased testis weight, decreased sperm count and motility, decreased numbers of spermatogenic cells and spermatids, necrosis of spermatogenic cells, atrophy of testes, and hyperplasia of Leydig cells	(Kumar et al., 2001)	High
Repro-ductive	Develop-mental	Rat, F344, F (n=8-12 dams/group)	Oral, gavage (corn oil)	0, 10.1, 32, 101, 320, 475, 633, 844 or 1125 mg/kg-day	Gestation days 6-15	Reproductive effects and maternal toxicity NOAEL= 320 mg/kg-day (F)[8]	Delayed parturition and decreased dam body weight gain GD 6-20	(Narotsky et al., 1995)	High

Target Organ/ System	Study Type	Species/ Strain/Sex (Number/ group)[1]	Exposure Route	Doses/ Concentrations[2]	Duration[3]	Effect Dose/ Concentration[4] (mg/m3 or mg/kg-day) (Sex)	Effect[5]	Reference[6]	Data Quality Evaluation[7]
Repro-ductive	Repro-ductive	Rat, F344, M/F (n=40/group [20 pairs/group],	Oral, diet	0 or 389 mg/kg-d (estimated) (0 or 0.60%, micro-encapsulated) Mating pairs were control male x control female, control male x 0.60% female, and 0.60% male x control female	In a crossover mating trial, breeding pairs that were exposed continuously to TCE in the feed were cohabited for 7 days and then separated to allow the female to deliver	LOAEL= 389 mg/kg-day (estimated)[8] (parental reproductive function)	Decreased mating index for TCE-exposed male or female groups	(George et al., 1986)	High

Target Organ/ System	Study Type	Species/ Strain/Sex (Number/ group)[1]	Exposure Route	Doses/ Concentrations[2]	Duration[3]	Effect Dose/ Concentration[4] (mg/m3 or mg/kg-day) (Sex)	Effect[5]	Reference[6]	Data Quality Evaluation[7]
Repro-ductive	Repro-ductive	Rat, F344, M/F (n=40/group [20 pairs/group], 80 controls	Oral, diet	0, 72, 186 or 389 mg/kg-day (estimated) (0, 0.15, 0.30 or 0.60%, micro-encapsulated)	Breeders were exposed continuously to TCE in the feed; sexes were housed separately for 1 week premating, then males and females from the same dose group were randomly paired and cohabited for 13-14 weeks; pregnant females were exposed throughout gestation	LOAEL= 72 mg/kg-day (estimated) (M/F)[8]	Significant decrease in postpartum dam body weight at all doses in F0 and F1 rats; significant decrease in terminal body weight in both sexes	(George et al., 1986)	High
Repro-ductive	Short-term	Mouse, CD-1, M (n=4/group)	Inhalation, vapor, whole body	0 or 5429 mg/m3 (0 or 1000 ppm)	6 hours/day, 5 days/week for 1-4 weeks	LOAEL= 5429 mg/m3 (M)[8]	Effects on epididymis epithelium	(Kan et al., 2007)	Low

Target Organ/ System	Study Type	Species/ Strain/Sex (Number/ group)[1]	Exposure Route	Doses/ Concentrations[2]	Duration[3]	Effect Dose/ Concentration[4] (mg/m3 or mg/kg-day) (Sex)	Effect[5]	Reference[6]	Data Quality Evaluation[7]
Repro-ductive	Short-term/Sub-chronic	Mouse, CD-1, M (n=4-27/group)	Inhalation, whole body	0 or 5429 mg/m3 (0 or 1000 ppm)	6 hours/day, 5 days/week for 1-6 weeks	LOAEL= 5429 mg/m3 (M)[8]	Sperm effects (decreased in vitro sperm-oocyte binding and reduced in vivo fertilization)	(Xu et al., 2004)	High
Develop-mental	Develop-mental	Rat, Sprague-Dawley, F (n=55 controls and 9-13/dosed group)	Oral, drinking water	0, 0.00045, 0.048, 0.218, or 129 mg/kg-d (0, 0.0025, 0.25, 1.5 or 1100 ppm)	Throughout pregnancy (22 days)	NOAEL= 0.048 mg/kg-d (F)[8]	Statistically significant increase in percentage of abnormal hearts and the percentage of litters with abnormal hearts at 0.048 mg/kg-d (250 ppb) and higher	(Johnson et al., 2003)	Medium
Develop-mental	Develop-mental	Rat, F344, F (n=8-12 dams/group)	Oral, gavage (corn oil)	0, 10.1, 32, 101, 320, 475, 633, 844 or 1125 mg/kg-day	Gestation days 6-15	NOAEL= 32 mg/kg-day for dose-related increase (M/F pups combined); NOAEL= 844 mg/kg-d for statistically significant increase (M/F pups combined)[8] BMDL= 60 mg/kg-day[8]	Increased percentage of pups with eye defects	(Narotsky et al., 1995)	High

Target Organ/ System	Study Type	Species/ Strain/Sex (Number/ group)[1]	Exposure Route	Doses/ Concentrations[2]	Duration[3]	Effect Dose/ Concentration[4] (mg/m3 or mg/kg-day) (Sex)	Effect[5]	Reference[6]	Data Quality Evaluation[7]
Develop-mental neuro-toxicity	Repro-ductive	Rat, F344, M/F (n=40/group [20 pairs/group], 80 controls	Oral, diet	0, 72, 186 or 389 mg/kg-day (estimated) (0, 0.15, 0.30 or 0.60%, micro-encapsulated	Breeders were exposed continuously to TCE in the feed;; pregnant females were exposed throughout gestation	LOAEL= 72 mg/kg-day (estimated) (M/F pups)[8]	Open field testing in pups: a statistically significant dose-related trend toward increased time required for M and F pups to cross the first grid in the test device; Statistically significant decreased F1 body weight at all doses on PNDs 21 and 80.	(George et al., 1986)	High
Develop-mental neuro-toxicity	Develop-mental	Mouse, NMRI, M (n=12 male pups from 3-4 different litters/group of non-dosed dams)	Oral, gavage (fat emulsions prepared from egg lecithin and peanut oil)	0, 50 or 290 mg/kg-day	Postnatal days 10-16	Developmental LOAEL= 50 mg/kg-day (M pups)[8]	Decreased rearing activity on postnatal day 60 (M pups)	(Fredriksson et al., 1993)	Medium

[1]Species/strain, sex of animals included in the study.
[2]Doses and concentrations
[3]Acute exposures defined as those occurring within a single day (<24 hr). Short-term exposures are defined as 1-30 days. Subchronic exposures are defined as 30-90 days. Chronic exposures are defined as >90 days, or 10% or more of a lifetime.
[4]Units are mg/m3 or ppm for inhalation exposure and mg/kg-day for oral exposure; sex is identified if one sex has a lower POD; this includes only the PODs identified by the study authors.
[5]The effect(s) listed were the most sensitive effects observed for that target organ/system in that study (i.e., the effect(s) upon which the POD was based).
[6]This column lists the primary reference for the reported data.
[7]Information included in this column is the result of the data quality evaluation for all acceptable studies (those with an overall rating of high, medium or low). Unacceptable studies are not included in this table.
[8]NOAEL/LOAEL/LC50 values of this row were IRIS conclusions [EPA (U.S. Environmental Protection Agency). 2011. *Toxicological Review of Trichloroethylene (CAS No. 79-01-6)*. EPA/635/R-09/011F. Integrated Risk Information System, Office of Research and Development, Washington, DC.]
[9]EPA determined NOAEL/LOAEL/LC50 values of this row based on information presented in the IRIS document (EPA, 2011) and/or in the original study report.

2 Summary of Epidemiology Studies Considered for Dose-Response Assessment of TCE

Target Organ/ System	Outcome/ Endpoint	Study Population	Exposure	Results	Reference	Data Quality Evaluation
Cancer	Renal cell cancer risk	Cases (n=86) were occupational workers from the Arve Valley (France). Age-and gender-matched controls were identified from the same geographical area (n=316).	Exposure estimated by JEM and occupational questionnaire (5 exposure groups: 1-35 35-50, 50-75, 75-100, >100 ppm). Multivariate modeling using exposed/ unexposed, cumulative dose, and cumulative dose with peak exposures. Supplemental material reported low, medium, and high cumulative doses (ppm*year) for cases and controls.	OR for high cumulative TCE dose plus peaks was 2.73 (1.06-7.07) (8 cases; 14 controls). The OR for high cumulative dose (without peaks) was 2.16 (1.02-4.60) (16 cases, 37 controls). The OR was not statistically significant after adjusting for exposure to cutting fluids (suggested lack of statistical power).	(Charbotel et al., 2006)	High
Neurological/ Behavior	Nerve function tests including autonomic nerve function, trigeminal nerve function, peripheral motor nerve function, and peripheral sensory nerve function	31 exposed male print workers (mean age 44 years) and 28 unexposed male controls (mean age 45 years) from the same plant matched for physical job activity, education, nationality, and age. The exposed workers had been employed for an average of 16 years (SD 9 years).	Mean cumulative TCE exposure based on average (704 ppm) TCE exposure and years of exposure.	Significant effects of the mean cumulative TCE exposure were observed for trigeminal nerve function (increased latency in masseter reflex) and peripheral sensory nerve function (reduction in the sensory nerve conduction velocity and prolongation in the sensory nerve refractory period). No significant changes were observed for autonomic nerve function or peripheral motor nerve function.	(Ruijten et al., 1991)	Medium

Target Organ/ System	Outcome/ Endpoint	Study Population	Exposure	Results	Reference	Data Quality Evaluation
Reproductive	Semen parameters including volume, total sperm count, sperm viability, motility, and morphology	85 male workers (mean age 28 years-old) exposed to TCE in an electronics factory (Singapore). Average exposure duration was 5.1 years (SD 2.1 years)	Urinary tetrachloroacetic acid (mg/g creatinine) collected on day of semen collection. Mean (range) urinary tetrachloroacetic acid concentration of 22.4 (0.8-136.4) mg/g creatinine	Adjusted prevalence rate ratio for hyperzoospermia (sperm density of >120 million sperm/mL ejaculate) was increased at urinary TCA concentrations >75 mg/g creatinine. Sperm density was also increased among workers with high exposure (uTCA >25 mg/g creatine) compared to workers with low exposure (uTCA <25 mg/g creatine). Decreased sperm morphology was also observed. No significant associations observed other sperm parameters	(Chia et al., 1996)	Medium

3 References

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