



Human Health Risk Assessment of Trichloroethylene from Industrial Complex A

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This study investigated the human health risks of trichloroethylene from Industrial Complex A. The excessive carcinogenic risks for central tendency exposure were 1.40×10^{-5} for male and female residents in the vicinity of Industrial Complex A. The excessive cancers risk for reasonable maximum exposure were 2.88×10^{-5} and 1.97×10^{-5} for males and females, respectively. These values indicate that there are potential cancer risks for exposure to these concentrations. The hazard index for central tendency exposure to trichloroethylene was 1.71 for male and female residents. The hazard indexes for reasonable maximum exposure were 3.27 and 2.41 for males and females, respectively. These values were over one, which is equivalent to the threshold value. This result showed that adverse cancer and non-cancer health effects may occur and that some risk management of trichloroethylene from Industrial Complex A was needed.

Key words: Risk assessment, Trichloroethylene, Volatile organic compounds, A industrial complex, Passive sampler

INTRODUCTION

Trichloroethylene (TCE) is used for vapor degreasing and as a solvent. In the past, trichloroethylene was used as an extractant in food processing. This was discontinued in 1975, when on the basis of liver tumors in mice, the National Cancer Institute (NCI) issued an alert warning that trichloroethylene may be a carcinogen. TCE has previously been shown to be carcinogenic in the liver via experiments (Herren-Freund *et al.*, 1987; Maltoni *et al.*, 1988).

The adverse non-cancer effects associated with TCE exposure via inhalation include hepatic, renal, neurological, immunological, reproductive, and developmental effects (Lilis *et al.*, 1969; Dorfmueller *et al.*, 1979). The most sensitive adverse effects observed, which were used as the primary basis for the reference concentration, were those affecting the immune system and the developing fetus and were based on route-to-route extrapolation via oral studies. Additional support for the Reference Concentration (RfC) was based on adverse effects on the kidneys (Keil *et al.*, 2009; Johnson *et al.*, 2003).

The knowledge of the acute human toxicity of TCE

comes mainly from its use as an anesthetic (Dobkin and Byles, 1963). Tachypnea and ventricular arrhythmias are correlated with overexposure (inhaled concentrations greater than 15,000 ppm). Systemic toxicity is low following anesthesia, but occasionally, hepatotoxicity has been reported, which is generally attributed to breakdown of the TCE to dichloroacetylene and phosgene by the soda-lime that is present in some recirculatory anesthesia machines (Foy *et al.*, 1996).

Elevated risks for kidney cancer have been observed across many independent studies. Twenty-four studies in which there was a high likelihood of TCE exposure in individual study subjects (e.g., based on job-exposure matrices or biomarker monitoring) and which were judged to have met, to a sufficient degree, the standards of epidemiologic design and analysis were identified in a systematic review of the epidemiologic literature. Of the 15 of these 24 studies reporting the risk of kidney cancer (Zhao *et al.*, 2005; Charbotel *et al.*, 2006; Radican *et al.*, 2008; Moore *et al.*, 2010), most estimated Relative Risks (RRs) between 1.1 and 1.9 for overall exposure to TCE. Six of these 15 studies reported statistically significantly increased risks for either overall exposure to TCE (Brüning *et al.*, 2003; Moore *et al.*, 2010; Raaschou-Nielsen *et al.*, 2003) or for one of the highest TCE exposure groups (Raaschou-Nielsen *et al.*, 2003; Zhao *et al.*, 2005; Charbotel *et al.*, 2006; Moore *et al.*, 2010). Thirteen other cohort, case-control, and

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geographic-based studies were given less weight because of the lesser likelihood of TCE exposure among their subjects and other study design limitations that would decrease statistical power and study sensitivity.

TCE was characterized as “carcinogenic to humans” by the EPA in the USA. This hazard descriptor is used when there is convincing epidemiologic evidence for a causal association between human exposure and cancer. Convincing evidence is found in the consistency of the kidney cancer findings (Maltoni *et al.*, 1988; Fukuda *et al.*, 1983; Henschler *et al.*, 1980). The consistency of the increased kidney cancer RR estimates across a large number of independent studies with different designs and populations and from different countries and industries provides compelling evidence, given the difficulty, a priori, of detecting effects in epidemiologic studies when the RRs are modest and the cancers are relatively rare, and therefore, individual studies have limited statistical power. This strong consistency argues against chance, bias, and confounding as explanations for the elevated kidney cancer risks. In addition, statistically significant exposure-response trends are observed in high-quality studies.

This study was performed in order to discover whether control is needed after the human health risk assessment for the TCE emitted from Industrial Complex A is evaluated. Industrial Complex A is a large-scale industrial complex designed for rearranging capital area and bringing in companies that create pollution. During chemical, leather, dyeing, and metal enterprises in Industrial Complex A, volatile organic compounds (VOCs) are emitted. A large-scale residential area was created in the neighboring areas of Industrial Complex A. The residential area was close to the industrial complex, and VOC emissions are increasing along with the increasing number of vehicles and the use of organic solvents by the companies located in the complex, so human health risks related to TCE could be an issue.

MATERIALS AND METHODS

Exposure assessment. In this study, the TCE concentration that was already presented in a journal was used for

Table 1. Comparison with TCE concentrations measured in other areas

Sampling site	Mean (Range) (ppb)	Reference
A industrial area (Korea)	0.8 (0.7~0.9)	(Na <i>et al.</i> , 2001)
B industrial area (Korea)	0.06 (0.01~0.31)	(Shin HS, 2004)
Urban and areas near emission sources (USA)	0.71 (0.04~1.2)	(Gist and Burg, 1995)

an assessment of the reliability of exposure. Na *et al.* showed the TCE concentration in Industrial Area A (Na *et al.*, 2001), Shin *et al.* showed the average concentration of TCE in Industrial Area B (Shin and Ahn, 2004), and Gist *et al.* showed the TCE concentration in the urban areas near emission sources in the USA (Gist and Burg, 1995) (Table 1).

Exposure scenario.

Daily Average Inhalation Rate (DAIR): The long-term exposure inhalation rate, classified according to gender and age, was taken from the Korean Exposure Factors Handbook (KEFH). These values were calculated by estimation via heart rate. For this process, in a small sample classified according to gender and age, a regression equation including respiration volume and heart rate had been previously calculated. The mean DAIRs for male and female Korean adults are 15.7 and 12.8 m³/day, respectively, and the standard deviations are 1.2 and 0.9 m³/day (Kim *et al.*, 2006).

Exposure time, frequency, and duration: Conservative values were used for exposure time, frequency, and duration, considering residents who do not immigrate to other areas and live out their entire lives. Therefore, 24 hrs was used for the exposure time, 365 days a year was used for the frequency, and the life expectancy was used for the duration.

Body weight: The body weight, classified according to gender and age, was taken from KEFH. The mean body weights for male and female Korean adults are 69.16 and 56.37 kg, respectively, and the standard deviations are 9.79 and 7.81 kg, respectively (Kim *et al.*, 2006).

Life expectancy: 78.6 years was used for life expectancy, as recommended in KEFH (Kim *et al.*, 2006).

Risk characterization. Human exposure doses (lifetime average daily doses; LADDs) were derived as shown in Equation 1.

$$\text{LADDs} = (\text{AC} \times \text{DAIR} \times \text{ET} \times \text{EF} \times \text{ED}) / (\text{BW} \times \text{LT} \times \text{AT} \times \text{AF}) \quad (\text{Eq. 1})$$

LADDs: human exposure doses (mg/kg-day)

AC: concentration in air (mg/m³)

DAIR: daily average inhalation rate (m³/day)

ET: exposure time (hr/day)

EF: exposure frequency (day/year)

ED: exposure duration (year)

BW: body weight (kg)

LT: life expectancy (year)

AT: average exposure time (hr/day)

AF: average exposure frequency (day/year)

The Toxicological Reference Value (TRV) for calculating non-carcinogenic risk was derived as shown in Equation 2, with a Point Of Departure (POD) such as NOAEL, LOAEL, or BMDL and an uncertainty factor (UF). For cal-

culating carcinogenic risk, the Unit Risk (UR) was used.

$$\text{TRV} = \text{POD}/\text{UF} \quad (\text{Eq. 2})$$

Non-carcinogenic risk was calculated via the Hazard Index (HI), which was derived as shown in Equation 3, with human exposure doses and the toxicological reference value. Carcinogenic risk was calculated via the excessive carcinogenic risk (ECR), which was derived as shown in Equation 4, with human exposure doses and unit risk.

$$\text{HI} = \text{LADDs}/\text{TRV} \quad (\text{Eq. 3})$$

$$\text{ECR} = \text{LADDs} \times \text{UR} \quad (\text{Eq. 4})$$

RESULTS

Exposure assessment for airborne TCE. Na *et al.* showed 0.8 ppb in Industrial Area A (Na *et al.*, 2001), Shin *et al.* showed the average concentration of TCE in Industrial Area B to be 0.06 ppb (Shin and Ahn, 2004), and Gist *et al.* showed the TCE concentration to be 0.71 ppb (0.04~1.2 ppb) in urban areas near emission sources in the USA (Gist and Burg, 1995) (Table 1).

In this study, the TCE concentration in Industrial Area A measured by Na *et al.* (Na *et al.*, 2001) was used in the risk

Table 2. Calculated Lifetime Average Daily Doses (LADDs) for Trichloroethylene (TCE) from Industrial Complex A

	LADDs (mg/kg-day)	
	CTE	RME
Male	9.74×10^{-4}	1.87×10^{-3}
Female	9.75×10^{-4}	1.37×10^{-3}

characterization.

Risk characterization for airborne TCE. The central tendency exposure (CTE) of LADDs to TCE were 9.74×10^{-4} and 9.75×10^{-4} mg/kg-day for male and female residents in the vicinity of Industrial Complex A, respectively, and the reasonable maximum exposure (RME) of LADDs were 1.87×10^{-3} and 1.37×10^{-3} mg/kg-day for males and females, respectively (Table 2).

The toxicological reference value was derived via the ratio of Point Of Departure (POD) to UF. The PODs of TCE were LOAEL (HEC₉₉) 0.19 mg/m³ and BMDL₉₉ (HEC₉₉) 0.021 mg/m³. The UFs of each POD are 100 and 10. The POD and UF values were suggested by the Integrated Risk Information System (IRIS) of the US EPA. The toxicological reference value of TCE was 2×10^{-3} mg/m³. The unit of concentration was converted to the unit of a dose. Applying 70 kg and 20 mg/m³ as the average body weight and inhalation rate of an American, 5.71×10^{-4} mg/kg-day was used to derive the HI (Table 3).

The HIs for CTE to TCE were 1.71 for male and female residents in the vicinity of Industrial Complex A. The HIs for RME were 3.27 and 2.41 for males and females, respectively (Table 4).

The unit risk was suggested by the Integrated Risk Information System (IRIS). The unit risk from inhalation exposure to TCE was 4.1×10^{-6} per $\mu\text{g}/\text{m}^3$. As with calculating the non-carcinogenic risk, the unit of concentration was converted to the unit of dose. Applying 70 kg and 20 mg/m³ as the average body weight and inhalation rate of an American, 1.44×10^{-5} per $\mu\text{g}/\text{kg}\cdot\text{day}$ was used to derive the ECR. The ECR for CTE was 1.40×10^{-5} for male and female res-

Table 3. Calculated Toxicological Reference Value (TRV) of Trichloroethylene (TCE) from Industrial Complex A

Critical effect	Decreased thymus weight in female B6C3F ₁ mice (Keil <i>et al.</i> , 2009)	Increased fetal cardiac malformations in Sprague-Dawley rats (NTP, 1988)
	LOAEL (HEC ₉₉) 0.19 mg/m ³	BMDL ₉₉ (HEC ₉₉) 0.021 mg/m ³
POD		
UF _H	3	3
UF _A	3	3
UF _S	1	1
UF _L	10	1
UF _D	1	1
Total UF	100	10
TRV	$0.002 \text{ mg}/\text{m}^3 = 5.71 \times 10^{-4} \text{ mg}/\text{kg}\cdot\text{day}$	

UF_H: Intraspecific uncertainty factor. Three was applied to account for possible toxicodynamic differences in sensitive humans because the probabilistic human PBPK model used in this assessment incorporates the best available information about variability in the toxicokinetic disposition toward TCE in humans, but does not account for humans who may be sensitive due to toxicodynamic factors.

UF_A: Interspecific uncertainty factor. Three was applied to account for toxicodynamic uncertainty when the use of the PBPK models to extrapolate internal doses from mice to humans reduces toxicokinetic uncertainty, but does not account for the possibility that humans may be more sensitive than mice to TCE due to toxicodynamic differences.

UF_S: Subchronic-to-Chronic-Duration uncertainty factor. One was applied when the exposure is considered chronic.

UF_L: LOAEL-to-NOAEL uncertainty factor. Ten was applied when the POD is a LOAEL for an adverse effect.

UF_D: Database uncertainty factor. The database UF is intended to account for the potential for deriving an underprotective RfD/RfC as a result of an incomplete characterization of the chemical's toxicity.

Table 4. Acquired Hazard Index (HI) of TCE from Industrial Complex A

	HI	
	CTE	RME
Male	1.71	3.27
Female	1.71	2.41

Table 5. Acquired Excessive Cancer Risk (ECR) of TCE from Industrial Complex

	ECR	
	CTE	RME
Male	1.40×10^{-5}	2.88×10^{-5}
Female	1.40×10^{-5}	1.97×10^{-5}

idents in vicinity of Industrial Complex A, and the ECRs for RME were 2.88×10^{-5} and 1.97×10^{-5} for males and females, respectively (Table 5).

DISCUSSION

The general population is exposed to TCE at low concentrations (in the parts per billion ranges) in air, water, and food. The reduction of the use of the chemical in anesthesia, solvent extraction, the fumigation of foodstuffs, and the dry-cleaning of textiles has reduced exposure from these sources. Exposure during the production of TCE is relatively low because of the nature of the process. Industrial uses, such as metal degreasing, can involve high levels of exposure. The respiratory route is the principal route of exposure, with dermal exposure being an additional route. Oral intake is insignificant in industrial settings (Landrigan *et al.*, 1987). TCE production in the United States began in the early 1920s. TCE was used as a replacement for petroleum distillates in the dry-cleaning industry and became the solvent of choice for vapor degreasing in the 1930s. TCE's use as a degreaser decreased in the 1960s due to toxicity concerns and the increasing popularity of 1,1,1-trichloroethane (TCA) (Dorherty, 2000). An estimated 3.5 million workers are exposed to TCE (Page, 1979). The recommended threshold limit value for industrial exposure to TCE is 50 ppm, and the Federal OSHA standard for TCE is 100 ppm. The California standard is set at 25 ppm.

ACGIH has designated TCE as A5, which means "not suspected as a human carcinogen." However, following the US EPA, TCE is characterized as "carcinogenic to humans" by all routes of exposure. This conclusion is based on convincing evidence of a causal association between TCE exposure in humans and kidney cancer. The human evidence of carcinogenicity from epidemiologic studies of TCE exposure is strong for Non-Hodgkin Lymphoma (NHL) (Morgan and Cassady, 2002; Vartiainen *et al.*, 1993), but

less convincing than it is for kidney cancer and more limited for liver and biliary tract cancer (Raaschou-Nielsen *et al.*, 2003).

Risk characterization is an integral component of the risk assessment process for both ecological and health risks, i.e., it is the final, integrative step in risk assessment. As defined in the risk characterization policy, the risk characterization integrates information from the preceding components of the risk assessment and synthesizes an overall conclusion about risk that is complete, informative, and useful for decision makers. In essence, a risk characterization conveys the risk assessor's judgment as to the existence and nature of human health or ecological risks (Williams and Paustenbach, 2002).

For a health risk assessment, the National Academy of Sciences (NAS) describes a four-step paradigm (Foster *et al.*, 2000). For each step, the relevant and scientifically reliable information is evaluated. In addition, the related uncertainties and science policy choices are described: a) hazard identification -- the determination of whether a particular chemical is or is not causally linked to particular health effects, b) dose-response assessment -- the determination of the relationship between the magnitude of exposure and the probability of the occurrence of the health effects in question, c) exposure assessment -- the determination of the extent of human exposure before or after the application of regulatory controls, and d) risk characterization -- the description of the nature and often the magnitude of human risk, including attendant uncertainty.

An adult-based inhalation unit risk estimate of 4.1×10^{-6} per $\mu\text{g}/\text{m}^3$ was suggested by the IRIS, EPA. The airborne concentration of TCE from Industrial Complex A was 0.8 ppb ($4.29 \mu\text{g}/\text{m}^3$). This concentration means that the risk was 1.40×10^{-5} for men and women and that the risks of RME were 2.88×10^{-5} and 1.97×10^{-4} for men and women, respectively.

In general, the US EPA considers excess cancer risks that are below about 1 chance in 1,000,000 (1×10^{-6}) to be so small as to be negligible and risks above 1×10^{-6} to be sufficiently large that some sort of remediation is desirable. Excess cancer risks that range between 1×10^{-6} and 1×10^{-4} are generally considered to be acceptable, although this is evaluated on a case-by-case basis, and the EPA may determine that risks lower than 1×10^{-4} are not sufficiently protective and warrant remedial action. When the EPA controls hazardous air pollutants from mobile sources, the standards are finalized in the rules so as to reduce both the number of people above the 1 in 100,000 cancer risk level and the average population cancer risk by reducing exposures to air toxins from mobile sources.

For the non-cancer risk, the CTE of HI for TCE was 1.71 for male and female residents in the vicinity of Industrial Complex A, and the RMEs of HI were 3.27 and 2.41 for males and females, respectively. The US EPA holds that

if the HQ for a chemical is equal to or less than one, there is no appreciable risk that non-cancer health effects will occur. If the HQ exceeds one, there is some possibility that non-cancer effects may occur. The values obtained in this study were over one, which is equivalent to the threshold value.

In this study, the ECR for CTE was 1.40×10^{-5} for male and female residents in the vicinity of Industrial Complex A, and the ECRs for RME were 2.88×10^{-5} and 1.97×10^{-5} for males and females, respectively. These values indicate that there are potential cancer risks due to exposure to these concentrations. The HI for CTE to trichloroethylene was 1.71 for male and female residents in the vicinity of Industrial Complex A, and the HIs for RME were 3.27 and 2.41 for male and female residents, respectively. These values were over one, which is equivalent to the threshold value. This result showed that some risk management of TCE at Industrial Complex A was needed.

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