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Toluene

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Chapter 1 Summary Tables

Table 1 provides a summary of health- and welfare-based values resulting from an acute and chronic evaluation of toluene. Table 2 provides summary information on toluene's physical/chemical data.

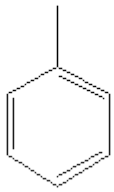
Table 1 Health- and Welfare-Based Values

Short-Term Values	**Concentration**	**Notes**
$^{acute}ESL$ [1 h] (HQ = 0.3)	4,500 µg/m^3 (1,200 ppb)	**Critical Effect(s):** eye and nose irritation; increased occurrence of headache, dizziness, and intoxication in human male volunteers
Acute ReV (HQ = 1)	15,000 µg/m^3 (4,000 ppb) *	**Critical Effect(s):** Same as above
$^{acute}ESL_{odor}$	3,500 µg/m^3 (920 ppb)* **Short-Term ESL for Air Permit Reviews**	Geometric Mean of 50% population odor detection concentrations (revised based on TCEQ 2012)
$^{acute}ESL_{veg}$	---	No data found
Long-Term Values	**Concentration**	**Notes**
$^{chronic}ESL_{nonlinear(nc)}$ (HQ = 0.3)	1,200 µg/m^3 (330 ppb) **Long-Term ESL for Air Permit Reviews**	**Critical Effect:** Color vision impairment in occupational workers
Chronic ReV (HQ = 1)	4,100 µg/m^3 (1,100 ppb)*	**Critical Effect(s):** Same as above
$^{chronic}ESL_{linear(c)}$ $^{chronic}ESL_{nonlinear(c)}$	---	Inadequate data
$^{chronic}ESL_{veg}$	---	No data found

* Values that may be used for evaluation of air monitoring data

Abbreviations used: **HQ**, hazard quotient; **ppb**, parts per billion; **µg/m^3**, micrograms per cubic meter; **h**, hour; **ESL**, Effects Screening Levels; **ReV**, Reference Value; **$^{acute}ESL$**, acute health-based ESL; **$^{acute}ESL_{odor}$**, acute odor-based ESL; **$^{acute}ESL_{veg}$**, acute vegetation-based ESL; **$^{chronic}ESL_{nonlinear(nc)}$**, chronic health-based ESL for nonlinear dose-response noncancer effects; **$^{chronic}ESL_{linear(c)}$**, chronic health-based ESL for linear dose-response cancer effect; **$^{chronic}ESL_{nonlinear(c)}$**, chronic health-based ESL for nonlinear dose-response cancer effect; and **$^{chronic}ESL_{veg}$**, chronic vegetation-based ESL

Table 2 Chemical and Physical Data

Parameter	**Value**	**Reference**
Molecular Formula and Structure	 C7-H8 (C6H5CH3)	ChemFinder 2006
Molecular Weight	92.14	Hazardous Substances Data Bank (HSDB) (2000)
Physical State	liquid	HSDB (2000)
Color	colorless	HSDB (2000)
Odor	Sweet, pungent, benzene-like	HSDB (2000)
CAS Registry Number	108-88-3	HSDB (2000)
Synonyms	Methylbenzene, Methylbenzol, Phenyl methane, Toluol	HSDB (2000)
Solubility in water	526 mg/l @ 25 ^{o}C	HSDB (2000)
Log K_{ow}	Log K_{ow} = 2.73	HSDB (2000)
Vapor Pressure	28.4 mm Hg @ 25 ^{o}C	HSDB (2000)
Vapor Density (air = 1)	3.1	HSDB (2000)
Density (water = 1)	0.8636 @ 25 ^{o}C/4 ^{o}C	HSDB (2000)
Melting Point	-94.9 ^{o}C	HSDB (2000)
Boiling Point	110.6 ^{o}C	HSDB (2000)
Conversion Factors	1 ppb = 3.76 µg/m^3 1 µg/m^3 = 0.27	Toxicology Section

Chapter 2 Major Uses or Sources

Toluene is widely used in the chemical manufacturing industry. It is used as a raw material in the production of benzene, solvent-based cleaning agents, household aerosols, nail polish, paints and thinners, lacquers, adhesives, and as a gasoline additive. Major toluene emission sources include motor vehicles, aircraft, petroleum refineries and terminals, rubber and paint manufacturing, varnishes and lacquers, metal degreasing, printing, and tobacco smoke.

Chapter 3 Acute Evaluation

3.1 Health-Based Acute ReV and ESL

3.1.1 Physical/Chemical Properties and Key Studies

Toluene is a liquid that is moderately soluble in water and has a moderate vapor pressure. Because of its small molecular weight and other physical/chemical properties, toluene is rapidly absorbed from the respiratory tract. The main chemical and physical properties of toluene are summarized in Table 2.

There have been numerous toxicity studies conducted in animals and in humans after exposure to toluene. These studies are discussed in detail by ATSDR (2000) and USEPA (2005). Furthermore, there is an abundance of well conducted human inhalation studies from which to choose and identify a point of departure (POD) for toluene. Since human data are a preferred source from which to base a toxicity assessment, a human study conducted by Andersen et al. (1983) was chosen as the key study. Sixteen healthy young human male subjects were exposed to 0, 10, 40, or 100 ppm toluene for 6 hours (hs) on 4 consecutive days using an inhalation chamber (Andersen et al. 1983). During the 100 ppm toluene exposures, statistically significant increased irritation was experienced in the eyes and nose, but not in the throat or lower airways. There was also a statistically significant increase in the occurrence of headaches, dizziness, and feelings of intoxication during the 100 ppm exposures, but not at the other concentrations. No significant adverse effects were reported at 10 or 40 ppm.

Numerous studies regarding acute exposures in humans inhaling toluene in the range of 40 to 700 ppm were also considered. The following 3 supporting studies were chosen because they demonstrate that neurotoxicity resulting from toluene exposure occurs at concentrations above 40 ppm:

- Reaction time and perceptual speed were studied among 12 young male subjects exposed by inhalation to toluene concentrations ranging from 100 to 700 ppm, in four 20 minute exposures (Gamberale et al. 1972). Statistically significant impaired reaction time and perceptual speed were observed at 300 and 700 ppm, respectively. The no-observed-adverse-effect-level (NOAEL) was observed to be 100 ppm.
- Echeverria et al. (1989) reported a lowest-observed-adverse-effect-level (LOAEL) of 75

ppm for neurological effects in humans. Forty two students were exposed by inhalation to 0, 75, and 150 ppm toluene for a 7 h period. A complete battery of 12 tests (neurobehavioral) was administered before and after each exposure. Toluene caused a dose-dependent impairment of function on digit span pattern recognition, the one hole test, and pattern memory.

- Baelum et al. (1985) reported a LOAEL of 100 ppm for neurological effects in humans. Two groups of 43 occupationally exposed subjects were exposed by inhalation to clean air, or to air containing 100 ppm toluene for 6.5 hs in a climate chamber. A battery of 10 tests of visuomotor coordination, visual performance, and cortical function were administered during the 6.5 h exposure period. Toluene exposure decreased performance on four of the neurobehavioral tests. Three of these tests were of visual perseverance, and the fourth test affected was the simple peg board test of visuomotor function.

3.1.2 Mode of Action and Dose Metric

Toluene is rapidly absorbed from the respiratory tract, and has been detected in human arterial blood within 10 seconds after initiation of inhalation exposure. Animal and human studies indicate that pulmonary absorption for toluene is 85-90% during brief exposures (within minutes), and is closer to 50% during longer exposures (< 1 h). Toluene is distributed throughout the body. Higher toluene concentrations can be found in tissues having high lipid content and in high vascular tissues (e.g., liver, kidney, brain). Toluene is metabolized in the liver, primarily to hippuric acid and benzoyl glucuronide, which are both readily excreted in the urine. Toluene excretion from the body is rapid, and its retention time is considered to be less than 24 hs, therefore bioaccumulation of toluene is unlikely.

Inhalation is the primary route of acute toluene exposure, and neurological effects (e.g., central nervous system [CNS] depression) are the most sensitive endpoints. Although the mechanisms underlying toluene's observed neurotoxicity are not fully understood, it appears to be related to concentrations of the parent compound (rather than metabolites) reaching the brain (Van Asperen et al. 2003). Available data indicate that toluene concentrations in the brain determine the CNS effects, and that at a constant exposure concentration, levels in the blood and brain will rapidly reach a steady state. Once the steady state is reached, exposure concentration is the primary factor for toluene induced CNS effects, and not exposure duration. Therefore, exposure concentration of the parent compound is considered the appropriate dose metric for acute toluene exposure both for neurological effects and for producing mild sensory irritation. Based on the above information, sensory irritation in humans is considered to have a threshold (i.e., a nonlinear MOA) because it is concentration dependent.

3.1.3 Point of Departure (POD) for the Key Study and Dosimetric Adjustments

Andersen et al. (1983) was conservatively chosen as toluene's key acute study, because of its low no-observed-adverse-effect-level (NOAEL) of 40 ppm. This study was also chosen by Cal

EPA (1999) and ATSDR (2000) as their key study. After choosing the NOAEL of 40 ppm as the POD_{HEC}, we considered adjusting the NOAEL from a subacute to an acute exposure duration following guidance in Section 3.2.2 from *Guidelines to Develop Effects Screening Levels, Reference Values, and Unit Risk Factors* (hereafter referred to ESL Guidelines (TCEQ 2006). However, since exposure concentration and not duration plays a role in toluene's effects of mild sensory irritation, no adjustment was deemed necessary, and the POD for a 1 h exposure was assumed to be 40 ppm.

3.1.4 Adjustments of the POD_{HEC}

Since sensory irritation in humans produced by toluene is considered to have a threshold (i.e., a nonlinear MOA), uncertainty factors (UFs) were applied to the POD_{HEC}. An UF of 10 for intraspecies variability (UF_H) was used to account for sensitive subpopulations and a database UF of 1 (UF_D) was used since the toxicological database for toluene is extensive (ATSDR 2000; USEPA 2005). The acute ReV was calculated as follows:

$$\begin{aligned} \text{Acute ReV} &= POD_{HEC} / (UF_H \times UF_D) \\ &= 40 \text{ ppm} / (10 \times 1) \\ &= 4 \text{ ppm} \\ &= 4{,}000 \text{ ppb} \end{aligned}$$

3.1.5 Health-Based Acute ReV and $^{acute}ESL$

The acute ReV of 4,000 ppb (15,000 µg/m^3) was rounded to two significant figures at the end of all calculations. Rounding to two significant figures, the acute ReV is 15,000 µg/m^3 (4,000 ppb). The rounded acute ReV was then used to calculate the $^{acute}ESL$. At the target hazard quotient of 0.3, the $^{acute}ESL$ is 4,500 µg/m^3 (1,200 ppb) (Table 3).

Table 3 Derivation of the Acute ReV and ^{acute}ESL

Parameter	**Summary**
Study	Andersen et al. 1983
Study population	16 healthy human male volunteers
Study quality	High
Exposure Methods	6 h/day for 4 days at inhalation exposures of 0, 10, 40 and 100 ppm
LOAEL	100 ppm
NOAEL	40 ppm
Critical Effects	Eye and nose irritation, plus headaches, dizziness and intoxication
POD_{HEC}	40 ppm (NOAEL)
Exposure Duration	6 h/day for 4 days
Extrapolation to 1 h exposure	Concentration dependent; no adjustment needed
Extrapolated 1 h concentration (POD_{ADJ})	40 ppm
Total Uncertainty Factors (UFs)	10
Interspecies UF	NA
Intraspecies UF	10
LOAEL UF	NA
Incomplete Database UF *Database Quality*	1 High
Acute ReV [1 h] (HQ = 1)	**15,000 µg/m^3 (4,000 ppb)**
^{acute} ESL [1 h] (HQ = 0.3)	**4,500 µg/m^3 (1,200 ppb)**

3.2 Welfare-Based Acute ESLs

3.2.1 Odor Perception (Revised March 21, 2014)

Toluene has a sweet, pungent, benzene-like odor with a wide odor threshold range of 0.17 to 40 ppm for detection, and a range of 1.7 to 67 ppm for recognition. The following studies which have been reviewed/accepted by the American Industrial Hygiene Association (AIHA 1989) and by USEPA (1992) reported a 50% odor detection threshold for toluene (from the oldest study to the most current studies):

- 0.94 mg/m^3 (0.25 ppm) Stalker (1963);
- 140 mg/m^3 (37 ppm) May (1966);
- 60 mg/m^3 (16 ppm) Dravnieka (1974);
- 25.4 mg/m^3 (6.7 ppm) Punter (1980);
- 0.64 mg/m^3 (0.17 ppm) Hellman (1974);
- 3.5 mg/m^3 (0.92 ppm) Hoshika (1993) (measured by the Japanese triangle bag method);
- 3.7 mg/m^3 (0.99 ppm) Hoshika (1993) (measured by the Dutch Standardized Method in the Netherlands);
- 1.39 ppm Van Doorn (2002) (measured by the Dutch Standardized Method);
- 1.59 ppm Van Doorn (2002) (measured by the European Standardized Method); and
- 1.24 mg/m^3 (0.33 ppm) Nagata (2003)

According to the guidelines for setting odor-based ESLs in TCEQ (2012), odor detection values defined as the highest quality level of odor thresholds (Level 1) will be considered first in setting the $^{acute}ESL_{odor}$ values. The odor detection thresholds reported by Hoshika (1993), van Doorn (2002), and Nagata (2003) were determined by the standardized methods of measuring odor and are defined as Level 1 quality data. The odor thresholds reported by others, however, are defined as Level 3 quality data. Therefore, only the standardized odor detection thresholds determined by Hoshika (1993), van Doorn (2002), and Nagata (2003) were used to set the $^{acute}ESL_{odor}$. Because more than one Level 1 study was located, the geometric mean of the 50% odor detection thresholds from these studies was calculated. Accordingly, the $^{acute}ESL_{odor}$ for toluene is 3.47 mg/m^3 (0.92 ppm) or 3,500 µg/m^3 (920 ppb) (rounded to two significant figures). Because odor is a concentration-dependent effect, the same 1-h $^{acute}ESL_{odor}$ can be assigned to all averaging times for monitoring and modeling samples.

3.2.2 Vegetation Effects

Data is not available.

3.3 Short-Term ESL and Values for Air Monitoring Evaluation

The acute evaluation resulted in the derivation of the following acute values:

- ReV = 15,000 µg/m^3 (4,000 ppb),
- ^{acute}ESL = 4,500 µg/m^3 (1,200 ppb)
- ^{acute}ESL$_{odor}$ = 3,500 µg/m^3 (920 ppb)

The short-term ESL for air permit evaluations is the ^{acute}ESL$_{odor}$ of 3,500 µg/m^3 (920 ppb) since it is lower than the ^{acute}ESL of 4,500 µg/m^3 (1,200 ppb) (Table 1). For evaluation of ambient air monitoring data, the ^{acute}ESL$_{odor}$ of 3,500 µg/m^3 (920 ppb) is lower than the acute ReV of 15,000 µg/m^3 (4,000 ppb) (Table 1), although both values will be used for the evaluation of air data (Table 1).

Chapter 4 Chronic Evaluation

4.1 Noncarcinogenic Potential

4.1.1 Physical/Chemical Properties and Key Studies

Refer to Section 3.1.1 for a discussion of physical/chemical properties.

There is a substantial database for subchronic and chronic animal and human inhalation exposure to toluene (ATSDR 2000; USEPA 2005). Some of toluene's reported chronic CNS effects resulted from chronic toluene abuse through "glue or solvent-sniffing" or inhalation of other commercial products. Unfortunately, results from these studies are often confounded by subjects abusing other solvents and mixtures of solvents. Human occupational studies with NOAELs in the range of 25 to 50 ppm have been identified. A well-conducted occupational study by Zavalic et al. (1998) was chosen as the key study, with a reported NOAEL of 32 ppm. This study is also cited in the United States Environmental Protection Agency Integrated Risk Information System (IRIS) and by Cal EPA, and was chosen as the key study by ATSDR (2000) in developing their chronic Minimum Risk Level (MRL). Three groups of Croatian workers occupationally exposed by inhaling toluene at 0, 32, and 132 ppm over a 10+ year period were examined by means of interviews, medical examination, and by color vision testing using the Lanthony desaturated panel D-15 test. A significant (10-14%) increase in color confusion index (CCI) for both eyes was reported in the 132 ppm exposure group. No adverse health effects were reported in the 32 ppm exposure group, therefore the 32 ppm was designated as a NOAEL.

Several supporting chronic human inhalation studies were also considered. The following three studies report a LOAEL at 50 ppm and above as critical endpoints for vision/auditory impairment and neurobehavioral effects:

- Foo et al. (1990) conducted an occupational inhalation study of 30 female workers

exposed to toluene vapor concentrations of 13 ppm (control group) and 88 ppm (exposed group) over a 5.7 year period. A significant decrease in neurobehavioral performance, which included the Benton visual retention test, visual reproduction, trail making, grooved pegboard, digit span, finger tapping, and simple reaction time, was observed in the 88 ppm exposure group. This exposure concentration was designated as the LOAEL.

- Orabeck and Nise (1989) observed impairment in neuropsychometric tests among 30 rotogravure printers from 2 Swedish printing plants exposed to toluene over a 29 year period. Statistically significant higher occurrences of fatigue, short-term memory problems, concentration difficulty, and mood lability were observed. Since exposure concentrations changed over the 29 year period, the LOAEL is estimated to be somewhere within the range of 11.2 to 453 ppm. A representative exposure concentration of 140 ppm was determined.
- Vrca et al. (1997) studied 49 printing press workers occupationally exposed to toluene for approximately 21.6 years. Toluene exposure concentrations were estimated to range anywhere from 40 to 60 ppm. Significantly reduced wave amplitude of visual evoked potentials, and as well as increased latency of auditory evoked potentials were noted. The estimated LOAEL was considered to be 50 ppm.

4.1.2 Mode of Action and Dose Metric

As previously stated, toluene is rapidly absorbed from the respiratory tract, and distributed throughout the body. Inhalation is the primary route for chronic toluene exposure, and neurological effects are the most sensitive endpoints. Toluene exposure concentration is considered the appropriate dose metric. Since the mode of action whereby toluene produces neurological effects is unknown but is considered to be dependent on concentration, neurological effects in humans are considered to have a threshold (i.e., a nonlinear MOA).

4.1.3 Dosimetric Adjustment to POD_{HEC}

The NOAEL of 32 ppm based on color vision impairment was chosen as the occupational point-of-departure (POD_{OC}). In accordance with Section 4.2.1 of the ESL Guidelines (TCEQ 2006), the NOAEL was adjusted from a human occupational exposure to represent a more appropriate POD based on the ventilation rate and exposure duration for the general population (POD_{HEC}). Using the following equation:

$POD_{HEC} = POD_{OC} \times (VE_{ho}/VE_h) \times [(days/week_{oc}) / (days/week_{res})]$

where: VE_{ho} = occupational ventilation rate for an 8-h day (10 m^3/day)

VE_h = non-occupational ventilation rate for a 24-h day (20 m^3/day)

$days/week_{oc}$ = occupational exposure frequency (5 days)

$days/week_{res}$ = residential exposure frequency (7 days)

POD_{HEC} = 32 ppm x [10 m^3/day/20 m^3/day] x [5 day/7 day] = 11.4 ppm

4.1.4 Adjustments of the POD_{HEC}

Since neurological effects in humans produced by toluene is considered to have a threshold (i.e., a nonlinear MOA), uncertainty factors (UFs) were applied to the POD_{HEC}. An UF_H of 10 was used to account for sensitive subpopulations, a subchronic-to-chronic UF (UF_{Sub}) of 1 was used because a 10-year human study was available, and a UF_D of 1 was used since the chronic toxicological database for toluene is extensive (ATSDR 2000; USEPA 2005). The chronic ReV was calculated as follows:

$$\begin{aligned} \text{chronic ReV} &= POD_{HEC} / (UF_H \times UF_{Sub} \times UF_D) \\ &= 11.4 \text{ ppm} / (10 \times 1 \times 1) \\ &= 1.14 \text{ ppm} \\ &= 1140 \text{ ppb} \end{aligned}$$

4.1.5 Health-Based Chronic ReV and $^{chronic}ESL_{nonlinear(nc)}$

The chronic ReV value based on neurological effects was rounded to two significant figures at the end of all calculations. Rounding to two significant figures, the chronic ReV is 1100 ppb (4100 µg/m^3). The rounded chronic ReV was then used to calculate the $^{chronic}ESL_{nonlinear(nc)}$. At the target hazard quotient of 0.3, the $^{chronic}ESL_{nonlinear(nc)}$ is 330 ppb (1200 µg/m^3) (Table 4).

Table 4 Derivation of the Chronic ReV and $^{chronic}ESL_{nonlinear(nc)}$

Parameter	**Summary**
Study	Occupational exposure workers inhaling toluene (Zavalic et al. 1998a)
Study population	3 groups of workers occupationally exposed to toluene
Study quality	High
Exposure Method	10+ years of inhalation exposure at 0, 32 and 132 ppm
Critical Effects	Color vision impairment
POD_{OC}	32 ppm (NOAEL)
Exposure Duration	8 h/day, 5 days/week, for 10+ years
Extrapolation to continuous exposure (POD_{ADJ})	NA
POD_{HEC} Dosimetry adjustment from occupational to general human population	11 ppm
Total UFs	10
Interspecies UF	NA
Intraspecies UF	10
LOAEL UF	NA
Subchronic to chronic UF	NA
Incomplete Database UF *Database Quality*	1 High
Chronic ReV (HQ = 1)	4,100 µg/m^3 (1,100 ppb)
$^{chronic}ESL_{nonlinear(nc)}$ (HQ = 0.3)	1,200 µg/m^3 (330 ppb)

4.2 Carcinogenic Potential

Data are inadequate for an assessment of human carcinogenic potential via the inhalation pathway for toluene. The United States Environmental Protection Agency (USEPA, 2005) classifies toluene as not likely to be carcinogenic to humans. The International Agency for Research on Cancer (IARC, 1994), and the American Conference of Governmental Industrial Hygienists (ACGIH, 2006) determined that toluene is not classifiable as a human carcinogen.

4.3 Welfare-Based Chronic ESL

No data found

4.4 Long-Term ESL and Values for Air Monitoring Evaluation

The chronic evaluation resulted in the derivation of the following chronic values:

- Chronic ReV = 4,100 µg/m^3 (1,100 ppb)
- $^{chronic}ESL_{nonlinear(nc)}$ = 1,200 µg/m^3 (330 ppb)

The long-term ESL for air permit evaluations is the $^{chronic}ESL_{nonlinear(nc)}$ of 1,200 µg/m^3 (330 ppb) (Table 1). For evaluation of monitoring data, the chronic ReV of 4,100 µg/m^3 (1,100 ppb) is used (Table 1).

Chapter 5 References

5.1 References Cited in the DSD

Agency for Toxic Substances and Disease Registry (ATSDR). 2000. Toxicological profile for toluene. Available from ATSDR, Public Health Service, U.S. Department of Health and Human Services, Atlanta, GA. www.atsdr.cdc.gov/toxprofiles.

Andersen, I, GR Lundqvist, L Molhave, et al. 1983. Human response to controlled levels of toluene in six-h exposures. *Scand J Work Environ Health* 9:405-18.

Baelum, J, I Andersen, GR Lundqvist, et al. 1985. Response of solvent-exposed printers and unexposed controls to six-hour toluene exposure. *Scand J Work Environ Health* 11:271-80.

California Environmental Protection Agency (Cal EPA 1999). Office of Environmental Health Hazard Assessment (OEHHA), Berkeley, CA.

ChemFinder.com. 2006. n-Hexane. ChemFinder.com Database and Internet Searching. http://chemfinder.cambridgesoft.com/result.asp.

Dravnieks, A. 1974. A building-block model for the characterization of odorant molecules and their odors. *Ann N Y Acad Sci* 237 (0):144-63.

Echeverria, D, L Fine, G Langolf, et al. 1989. Acute neurobehavioral effects toluene. *Br J Med* 46:483-95.

Foo, SC, J Jeyarathnam, and D Koh. 1990. Chronic neurobehavioral effects of toluene. *Br J Ind Med* 47: 480-84.

Gamberale, F, and M Hultengren. 1972. Toluene exposure. II. Psychophysiological functions. *Work Environ Health* 9:131-39.

Hazardous Substances Data Bank. 2000. United States National Library of Medicine,

http://toxnet.nlm.nih.gov/cgi-bin/sis/search/f?./temp/~aJJC1z:1

Hellman, TM, and FH Small. 1974. Characterization for the odor properties of 101 petrochemicals using sensory methods. *J Air Pollut Control Assoc* 24:979-82.

Hoshika, Y, T Imamura, G Muto, LJ van Gemert, JA Don and JI Walpot. 1993. International comparison of odor threshold values of several odorants in Japan and in The Netherlands. *Environ Res* 61: 78-83.

May, J. 1966. Geruchsschwellen von Losemitteln zur Bewetertug von Losemittelgeruchen in der Luft [Odor thresholds of solvents for assessment of solvent odors in the air] *Staub Reinhalt* 26 385-389.

Nagata Y. 2003. Measurement of odor threshold by triangle odor bag method. Odor Measurement Review, Japan Ministry of the Environment. Pp. 118-127. Available from: http://www.epa.gov/oppt/aegl/pubs/rest101.htm

Orabeck, P, and G Nise. 1989. Neurasthenic complaints and psychometric function of toluene exposed rotogravure printers. *Am J Ind Med* 16:67-77.

Punter, PH. 1983. Mesurement of human olfactory thresholds for several groups of structurally related compounds. Chem Senses 7(3-4):215-235.

Stalker, WW. 1963. Defining the Odor Problem in a Community. *Am Ind Hyg Assoc J* 24:600-605.

Texas Commission on Environmental Quality (TCEQ). 2006. Guidelines to Develop Effects Screening Levels, Reference Values, and Unit Risk Factors. Chief Engineer's Office. RG-442.

Texas Commission on Environmental Quality (TCEQ). 2012. TCEQ guidelines to develop toxicity factors (Revised RG-442). Office of the Executive Director. Available from: http://www.tceq.texas.gov/publications/rg/rg-442.html

United States Environmental Protection Agency (USEPA). 2005. Toxicological review of toluene in support of summary information on the integrated risk information system (IRIS). EPA/635/R-05/004.

Van Asperan, J, WR Rijcken, and JH Lammers. 2003. Application of physiologically based toxicokinetic modeling to study the impact of the exposure scenario on the toxicokinetics and the behavioral effects of toluene in rats. *Toxicol Lett* 138:51-62.

van Doorn R, MW Ruijten, and T van Harreveld. 2002. Guidance for the Application of Odor in Chemical Emergency Response. Version 2.1; August 29, 2002. Presented at the NAC/AEGL-Meeting September 2002, Washington DC.

Vrca, A, D Bozicevic, V Bozikov, et al. 1997. Brain stem evoked potentials and visual evoked potentials in relation to the length of occupational exposure to low levels of toluene. *Acta Medica Croatica* 51:215-19.

Zavalic, M, Z Mandic, R Turk, et al. 1998. Quantitative assessment of color vision impairment in workers exposed to toluene. *Am J Ind Med* 33:297-304.

5.2 Other Studies and Documents Reviewed by the TS

Abbate, C, C Giorgianni, F Munao, et al. 1993. Neurotoxicity induced by exposure to toluene: an electrophysiologic study. *Int Arch Occup Environ Health 64*:389-92.

American Conference of Governmental Industrial Hygienists (ACGIH). 2001. Documentation of the threshold limit value for toluene. Cincinnati, OH.

Bale, A, M Jackson, Q Krantz, et al. 2007. Evaluating the NMDA-glutamate receptor as a site of action for toluene, in vivo. *Toxicological Sciences* 98(1):159-66.

Boey, KW, SC Foo, J Jeyaratnam. 1997. Effects of occupational exposure to toluene: a neuropsychological study on workers in Singapore. *Ann Acad Med Singapore* 26:84-7.

Bushnell, P, W Oshiro, T Samsam, et al. 2007. A dosimetric analysis of the acute behavioral effects of inhaled toluene in rats. *Toxicological Sciences* 99(1):181-89.

Eisenberg, D. 2003. Neurotoxicity and mechanism of toluene abuse. *Einstein Quart J Bio Med* 19:150-59.

Government of Canada, Health and Welfare Canada, Environment Canada. 1992. Priority substances list assessment. Report No. 4 toluene.

Morata, TC, AC Fiorini, FM Fischer, et al. 1997. Toluene-induced hearing loss among rotogravure printing workers. *Scand J Work Environ Health* 23:289-98.

Neubert, D, C Gericke, B Hanke, et al. 2001. Multicenter field trial on possible health effects of toluene. II. Cross-sectional evaluation of acute low-level exposure. *Toxicology* 168:139-83.

Risk Assessment Information System (RAIS). 1994. Toxicity profiles-toxicity summary for toluene. Oak Ridge National Laboratory, Oak Ridge, TN.

Songnian, YIN, LI Guilan, HU Yitang, et al. 1987. Symptoms and signs of workers exposed to benzene, toluene or the combination. *Industrial Health* 25:113-30.

Tanaka, K, T Maeda, T Kobayashi, et al. 2003 A survey of urinary hippuric acid and subjective

symptoms among occupational low toluene exposed workers. *Fukushima J Med Sci* 49:129-39.

Zupanic, M, P Demes, A Seeber. 2002. Psychomotor performance and subjective symptoms at low level toluene exposure. *Occup Environ Med* 59:263-68.