Development Support Document
Original: October 8, 2009
Revised: March 14, 2014
Revised Odor Value: September 14, 2015

Hydrogen Chloride

CAS Registry Number: 7647-01-0

Prepared by

Shannon Ethridge, M.S., D.A.B.T.

Toxicology Division

Office of the Executive Director
TEXAS COMMISSION ON ENVIRONMENTAL QUALITY

Revision History

Original Development Support Document (DSD) posted as final on October 8, 2009.

Revised DSD March 14, 2014: The DSD was revised based on updated guidance from USEPA (2012) (i.e., for the chronic reference value, dosimetric adjustments were performed as a Category 1 vapor based on updated recommendations on animal-to-human dosimetric adjustments in USEPA (2012): the default regional gas dose ratio for the extrathoracic region ($RGDR_{ET}$) is 1.)

Revised DSD September 14, 2015: An odor-based value was provided because hydrogen chloride has an irritating, pungent odor (TCEQ 2015).

TABLE OF CONTENTS

REVISION HISTORY ..... **I**

TABLE OF CONTENTS ..... **II**

LIST OF TABLES ..... **III**

ACRONYMS AND ABBREVIATIONS ..... **IV**

CHAPTER 1 SUMMARY TABLES **1**

CHAPTER 2 MAJOR USES OR SOURCES **4**

CHAPTER 3 ACUTE EVALUATION **4**

3.1 HEALTH-BASED ACUTE REV AND ESL 4
3.1.1 Physical/Chemical Properties and Essential Data *4*
3.1.1.1 Physical/Chemical Properties 4
3.1.1.2 Essential Data and Key Study 4
3.1.2 Mode-of-Action (MOA) Analysis *6*
3.1.3 Dose Metric *6*
3.1.4 Point of Departure (POD) for the Key Study *6*
3.1.5 Dosimetric Adjustments *7*
3.1.6 Critical Effect and Adjustment of POD_{HEC} *7*
3.1.7 Health-Based Acute ReV and $^{acute}ESL$ *7*
3.1.8 Comparison of Results *8*
3.2 WELFARE-BASED ACUTE ESLS 9
3.2.1 Odor Perception *9*
3.2.2 Vegetation Effects *9*
3.3 SHORT-TERM ESL 11
3.4 ACUTE INHALATION OBSERVED ADVERSE EFFECT LEVEL 11

CHAPTER 4 CHRONIC EVALUATION **11**

4.1 NONCARCINOGENIC POTENTIAL 11
4.1.1 Physical/Chemical Properties and Essential Data *11*
4.1.1.1 Human Studies 11
4.1.1.2 Animal Studies 12
4.1.2 MOA Analysis and Dose Metric *13*
4.1.3 POD for the Key Study *13*
4.1.4 Dosimetric Adjustments *13*
4.1.4.1 Exposure Duration Adjustments 13
4.1.4.2 Default Dosimetry Adjustments from Animal-to-Human Exposure 13
4.1.5 Critical Effect and Adjustment of POD_{HEC} *15*
4.1.6 Health-Based Chronic ReV and $^{chronic}ESL_{threshold(nc)}$ *15*
4.1.7 Comparison of Results *16*
4.2 CARCINOGENIC POTENTIAL 16
4.3 WELFARE-BASED CHRONIC ESL 17
4.4 LONG-TERM ESL 17
4.5 CHRONIC OBSERVED ADVERSE EFFECT LEVEL 17

CHAPTER 5 REFERENCES 18

5.1 REFERENCES CITED IN THE DEVELOPMENT SUPPORT DOCUMENT 18

LIST OF TABLES

TABLE 1 AIR MONITORING COMPARISON VALUES (AMCVS) FOR AMBIENT AIR [A] 1
TABLE 2 AIR PERMITTING EFFECTS SCREENING LEVELS (ESLS) 2
TABLE 3 CHEMICAL AND PHYSICAL DATA 3
TABLE 4 DERIVATION OF THE ACUTE REV AND ^{ACUTE}ESL 8
TABLE 5 DERIVATION OF THE CHRONIC REV AND ^{CHRONIC}ESL $_{THRESHOLD(NC)}$ 16

Acronyms and Abbreviations

Acronyms and Abbreviations	Definition
ACGIH	American Conference of Governmental Industrial Hygienists
ADH	aldehyde dehydrogenase
AEGL	Acute Exposure Guideline Levels
ATSDR	Agency for Toxic Substances and Disease Registry
^{0} C	degrees centigrade
BMR	benchmark response
CNS	central nervous system
ConA	Concanavalin A
CRO	crotonaldehyde
DSD	development support document
EC_{50}	Effective concentration at a 50% response level
ESL	Effects Screening Level
$^{acute}ESL$	acute health-based Effects Screening Level for chemicals meeting minimum database requirements
$^{acute}ESL_{generic}$	acute health-based Effects Screening Level for chemicals not meeting minimum database requirements
$^{acute}ESL_{odor}$	acute odor-based Effects Screening Level
$^{acute}ESL_{veg}$	acute vegetation-based Effects Screening Level
$^{chronic}ESL_{threshold(c)}$	chronic health-based Effects Screening Level for threshold dose response cancer effect
$^{chronic}ESL_{threshold(nc)}$	chronic health-based Effects Screening Level for threshold dose response noncancer effects
$^{chronic}ESL_{nonthreshold(c)}$	chronic health-based Effects Screening Level for nonthreshold dose response cancer effects
$^{chronic}ESL_{nonthreshold(nc)}$	chronic health-based Effects Screening Level for nonthreshold dose response noncancer effects
$^{chronic}ESL_{veg}$	chronic vegetation-based Effects Screening Level
EU	European Union

Acronyms and Abbreviations	Definition
GC	gas chromatography
GLP	good laboratory practice
hr	hour
$H_{b/g}$	blood:gas partition coefficient
$(H_{b/g})_A$	blood:gas partition coefficient, animal
$(H_{b/g})_H$	blood:gas partition coefficient, human
HEC	human equivalent concentration
HQ	hazard quotient
HSDB	Hazardous Substance Data Base
IARC	International Agency for Research on Cancer
IC_{50}	Inhibitory concentration at a 50% response level
IL	interleukin
IPCS	International Programme on Chemical Society
IRIS	USEPA Integrated Risk Information System
kg	kilogram
LC_{50}	concentration causing lethality in 50% of test animals
LD_{50}	dose causing lethality in 50% of test animals
LPS	lipopolysaccharide
LOAEL	lowest-observed-adverse-effect-level
LTD	Limited toxicity data
MW	molecular weight
µg	microgram
$\mu g/m^3$	micrograms per cubic meter of air
mg	milligrams
mg/m^3	milligrams per cubic meter of air
min	minute
MOA	mode of action

Acronyms and Abbreviations	Definition
n	number
NAC	National Advisory Committee
NIOSH	National Institute for Occupational Safety and Health
NOAEL	no-observed-adverse-effect-level
NOEL	no-observed-effect-level
NRC	National Research Council
OAEL	Observed adverse effect level
OSHA	Occupational Safety and Health Administration
PBPK	physiologically based pharmacokinetic
POD	point of departure
POD_{ADJ}	point of departure adjusted for exposure duration
POD_{HEC}	point of departure adjusted for human equivalent concentration
ppb	parts per billion
ppm	parts per million
RD_{50}	50% reduction in respiration rate
ReV	reference value
RGDR	regional gas dose ratio
ROS	Reactive oxygen species
RP	Relative potency
RP_{GM}	Geometric mean of relative potency endpoints
SA	surface area
SD	Sprague-Dawley
TCEQ	Texas Commission on Environmental Quality
TD	Toxicology Division
UF	uncertainty factor
UF_H	interindividual or intraspecies human uncertainty factor

Acronyms and Abbreviations	Definition
UF_A	animal to human uncertainty factor
UF_{Sub}	subchronic to chronic exposure uncertainty factor
UF_L	LOAEL to NOAEL uncertainty factor
UF_D	incomplete database uncertainty factor
USEPA	United States Environmental Protection Agency
V_E	minute volume

Chapter 1 Summary Tables

Table 1 for air monitoring and Table 2 for air permitting provide a summary of health- and welfare-based values from an acute and chronic evaluation of hydrogen chloride (HCl). Please refer to Section 1.6.2 of the TCEQ Guidelines to Develop Toxicity Factors (TCEQ 2012) for an explanation of air monitoring comparison values (AMCVs), reference values (ReVs) and effects screening levels (ESLs) used for review of ambient air monitoring data and air permitting. Table 3 provides summary information on HCl's physical/chemical data.

Table 1 Air Monitoring Comparison Values (AMCVs) for Ambient Air [a]

Short-Term Values	Concentration	Notes
Acute ReV	**Short-Term Health** 660 µg/m^3 (450 ppb)	**Critical Effect:** Upper respiratory symptoms (sore throat, nasal discharge) and lower respiratory symptoms (pulmonary function, cough, chest pain) in exercising asthmatics
$^{acute}ESL_{odor}$	**Odor** 1100 µg/m^3 (770 ppb)	Irritating, pungent
$^{acute}ESL_{veg}$	- - -	$^{acute}ESL_{veg}$ not developed because the threshold concentration for adverse vegetative effects is substantially higher than human health-based acute ReV and $^{acute}ESL$
Long-Term Values	**Concentration**	**Notes**
Chronic ReV	**Long-Term Health** 26 µg/m^3 (18 ppb)	**Critical Effect:** Hyperplasia of nasal mucosa, larynx, and trachea in rats
$^{chronic}ESL_{nonthreshold(c)}$ $^{chronic}ESL_{threshold(c)}$	- - -	Data are inadequate for an assessment of human carcinogenic potential via the inhalation route
$^{chronic}ESL_{veg}$	- - -	No data found

[a] Hydrogen chloride is not monitored for by the TCEQ's ambient air monitoring program

Table 2 Air Permitting Effects Screening Levels (ESLs)

Short-Term Values	Concentration	Notes
^{acute}ESL [1 h] (HQ = 0.3)	**Short-Term ESL for Air Permit Reviews** 190 µg/m^3 (130 ppb) [a]	**Critical Effect:** Upper respiratory symptoms (sore throat, nasal discharge) and lower respiratory symptoms (pulmonary function, cough, chest pain) in exercising asthmatics
^{acute}ESL$_{odor}$	1100 µg/m^3 (770 ppb)	Irritating, pungent
^{acute}ESL$_{veg}$	- - -	^{acute}ESL$_{veg}$ not developed because threshold concentration for adverse vegetative effects is substantially higher than human health-based acute ReV and ^{acute}ESL
Long-Term Values	**Concentration**	**Notes**
^{chronic}ESL$_{threshold(nc)}$ (HQ = 0.3)	**Long-Term ESL for Air Permit Reviews** 7.9 µg/m^3 (5.4 ppb) [b]	**Critical Effect:** Upper respiratory tract effects in Sprague-Dawley rats
^{chronic}ESL$_{nonthreshold(c)}$ ^{chronic}ESL$_{threshold(c)}$	- - -	Data are inadequate for an assessment of human carcinogenic potential via the inhalation route
^{chronic}ESL$_{veg}$	- - -	No data found

[a] Based on the acute ReV of 660 µg/m^3 (450 ppb) multiplied by 0.3 to account for cumulative and aggregate risk during the air permit review

[b] Based on the chronic ReV of 26 µg/m^3 (18 ppb) multiplied by 0.3 to account for cumulative and aggregate risk during the air permit review

Table 3 Chemical and Physical Data

Parameter	**Value**	**Reference**
Molecular Formula	HCl	HSDB 2008
Chemical Structure	H–Cl	HSDB 2008
Molecular Weight	36.47	HSDB 2008
Physical State	Gas at room temperature	ATSDR 2007
Color	Colorless to slightly yellow	ATSDR 2007
Odor	Irritating, pungent	HSDB 2008
CAS Registry Number	7647-01-0	HSDB 2008
Synonyms	Chlorohydric acid, hydrochloric acid, muriatic acid	HSDB 2008
Solubility in water	67.3 g/100 ml at 30°C (Highly soluble)	HSDB 2008
Log P_{ow}	0.25	INCHEM 2000
Vapor Pressure	3.54 x 10^4 mm Hg at 25°C	HSDB 2008
Vapor Density (air = 1)	1.27	HSDB 2008
Density	1.045 g/m^3 (liquid at 118.16 K)	HSDB 2008
Melting Point	-114.22°C	HSDB 2008
Boiling Point	-85.05°C	HSDB 2008
Conversion Factors	1 ppm = 1.47 mg/m^3 1 mg/m^3 = 0.679 ppm	ACGIH 2001

Chapter 2 Major Uses or Sources

HCl is available commercially as an anhydrous gas or as an aqueous solution (hydrochloric acid/muriatic acid). Anhydrous HCl is used in making alkyl chlorides, in hydrochlorination, polymerization, alkylation, and nitration reactions. The acid is used where strong acids are needed (e.g., in activating oil wells, ore reduction, metallic pickling, electroplating metals, and food processing). Aqueous HCl is commonly called muriatic acid and is a component of commercial chemicals used to clean and disinfect swimming pools. Anthropogenic sources of HCl in air include fossil fuel burning (mainly coal), incineration of domestic and industrial waste, iron-steel manufacturing, the chemical and ceramic industries, glass manufacturing, cement production, and rocket firing. Natural sources of HCl in air include sea salt and emissions from volcanoes (Sturges and Harrison 1989, Lightowlers and Cape 1988, and Kamrin 1992).

Chapter 3 Acute Evaluation

3.1 Health-Based Acute ReV and ESL

3.1.1 Physical/Chemical Properties and Essential Data

3.1.1.1 Physical/Chemical Properties

HCl is a colorless to slightly yellow gas with an irritating, pungent odor. HCl is heavier than air and may cause asphyxiation in enclosed, poorly ventilated, or low-lying areas. HCl gas forms dense white vapors when exposed to air due to condensation with atmospheric moisture. The resulting vapor is highly corrosive and acidic. Because of its solubility, gaseous HCl will dissolve rapidly in cloud water or rain and be washed out of the atmosphere (Kamrin 1992). HCl is highly reactive and will be removed from the atmosphere by interacting with almost any surface (Kamrin 1992). Because of its reactive properties, long-range transport of HCl is unlikely, and the most significant levels are found near the emission sources. The main chemical and physical properties of HCl are summarized in Table 3.

3.1.1.2 Essential Data and Key Study

HCl gas is a strong irritant, causing irritation of the eye, nose, and throat. Inhalation of HCl gas at sufficiently high concentrations can also produce acute tracheobronchitis (characterized by cough, sore throat, chest pain, and lightheadedness); bronchoconstriction; and pulmonary edema (Ellenhorn and Barceloux, 1988).

Only one laboratory-controlled acute inhalation exposure study in humans was identified in the literature and was selected as the key study. Stevens et al. (1992) investigated the respiratory effects from inhaled HCl in exercising young adult asthmatics. Five male and five female asthmatics between the ages of 18 and 25 years were exposed to filtered air, 0.8 ppm HCl, and 1.8 ppm HCl via a silicon rubber half-face mask. The half-face mask was used to control for adverse effects on the eyes. All subjects inhaled the three different test atmospheres on different

days, separated by at least a week. Each exposure session lasted for 45 minutes which was divided into three equal periods: exercise, rest, exercise. The exercise periods consisted of walking on a treadmill at a speed of 2 miles per hour (h) at an elevation grade of 10%.

Tests of pulmonary function included forced expiratory volume in 1 second, forced expiratory volume, maximal flow at 50% and 75% of expired vital capacity, and total respiratory resistance and peak flow. No significant changes were observed in any of these parameters at either 0.8 or 1.8 ppm HCl. Subjects did not report any exposure-related increases in severity of upper respiratory, lower respiratory, or other symptoms at either concentration. Nasal work of breathing was measured using computer-assisted posterior rhinomanometry both before and after exposure. No treatment-related changes were observed in nasal work of breathing data. A No-Observed-Adverse-Effect-Level (NOAEL) of 1.8 ppm was identified for this study.

Other data concerning acute inhalation effects of HCl in humans are qualitative and do not provide enough information to make accurate exposure assessments. Elkins (1959) (as cited in ACGIH 2001) reported that HCl was immediately irritating when inhaled at concentrations of 5 ppm or more. Stokinger (1981) (as cited in ACGIH 2001) also reported that concentrations above 5 ppm were disagreeable. Henderson and Haggard (1943) (as cited in ACGIH 2001) reported that exposure of humans to 35 ppm caused irritation of the throat on short exposure and 50 to 100 ppm HCl was barely tolerable. Reactive airways dysfunction syndrome (RADS) has been observed in humans exposed to undetermined concentrations of HCl (Promisloff et al. 1990, Turlo and Broder 1989, Boulet 1988).

In humans, exposure to concentrated HCl vapor can cause corneal cell death, cataracts, and glaucoma. Exposure to dilute solutions can cause a stinging sensation and ulceration of the eye surface (ATSDR 2007). No studies were available that identified the concentration that causes eye irritation/damage in humans. Ocular effects in animals have been observed at higher concentrations than concentrations that cause respiratory tract irritation. Corneal opacities were observed in guinea pigs exposed to 680 ppm HCl for 30 minutes but not 320 ppm (Burleigh-Flayer et al. 1985). Cloudy corneas were observed in guinea pigs 90 days after exposure to 4,200 ppm HCl but not 500 ppm (Kaplan et al. 1993). In contrast, mild irritation was observed in guinea pigs exposed to 107 ppm for 30 minutes (Malek and Alarie 1989). Irritant effects were observed in baboons exposed to 810 - 17,290 ppm HCl for 5 minutes, increasing in severity from coughing and frothing at the mouth at lower concentrations to profuse salivation, blinking/rubbing of the eyes, and shaking of the head at higher concentrations (Kaplan et al. 1985).

No human developmental or reproductive studies were identified in the literature. One animal developmental study was identified (Pavlova 1976). In this study, female Wistar rats were exposed to 302 ppm HCl via inhalation for 1 h on the 9th day of gestation. This concentration was lethal to one-third of the animals tested with animals showing signs of severe dyspnea and cyanosis. Surviving animals exhibited decreased lung, liver, and kidney function. Increased

mortality was observed among the progeny of the treated animals. Fetal effects also included a decrease in kidney and lung function. The fetal effects observed were most likely secondary to maternal toxicity; therefore, this study did not demonstrate developmental effects of HCl.

Two animal reproductive toxicity studies were identified (Pavlova 1976 and Pavlova 1977). In Pavlova (1976), female Wistar rats were exposed to 302 ppm HCl for 1 h, 12 days prior to mating to determine if HCl had reproductive effects. Mortality was observed in one-third of exposed animals with signs of severe dyspnea and cyanosis. Surviving animals showed a reduction in lung and kidney function. Fetal mortality was not affected by HCl exposure. Progeny of treated animals showed decreased lung, liver, and kidney function. The effects were most likely a result of maternal toxicity; therefore, this study did not demonstrate reproductive effects of HCl.

Pavlova (1977), as reported in GEOMET Technologies, Inc. (1981), exposed female rats to 302 ppm HCl for 1 h, 12 – 16 days prior to mating. This concentration was lethal to 20 – 30% of the rats. Surviving animals had a decrease in blood oxygen saturation and effects in the kidney, liver, and spleen. The estrus cycle was altered in exposed rats. In rats mated 12 – 16 days after exposure and killed on day 21 of pregnancy, fewer live fetuses were observed. Other fetal effects included a decrease in weight and an increase in relative lung weights. The fetal effects were most likely a result of maternal toxicity; therefore, this study did not demonstrate reproductive effects of HCl.

Please refer to Acute Exposure Guideline Level (AEGL) (NRC 2004) for a comprehensive discussion of the acute toxicity of HCl.

3.1.2 Mode-of-Action (MOA) Analysis

As reported in NRC (2004), HCl is an upper repiratory irritant at relatively low concentrations and may cause damage to the lower respiratory tract at high concentrations. HCl exposure can also cause eye irritation/damage at undetermined concentrations. On contact with moisture, HCl dissociates almost completely. The hydrogen ions combine with water to form hydronium ions (H_3O^+) that can cleave organic molecules and cause cell death. HCl may enter the lower respiratory tract when the scrubbing mechanism of the upper respiratory tract is saturated.

3.1.3 Dose Metric

Since exposure concentration of the parent chemical is the most appropriate dose metric for HCl based on its MOA, exposure concentration of the parent chemical will be used as the dose metric.

3.1.4 Point of Departure (POD) for the Key Study

A free-standing NOAEL of 1.8 ppm based on a 45 minute exposure from the Stevens et al. (1992) study was used as the POD.

3.1.5 Dosimetric Adjustments

As stated in Section 3.2 of the TCEQ Toxicity Factors Guidelines (TCEQ 2012), a duration adjustment is required to convert a 45-minute concentration POD to a 1-h concentration POD_{ADJ} if both concentration and duration play a role in toxicity. Haber's Rule is applied in this situation to determine the 1-h concentration ($C_1^n \times T_1 = C_2^n \times T_2$). Since HCl toxicity is both concentration- and duration-dependent, and a concentration less than 1 h is being adjusted to 1 h, a value of "n" = 1 was used to calculate the POD_{ADJ} which is the most conservative of the two values empirically derived by ten Berge (1986) (TCEQ 2012).

$C_1^n \times T_1 = C_2^n \times T_2$

1.8^1 ppm x 0.75 h = C_2^1 x 1 hr

C_2 = 1.35 ppm

POD_{ADJ} = 1.35 ppm

3.1.6 Critical Effect and Adjustment of POD_{HEC}

As indicated in Section 3.1.1.2, data from human studies suggest that upper respiratory irritation is the most sensitive endpoint for acute exposure to HCl. The POD_{ADJ} is based on a free-standing NOAEL so no adverse effects were experienced by any of the test subjects at that concentration, although endpoints evaluated included upper respiratory symptoms (e.g., sore throat, nasal discharge) and changes in pulmonary function (Stevens et al. 1992).

The following uncertainty factors (UFs) were applied: a UF of 1 for human variability (UF_H) since the key study involved a potentially sensitive subpopulation (exercising asthmatics), and a UF of 3 to account for database uncertainty (UF_D). The database confidence is medium to high according to Table 4-2 in the TCEQ Toxicity Factors Guidelines (TCEQ 2012) and there is some uncertainty regarding the adverse effect level for eye irritation since the key study design prevented eye exposure. The total UF = 3.

ReV = POD_{ADJ} / (UF_H x UF_D)

ReV = 1.35 ppm / 3

ReV = 0.45 ppm = 450 ppb

3.1.7 Health-Based Acute ReV and ^{acute}ESL

Numbers were not rounded between equations until the acute ReV was calculated. Once the acute ReV was calculated, it was rounded to 2 significant figures. The rounded acute ReV was then multiplied by 0.3 to calculate the ^{acute}ESL, and the ^{acute}ESL subsequently rounded to 2 significant figures. As shown in Table 4, the acute ReV is 450 ppb (660 µg/m^3). The acute ReV was then used to calculate the ^{acute}ESL. At the target hazard quotient (HQ) of 0.3, the ^{acute}ESL is 130 ppb (190 µg/m^3).

3.1.8 Comparison of Results

The acute ReV of 660 µg/m^3 (450 ppb) calculated based on the POD value from Stevens et al. (1992) is more conservative than the California Environmental Protection Agency (CalEPA) Acute Reference Exposure Level (REL) of 2,100 µg/m^3 (1,400 ppb) based on the same study. The acute REL is higher than the acute ReV because CalEPA did not incorporate a UF_D of 3.

Table 4 Derivation of the Acute ReV and ^{acute}ESL

Parameter	**Summary**
Study	Stevens et al. (1992)
Study population	10 asthmatics (5 male and 5 female) aged 18-25 years
Study quality	High
Exposure Methods	45 minute inhalation exposure via half-face mask to 0, 0.8 and 1.8 ppm
Critical Effects	Upper respiratory symptoms (sore throat, nasal discharge) and lower respiratory symptoms (pulmonary function, cough, chest pain)
POD (original study)	1.8 ppm (free-standing NOAEL)
Exposure Duration	45 minute
POD_{ADJ} (extrapolated to 1-h concentration)	1.35 ppm (n = 1)
Total UFs	3
Interspecies UF	3
Intraspecies UF	Not applicable (NA)
LOAEL UF	NA
Incomplete Database UF	1
Database Quality	Medium to high
Acute ReV [1 h] (HQ = 1)	**660 µg/m^3 (450 ppb)**
^{Acute}ESL [1 h] (HQ = 0.3)	**190 µg/m^3 (130 ppb)**

3.2 Welfare-Based Acute ESLs

3.2.1 Odor Perception

HCl has a pungent, suffocating odor with reported odor thresholds ranging from 0.06 ppm to 10 ppm (Amoore and Hautula 1983, Heyroth 1963, Leonardos et al. 1969, and van Thriel et al. 2006). Based on an evidence integration approach and historical information (TCEQ 2015), the $^{acute}ESL_{odor}$ for HCl is 1100 µg/m^3 (770 ppb).

3.2.2 Vegetation Effects

HCl gas is known to cause severe plant injury but only when present at high concentrations, which is infrequent and irregular (Endress et al. 1978b). Numerous studies have been conducted to determine the effects of HCl gas exposure in plants. Some of the first studies were conducted in the early 1900s after vegetation effects were observed in Europe and Great Britain near soda factories. HCl gas is a by-product of the Le Blanc soda process in which sodium chloride is treated with sulfuric acid (Endress et al. 1978a). As reported by Endress et al. (1978a) and Lerman et al. (1978), Haselhoff and Lindau (1903) conducted extensive vegetation studies on various plant species and reported numerous adverse effects of HCl gas exposure. The seedlings of Viburnum and larch were killed after less than two days exposure to 5 – 20 ppm HCl. Adverse effects were also observed in other plant species at higher concentrations (1,000 – 2,000 ppm).

Haagen-Smit et al. (1952) investigated the effects of chemical components of smog on various plant species including spinach, sugar beets, endive, oats, and alfalfa. Two adjacent gas rooms were used; one room served as a fumigation chamber and the other served as a plant growing room. The rooms received a continuous fresh air supply, the temperature was maintained at approximately 22°C, and the relative humidity at about 60%. In all fumigations, the chemical was first brought up to the test concentration in the fumigation chamber. Then, test plants were brought into the fumigation chamber from the growing chamber. Test plants remained in the fumigation chamber for 4 to 6 h and were then returned to the growing chamber. No effects were observed in any of the plant species after 5 h exposure to 1 ppm HCl.

Shriner and LaCasse (1969) exposed 28-day old tomato plants (*Lycopersicon esculentum*) to 5 ppm HCl gas for 2 h at a relative humidity of 65%, a temperature of 31°C, and 3.9 x 10^4 ergs/ cm^2s^{-1}light irradiance. It was not clear if the experiment included appropriate controls. Adverse effects were reported at 5 ppm and included glazing of the lower surface of mature leaves due to collapse of the cells of the lower epidermis and adjacent spongy mesophyll. Mature leaves also had bifacial intercostal bronzing which was associated with a further collapse of the spongy mesophyll and eventual collapse of the palisade mesophyll. The effect level identified in this study was 5 ppm.

Means and Lacasse (1969) investigated the effects of HCl gas on 12 tree species. Coniferous and broadleaf seedlings (2 – 5 years old) were exposed to 3 – 43 ppm HCl for 4 h. The most sensitive species identified was *Liriodendron tulipfera,* which showed visible injury at 3 ppm.

Lerman et al. (1976) investigated the effects of HCl gas exposure on eight species of ornamental plants. Species included Aster, Calendula, Cornflower, Cosmos, Marigold (American), Marigold (French), Nasturtium, and Zinnia. Plants were exposed in a plexiglass exposure chamber for 20 minutes to 1 – 35 mg/m^3 HCl gas under conditions of 24 – 35°C and 50 – 70% relative humidity. The natural light intensity in the chamber was greater than 3.0 x 10^5 ergs/cm^2s^{-1}. Plants were observed for effects 23 h after exposure. Visible injury including traces of necrosis, discoloration, and lower surface bronzing were observed at 1.5 – 9 mg/m^3 in seven of eight species. A regression analysis was performed to determine what concentration of HCl caused a 10% relative injury. Using this analysis, Cosmos appeared to be the most sensitive species, with 6.5 mg/m^3 HCl (4.4 ppm) causing a 10% relative injury. The effect level identified in this study was determined to be 6.5 mg/m^3 (4.4 ppm) for a 20 minute exposure.

To determine the effects of a large, instantaneous release like that which would be associated with a solid fuel rocket launch or an accidental industrial release, Endress et al. (1978a) exposed pinto bean plants 8 days from seeding to 6.0, 11.3, 17.9, 21.1, 25.0, 25.7, 32.0, 41.3, or 54.2 mg/m^3 HCl gas (4.07, 7.67, 12.15, 14.33, 16.98, 17.45, 21.73, 28.04, 36.8 ppm) in an exposure chamber for 20 minutes. Two groups of controls were used; one group was exposed to filtered air in the chamber and another group was maintained without chamber influences. The relative humidity ranged from 32 – 40%, the temperature was 31 – 38°C, and the irradiation varied between 3.0 – 8.0 x 10^4 ergs/cm^2s^{-1}. Leaf tissue samples were collected immediately after and 30 min, 1 h, 2 h, 3 h, and 24 h after fumigation. Adverse effects were observed at all concentrations and included visible injury to the leaves (glazing of the abaxial leaf surface), collapse of epidermal cells, and plasmolysis of the epidermal protoplast. The severity of effects increased with increasing HCl concentration. The effect level identified in this study was 4.07 ppm for a 20 minute exposure.

As a follow-up to previous studies, Endress et al. (1978b) exposed pinto bean plants 8 days from seeding to filtered air or 25.35 ± 0.35 mg/m^3 HCl (16.7 ppm) for 20 minutes. Exposures occurred within an air chamber. A second group of control plants was maintained without chamber influences. The relative humidity was 23 – 36%, the temperature ranged from 36 – 38°C, and the irradiation varied between 0.4 –1.6 x 10^5 ergs/cm^2s^{-1} within the chambers during fumigation. Twenty-four hours after exposure, when visible injury symptoms were well expressed, tissue samples were collected from the lamina of primary leaves and used for electron microscopy. Adverse effects were observed at the only concentration of HCl used (16.7 ppm) and included injury symptoms on primary leaves (glazing of either or both leaf surfaces and necrosis of interveinal areas) as well as injury at the fine structural level (e.g., increased stromal density, disruption of cytoplasmic membranes, damaged or broken cell walls, degeneration of the plasmalemma). Cellular injury was variable, and the degree of injury was characterized based on the level of severity. The effect level identified in this study was 16.7 ppm.

The available data indicate that the threshold concentration for HCl-related adverse vegetation effects is between 1 ppm for no effects observed in several plant species exposed for 5 hours

(Haagen-Smit et al. 1952) and 3 ppm for a 4 hour exposure in *Liriodendron tulipfera* that caused visible injury (Means and Lacasse 1969). These concentrations are substantially higher than the one hour health-based acute ReV of 450 ppb and the ^{acute}ESL of 130 ppb. In this case, the development of a short-term vegetation based ESL ($^{acute}ESL_{veg}$) is not necessary to protect human health and welfare, and according to the TCEQ Toxicity Factors Guidelines (TCEQ 2012), an $^{acute}ESL_{veg}$ is not developed.

3.3 Short-Term ESL

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

- acute ReV = 660 µg/m^3 (450 ppb)
- ^{acute}ESL = 190 µg/m^3 (130 ppb)
- $^{acute}ESL_{odor}$ = 1100 µg/m^3 (770 ppb).

The short-term ESL for air permit reviews is the health-based ^{acute}ESL of 190 µg/m^3 (130ppb) (Table 2).

3.4 Acute Inhalation Observed Adverse Effect Level

Acute inhalation observed adverse effect levels of HCl in humans are qualitative and do not provide enough information to make accurate assessments. Therefore, an acute inhalation observed adverse effect level was not developed. However, Elkins (1959) (as cited in ACGIH 2001) reported that HCl was immediately irritating when inhaled at concentrations of 5 ppm or more. Stokinger (1981) (as cited in ACGIH 2001) also reported that concentrations above 5 ppm were disagreeable.

Chapter 4 Chronic Evaluation

4.1 Noncarcinogenic Potential

4.1.1 Physical/Chemical Properties and Essential Data

Physical and chemical properties of HCl are discussed in Section 3.1.1.1.

4.1.1.1 Human Studies

Few human studies are available on the chronic effects of HCl exposure. As cited by CalEPA (2000), Stockinger (1981) reported bleeding of the nose and gums and ulceration of the mucous membranes after repeated occupational exposure to HCl mist at high (but unquantified) concentrations. Kamrin (1992) reported that levels above 10 ppm lead to work impairment, above 50 ppm lead to work hindrance, and above 100 ppm lead to a work environment in which work is impossible (Lehmann 1886, Matt 1889, and Lehman et al. 1908 as cited in Kamrin 1992).

Ten Bruggen (1968) reported dental erosion after repeated occupational exposure to mineral acids. The study was conducted in three industrial areas (Manchester, Glasgow, and Wolverhampton) with a total number of 783 workers exposed to acids. Control workers came from acid-free departments of the firms participating in the study. Progressive erosions were observed in a dose-dependent manner with 50% of battery formation workers (high exposure) affected, 24.5% of galvanizing picklers (intermediate exposure), and 22.3% of non-galvanizing picklers (intermediate exposure). All other occupations (low exposure) showed a 7.3% incidence of progressive erosion. The level of erosion was positively correlated with duration of exposure with Grade 1 erosion (enamel loss) occurring in workers after more than 3 months of exposure, Grade 2 erosion (loss of enamel and dentine) occurring in workers after 2.5 to 5 years of exposure, and Grade 3 erosion (loss of enamel and dentine with exposure of secondary dentine) occurring in workers after 6 or more years of exposure. No information on exposure concentrations was given.

4.1.1.2 Animal Studies

Albert et al. (1982) exposed male Sprague-Dawley rats to sham air (control) or 10 ppm HCl gas for 6 hours per day (h/d), 5 days per week (d/wk), for life, although only results from the first 588 days of the study are presented in this paper. No changes in body weight or mortality were reported in HCl exposed animals compared to controls. Other experimental results were reported by Sellakumar et al. (1985).

Sellakumar et al. (1985) was a complete report of the Albert et al. (1982) study in which male Sprague-Dawley rats (99 animals per group) were exposed to sham air (control) or 10 ppm HCl gas for 6 h/day, 5 d/wk, for life. Animals were observed daily, weighed monthly, and allowed to die naturally or were sacrificed when moribund. No differences were observed in body weight or survival in exposed animals versus control animals. HCl did not induce any serious irritating effects in the nasal epithelium nor did any of the animals develop any preneoplastic or neoplastic lesions. Increased incidence of hyperplasia of the nasal mucosa (62/99 versus 51/99), larynx (22/99 versus 2/99), and trachea (26/99 versus 2/99) was observed in HCl exposed rats compared to air-exposed controls. The Toxicology Division (TD) considers hyperplasia to be a mild adverse effect in the absence of other notable adverse effects (i.e., organ weight changes, body weight changes); therefore, the TD determined 10 ppm to be a mild LOAEL for this study.

In a 90-day animal inhalation study, B6C3F1 mice and Sprague-Dawley and Fisher 344 rats (31 males and 31 females of each strain) were exposed to 0, 10, 20, or 50 ppm HCl for 6 h/day, 5 d/wk, for 90 days (Toxigenics, Inc. 1984). There was a small but significant decrease in body weight gain in male and female mice and male Fisher 344 rats in the high-exposure groups. No effects on hematology, clinical chemistry, or urinalysis were reported. Both strains of rats showed evidence of minimal to mild rhinitis at all concentrations. Lesions were observed in the anterior portion of the nasal cavity and were concentration- and time-related. Mice in all exposure groups developed “eosinophilic globules” in the epithelial cells lining the nasal turbinates. Mice exposed to50 ppm had cheilitis with accumulation of hemosiderin-laden

macrophages involving the perioral tissues after 90 days. The details on the histopathology results could not be determined because the TD could not obtain the complete report. Without the complete report, it was difficult to determine if the eosinophilic globules observed in mice were a significant adverse change over controls. The TD determined 50 ppm to be the LOAEL based on decreased body weight gain in male and female mice and male Fisher 344 rats, and cheilitis with accumulation of hemosiderin-laden macrophages involving the perioral tissues in mice.

In the absence of quantitative human data, the TD selected the Sellakumar et al. (1985) rat study as the key study to derive the chronic ReV because it was the only chronic animal inhalation study available.

4.1.2 MOA Analysis and Dose Metric

The MOA for chronic effects of HCl is similar to that for acute effects. Persistent cell injury from HCl exposure can lead to hyperplasia or an increase in the number of cells in the affected tissue. Since exposure concentration of the parent chemical is the most appropriate dose metric for HCl based on its MOA, exposure concentration of the parent chemical will be used as the dose metric.

4.1.3 POD for the Key Study

A mild LOAEL of 10 ppm was identified from the Sellakumar et al. (1985) study based on increased incidence of hyperplasia of the nasal mucosa, larynx, and trachea in rats.

4.1.4 Dosimetric Adjustments

4.1.4.1 Exposure Duration Adjustments

The POD from Sellakumar et al. (1985) of 10 ppm was adjusted to a continuous exposure concentration:

POD_{ADJ} = POD x D/24 x F/7

where: POD_{ADJ} = POD adjusted for exposure duration

D = duration (hours per day)

F = frequency (days per week)

POD_{ADJ} = 10 ppm x 6/24 x 5/7

POD_{ADJ} = 1.78 ppm

4.1.4.2 Default Dosimetry Adjustments from Animal-to-Human Exposure

A dosimetric adjustment from an animal concentration to a POD_{HEC} was performed for HCl, a category 1 gas producing respiratory effects in the extrathoracic (ET) and tracheobronchial (TB) regions.

4.1.4.2.1 Extrathoracic Region

The health effects HCL produces at lower concentrations are mainly respiratory tract effects in the extrathoracic region of the respiratory tract, so dosimetric adjustments were performed as a Category 1 vapor based on updated animal-to-human dosimetric recommendations in USEPA (2012). The default regional gas dose ratio for the extrathoracic region ($RGDR_{ET}$) is 1.

$POD_{HEC} = POD_{ADJ} \times RGDR_{ET}$
$= 1.78 \text{ ppm} \times 1$
$= 1.78 \text{ ppm}$
$= 1{,}780 \text{ ppb}$

The resulting $POD_{HEC(ET)}$ is 1,780 ppb.

4.1.4.2.2 Tracheobronchial Region

Animal-to-human dosimetric recommendations in USEPA (2012) for category 1 vapors for effects in the TB region are that procedures outlined in USEPA (1994) be followed. Therefore, for the tracheobronchial region the following equations from USEPA (1994) were used:

$POD_{HEC} = POD_{ADJ} \times RGDR$

where: $RGDR = (MV_A/SA_A)/(MV_H/SA_H) \times ((e\text{-}[SA_{ET}/MV]_A)/(e\text{-}[SA_{ET}/MV]_H))$

RGDR = Regional Gas Dose Ratio
MV_A = Minute volume of the animal
MV_H = Minute volume of the human
SA_A = Surface area of the region of concern in the animal
SA_H = Surface area of the region of concern in the human

Default surface area for the tracheobronchial (TB) region of the rat is 22.5 cm^2. The default surface area for the TB region of the human is 3200 cm^2. The MV_A for a male Sprague-Dawley rat with a default body weight for a chronic study of 0.523 kilograms is 329.5 ml/min. The default MV_H is 13,800 ml/min.

$RGDR_{TB} = ((MV/SA_{ET})_A/(MV/SA_{ET})_H) \times ((e\text{-}[SA_{ET}/MV]_A)/(e\text{-}[SA_{ET}/MV]_H))$
$RGDR_{TB} = ((329.5 \text{ ml/min}/22.5 \text{ cm}^2)/(13{,}800 \text{ ml/min}/3200 \text{ cm}^2)) \times (0.9554/0.9856)$
$RGDR_{TB} = 3.292$

The resulting $POD_{HEC(TB)}$ from the POD_{ADJ} of 1.78 ppm is 5.728 ppm.

Based on this method of calculation, the $POD_{HEC(ET)}$ of 1.78 ppm is lower than the $POD_{HEC(TB)}$ of 5.728 ppm. The TD chose to use the $POD_{HEC(ET)}$ of 1.78 ppm as the POD_{HEC} to be protective of effects in the ET and TB regions.

4.1.5 Critical Effect and Adjustment of POD_{HEC}

As discussed in Section 4.1.1.2, data from animal studies suggests that hyperplasia of nasal mucosa, larynx, and trachea are the most sensitive endpoints for chronic inhalation exposure to HCl and are considered the critical effects.

The following uncertainty factors (UFs) were applied to the POD_{HEC}:

- a UF_H of 10 for intraspecies variability to account for potentially sensitive members of the population,
- a UF_A of 3 for animal-to-human variability was used because a dosimetric adjustment was made to account for toxicokinetic differences but not toxicodynamic differences,
- a UF_L of 3 for the adjustment from a mild LOAEL to a NOAEL,
- a UF_D of 1 for database uncertainty. Although the database regarding chronic effects of HCl is considered low to medium according to Table 5-2 of the TCEQ Toxicity Factors Guidelines (2012), the MOA of HCl toxicity and data from available studies indicate that exposure would not be expected to cause reproductive or developmental effects and additional chronic inhalation studies would not be expected to provide information to suggest effects other than those observed in the available subchronic and chronic studies would be observed. Specifically, the chronic database lacks one additional chronic inhalation study although one well-conducted subchronic inhalation study in mice and rats is available. The database also lacks one two-generation reproductive toxicity study and one additional developmental toxicity study in a different species. A one-generation reproductive toxicity study is available and does not indicate that HCl is a reproductive toxicant and two developmental studies conducted in rats do not indicate that HCl is a developmental toxicant. In addition, HCl exerts point-of-entry effects and because there is insignificant distribution remote to the respiratory tract, we would not expect HCl to cause reproductive or developmental effects.
- The total UF = 100.

$$ReV = POD_{HEC} / (UF_H \times UF_A \times UF_L \times UF_D)$$
$$ReV = 1.78 \text{ ppm} / 100$$
$$ReV = 0.0178 \text{ ppm} = 17.8 \text{ ppb}$$

4.1.6 Health-Based Chronic ReV and $^{chronic}ESL_{threshold(nc)}$

When calculating, no numbers were rounded between equations until the chronic ReV was calculated. Once the chronic ReV was calculated, it was rounded to 2 significant figures. The rounded ReV was then used to calculate the ESL, and the ESL subsequently rounded to 2 significant figures. The chronic ReV is 18 ppb (26 µg/m^3) using the mild LOAEL of 10 ppm as the POD. At the target HQ of 0.3, the $^{chronic}ESL_{threshold(nc)}$ is 5.4 ppb (7.9 µg/m^3) (Table 5).

Table 5 Derivation of the Chronic ReV and $^{chronic}ESL_{threshold(nc)}$

Parameter	Summary
Study	Lifetime bioassay (Sellakumar et al. 1985)
Study Population	Male Sprague-Dawley Rats (99 rats per group)
Study Quality	High
Exposure Method	Lifetime exposure via whole-body inhalation to 0 or 10 ppm HCl
Critical Effects	Hyperplasia of nasal mucosa, larynx, and trachea
POD (original study)	10 ppm (mild LOAEL)
Exposure Duration	6 h/day 5 days/week for lifetime
Extrapolation to continuous exposure (POD_{ADJ})	1.78 ppm
POD_{HEC}	1.78 ppm (category 1 gas with point-of-entry effects, based on $RGDR_{ET}$ = 1)
Total UFs	100
Interspecies UF	3
Intraspecies UF	10
LOAEL UF	3 (mild effects)
Subchronic to chronic UF	NA
Incomplete Database UF	1
Database Quality	Low to medium
Chronic ReV (HQ = 1)	**26 µg/m^3 (18 ppb)**
$^{chronic}ESL_{nonlinear(nc)}$ (HQ = 0.3)	**7.9 µg/m^3 (5.4 ppb)**

4.1.7 Comparison of Results

The chronic ReV of 26 µg/m^3 (18 ppb) calculated based on the POD_{HEC} value from Sellakumar et al. (1985) is higher than the USEPA RfC of 20 µg/m^3 (14 ppb) and the CalEPA Chronic Reference Exposure Level (REL) of 9 µg/m^3 (6 ppb) based on Sellakumar et al. (1985) because updated recommendations for animal-to-human dosimetric adjustments were used for the ET region (USEPA 2012).

4.2 Carcinogenic Potential

One United States study of steel-pickling workers showed an excess risk for lung cancer in workers exposed primarily to HCl (standardized mortality ratio, 2.24 [95% confidence interval (CI), 1.02-4.25]; 9 deaths) (Beaumont et al. 1987). In a study conducted by Steenland et al. (1988) of the same cohort evaluated in Beaumont et al. (1987), an excess incidence of laryngeal

cancer was observed in steel picklers (relative risk, 2.6; 95% CI, 1.2-5.0; 9 cases). Two of the nine cases had been exposed only to acids other than sulfuric acid, and three had been exposed to a mixture of acids. Confounding by exposure to sulfuric acid could not be ruled out.

Bond et al. (1983) conducted a case-control study of primary intracranial neoplasms at a US chemical plant and found no association with exposure to HCl. Bond et al. (1985) found no positive association between HCl exposure and renal cancer in a case-control study. The odds ratio for HCl exposure was 0.90 (90% CE, 0.44-1.83) in comparison with the first control group and 0.86 (90% CE, 0.40-1.86) in comparison with the second control group. Bond et al. (1986, 1991) conducted a nested case-control study of chemical workers at a Dow chemical plant in Freeport, TX and found no association with lung cancer and HCl exposure. Sellakumar et al. (1985) reported no carcinogenic effects in rats exposed to 10 ppm HCl for a lifetime. *In vitro* assays with HCl provide conflicting evidence of the mutagenic potential of HCl (IARC 1992).

Based on the weight-of-evidence, IARC determined that HCl is not classifiable as to its carcinogenicity to humans because of inadequate evidence in humans and experimental animals. USEPA has not classified HCl as to its carcinogenic potential at this time. Based on the weight-of-evidence analysis, the TD determined that information to assess human carcinogenicity following inhalation exposure is not sufficient at this time.

4.3 Welfare-Based Chronic ESL

No chronic vegetation studies were identified for HCl.

4.4 Long-Term ESL

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

- chronic ReV = 26 µg/m^3 (18 ppb)
- $^{chronic}ESL_{threshold(nc)}$ = 7.9 µg/m^3 (5.4 ppb)

The long-term ESL for air permit evaluations is 7.9 µg/m^3 (5.4 ppb) (Table 2).

4.5 Chronic Observed Adverse Effect Level

The LOAEL value of 10 ppm identified from the Sellakumar et al. (1985) study (Table 5) was used as the POD for calculation of a chronic inhalation observed adverse effect level. No duration adjustment was made (TCEQ 2012). However, an animal-to-human dosimetric adjustment was made to calculate a $LOAEL_{HEC}$:

The $LOAEL_{HEC}$ was calculated using the following equation:

$LOAEL_{HEC}$ = LOAEL x $RGDR_{ET}$ (Section 4.1.4)

= 10 ppm x 1

= 10 ppm or 10,000 ppb

The $LOAEL_{HEC}$ determined from an animal study, where effects occurred in some animals, represents a concentration at which it is probable that similar effects could occur in some individuals exposed to this level over the same duration as used in the study or longer. Importantly, effects are not a certainty due to potential interspecies and intraspecies differences in sensitivity. The chronic inhalation observed adverse effect level of 15,000 µg/m^3 **(**10,000 ppb) is provided for informational purposes only (TCEQ 2012). As the basis for development of inhalation observed adverse effect levels is limited to available data, future studies could possibly identify a lower POD for this purpose.

The margin of exposure between the chronic inhalation observed adverse effect level of 10,000 ppb to the ReV of 18 ppb is a factor of approximately 555.

Chapter 5 References

5.1 References Cited in the Development Support Document

Agency for Toxic Substances and Disease Registry (ATSDR). 2007. Medical management guidelines for hydrogen choride. Atlanta, GA.

Albert RE, AR Sellakumar, S Laskin, M Kuschner, N Nelson, and CA Snyder. 1982. Gaseous formaldehyde and hydrogen chloride induction of nasal cancer in rats. *J Natl Cancer Inst* 68: 597-603.

American Conference of Governmental Industrial Hygienists (ACGIH). 2001. Hydrogen chloride. Threshold limit values for chemical substances and physical agents and biological exposure indices. Cincinnati, OH.

Amoore JE and E Hautala. 1983. Odor as an aide to chemical safety: odor thresholds compared with threshold limit values and volatilities for 214 industrial chemicals in air and water dilution. *J Appl Toxicol* 3: 272-290.

Beaumont JJ, J Leveton, K Knox, T Bloom, T McQuiston, M Young, R Goldsmith, NK Steenland, DP Brown, and WE Halperin. 1987. Lung cancer mortality in workers exposed to sulfuric acid mist and other acid mists. *JNCI* 79:911-921.

Bond GG, RR Cook, PC Wight, and GH Flores. 1983. A case-control study of brain tumor mortality in a Texas chemical plant. *J Occup Med* 25:377-386.

Bond GG, RJ Shellenberger, GH Flores, RR Cook, and WA Fishbeck. 1985. A case-control study of renal cancer mortality at a Texas chemical plant. *Am J Ind Med* 7:123-139.

Bond GG, GH Flores, RJ Shellenberger, JB Cartmill, WA Fishbeck, and RR Cook. 1986. Nested case-control study of lung cancer among chemical workers. *Am J Epidemiol* 124:53-66.

Bond GG, GH Flores, BA Stafford, and GW Olsen. 1991. Lung cancer and hydrogen chloride exposure: results from a nested case-control study of chemical workers. *J Occup Med* 33:958-961.

Boulet LP. 1988. Increases in airway responsiveness following acute exposure to respiratory irritants: Reactive airway dysfunction syndrome or occupational asthma? *Chest* 94:476-481.

Buckley LA, XZ Jiang, RA James, KT Morgan, and CS Barrow. 1984. Respiratory tract lesions induced by sensory irritants at the RD_{50} concentration. *Toxicol Appl Pharmacol* 74: 417-429.

California Environmental Protection Agency. 1999. Determination of acute reference exposure levels for airborne toxicants: hydrogen chloride.

California Environmental Protection Agency. 2000. Chronic toxicity summary: hydrogen chloride.

Dydek Toxicology Consulting (Dydek). 2014. Comments on DSD for hydrogen chloride. March 07, 2014. Dydek Toxicology Consulting, Austin, Texas.

Ellenhorn MJ and DG Barceloux. 1988. Medical Toxicology: Diagnosis and treatment of human poisoning. New York. Elsevier Science Publishing.

Endress AG, JT Kitasako, and OC Taylor. 1978a. Ultracytopathological characterization of leaves followign short-term exposures of hydrogen chloride gas. *Atmos Environ* 12:1383-1390.

Endress AG, TJ Swieki, OC Taylor. 1978b. Foliar and microscopic observations of bean leaves exposed to hydrogen chloride gas. *Environ Exp Bot* 18:139-149.

Godish TJ and NL Lacasse. 1970. Effects of hydrogen chloride gas on respiration, photosynthesis, and transpiration of tomato. *Phytopathology* 60:575.

Haagen-Smit AJ, EF Darley, M Zaitlin, H Hull, W Noble. 1952. Investigation of injury to plants from air pollution in the los angeles area. *Plant Phyiology* 27:18-34.

Hazardous Substances Data bank (HSDB). 2008. Online database: http://toxnet.nlm.nih.gov. Last accessed on December 2, 2008.

IARC (International Agency for Research on Cancer). 1992. IARC Monographs on the evluation

of carcinogenic risks to humans. Occupational exposures to mists and vapors from strong inorganic acids and other industrial chemicals. Lyon, France: IARC 54:189-211.

Kamrin MA. 1992. Workshop on the health effects of HCl in ambient air. *Reg Tox and Pharm* 15:73-82.

Kaplan HL, A Anzeuto, WG Switzer, and RK Hinderer. 1988. Effects of hydrogen chloride on respiratory response adn pulmonary function of the baboon. *J Toxicol Environ Health* 23:473-493.

GEOMET Technologies, Inc. 1981. Hydrogen chloride: Report 4, Occupational Hazard Assessment. U.S. Department of Health and Human Services, NIOSH, Cincinnati, OH. NTIS PB83-105296.

Leonardos G, Kendall, and NJ Barnard. 1969. Odor threshold determinations of 53 odorant chemicals. *J Air Pollut Control Assoc* 19:91-95.

Lerman S, OC Taylor, and EF Darley. 1976. Phytotoxicity of hydrogen chloride gas with a short-term exposure. *Atmos Environ* 10:873-878.

Lightowlers PJ and JN Cape. 1988. Sources and fate of atmospheric HCl in the U.K. and Western Europe. *Atmos Environ* 22:7-15.

Monse´ C, HC Broding, Frank Hoffmeyer et al. 2010. Use of a Calibration Gas Generator for Irritation Threshold Assessment and As Supplement of Dynamic Dilution Olfactometry. *Chem Sense* 35:523-530. Available from: http://chemse.oxfordjournals.org/content/35/6/523.full.pdf+html

NAS/NRC. 1976. Medical and biological effects of environmental pollutants, chlorine and hydrogen chloride. Washington, DC, National Academy of Sciences - National Research Council. 62, 92-144.

National Research Council (NRC). 2004. Hydrogen chloride: Acute Exposure Guideline Level (Final). in Acute Exposure Guideline Levels (AEGLs) for Selected Airborne Chemicals: Volume 4 Available from: http://www.epa.gov/opptintr/aegl/pubs/tsd52.pdf

Pavlova TE. 1976. Disturbance of development of the progeny of rats exposed to hydrogen chloride. *Bull Exp Biol Med* 82:1078-1081.

Promisloff RA, GS Lenchner, and AV Cichelli. 1990. Reactive airway dysfunction syndrome in three police officers following a roadside chemical spill. *Chest* 98:928-929.

Sellakumar AR, CA Snyde, JJ Solomon, and RE Albert. 1985. Carcinogenicity of formaldehyde

and hydrogen chloride in rats. *Toxicol Appl Pharmacol* 81:401-406.

Shriner DS and NL LaCasse. 1969. Histological response of tomato to hydrogen chloride gas. *Phytopathology* 59:1050.

Steenland K, T Schnorr, J Beaumont, W Halperin, and T Bloom. 1988. Incidence of laryngeal cancer and exposure to acid mists. *Br J Ind Med* 45:766-776.

Stevens B, JQ Koenig, V Rebolledo, QS Hanley, and DS Covert. 1992. Respiratory effects from the inhalation of hydrogen chloride in young adult asthmatics. *J Occup Med* 34:923-929.

Sturges WT and RM Harrison. 1989. The use of nylon filters to collect HCl: Efficiencies, interferences, and ambient conditions. *Atmos Environ* 23:1987-1996.

Swiecki TJ, AG Endress, OC Taylor. 1982. Histological effects of aqueous acids and gaseous hydrogen chloride on bean leaves. *Am J of Botany* 69:141-149.

Ten Bruggen Cate HJ. 1968. Dental erosion in industry. *Br J Ind Med* 25:249-266.

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

TCEQ. 2015. Approaches to derive odor-based values. Texas Commission on Environmental Quality. Office of the Executive Director, Austin, TX.

Toxigenics Inc.1984. 90-Day inhalation study of hydrogen chloride gas in B6C3F1 mice, Sprague-Dawley rats and Fischer-344 rats. Study conducted for CIIT, Research Triangle Park, NC. CIIT Docket No. 20915.

Turlo SM and I Broder. 1989. Irritant-induced occupational asthma. *Chest* 96:297-300.

USEPA. 1994. Methods for derivation of inhalation reference concentrations and application of inhalation dosimetry. EPA/600/8-90/066F. Office of Research and Development. Washington, D.C.

USEPA. 1995. Integrated risk information system health assessment of hydrogen chloride (CASRN 7647-01-0). Available from: www.epa.gov/ncea/iris/subst/0396.htm.

United States Environmental Protection Agency (USEPA). 2012 Advances in inhalation gas dosimetry for derivation of a reference concentration (RfC) and use in risk assessment. Washington, D.C. EPA/600/R-12/044).

van Thriel C, M Schäper, E Kiesswetter, S Kleinbeck, S Juran, M Blaszkewicz, HH Fricke, L

Altmann, H Berresheim, and T Brüning. 2006. From chemosensory thresholds to whole body exposures-experimental approaches evaluating chemosensory effects of chemicals. *Int Arch Occup Environ Health* 79(4): 308-21.