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Ammonia

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Acronyms and Abbreviations

Abbreviation	Definition
A	animals
AEGL	acute exposure guideline level
AMCV	air monitoring comparison value
°C	degrees Celsius
CalEPA	California Environmental Protection Agency
CNS	central nervous system
DSD	development support document
ESL	effects screening level
$^{acute}ESL$	acute health-based effects screening level for chemicals 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
F	exposure frequency, days per week
FeV	forced expiratory volume
h	hour
H	humans
Hg	mercury
HEC	human equivalent concentration

Abbreviation	Definition
HQ	hazard quotient
kg	kilogram
LOAEL	lowest-observed-adverse-effect-level
LOEL	lowest-observed-effect-level
MW	molecular weight
µg	microgram
$\mu g/m^3$	micrograms per cubic meter
mg	milligrams
mg/m^3	milligrams per cubic meter
min	minute
MOA	mode of action
n	number
N/A	not applicable
NAC	National Advisory Committee
NOAEL	no-observed-adverse-effect-level
PEFR	peak expiratory flow rate
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
ReV	reference value
TCEQ	Texas Commission on Environmental Quality
UF	uncertainty factor
UF_H	interindividual or intraspecies human uncertainty factor
UF_A	animal to human uncertainty factor
UF_{Sub}	subchronic to chronic exposure uncertainty factor

Abbreviation	Definition
UF_L	LOAEL to NOAEL uncertainty factor
UF_D	database uncertainty factor
USEPA	United States Environmental Protection Agency
VC	vital capacity

Chapter 1 Summary Tables

Table 1 for air monitoring and Table 2 for air permitting provide a summary of health- and welfare-based values resulting from an acute and chronic evaluation of ammonia. Please refer to Section 1.6.2 of *the TCEQ Guidelines to Develop Toxicity Factors* (TCEQ 2012) for an explanation of values used for review of ambient air monitoring data and air permitting. Table 3 provides summary information on ammonia's physical/chemical properties.

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

Short-Term Values	**Concentration**	**Notes**
Acute ReV	590 µg/m^3 (830 ppb) **Short-Term Health**	**Critical Effect(s):** Mild, transient upper respiratory symptoms and central nervous system (CNS) effects (eye discomfort, smell, headache, dizziness, and feelings of intoxication) in exposed human volunteers
$^{acute}ESL_{odor}$	3600 µg/m^3 (5200 ppb) **Odor**	Sharp, pungent, repellent
$^{acute}ESL_{veg}$	2000 µg/m^3 (2800 ppb) **Short-Term Vegetation**	**Critical Effect(s):** Foliar damage in tomato plants
Long-Term Values	**Concentration**	**Notes**
Chronic ReV	320 µg/m^3 (450 ppb) **Long-Term Health**	**Critical Effect(s):** Free-standing NOAEL for lack of significant differences in self-reported symptoms and/or measured lung function parameters in workers
$^{chronic}ESL_{threshold(c)}$ $^{chronic}ESL_{nonthreshold(c)}$	---	Data are inadequate for an assessment of human carcinogenic potential
$^{chronic}ESL_{veg}$	---	Insufficient data

[a] Ammonia is not monitored for by the TCEQ's ambient air monitoring program, so currently no ambient air data (i.e., peaks, annual averages, trends, etc.) are available to assess ammonia concentrations in Texas ambient air

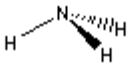
Table 2. Air Permitting Effects Screening Levels (ESLs)

Short-Term Values	Concentration	Notes
^{acute}ESL [1 h] (HQ = 0.3)	180 µg/m^3 (250 ppb) [a] **Short-Term ESL for Air Permit Reviews**	**Critical Effect:** Mild, transient upper respiratory symptoms and central nervous system (CNS) effects (eye discomfort, smell, headache, dizziness, and feelings of intoxication) in exposed human volunteers
^{acute}ESL$_{odor}$	3600 µg/m^3 (5200 ppb)	Sharp, pungent, repellent
^{acute}ESL$_{veg}$	2000 µg/m^3 (2800 ppb) **Short-Term Vegetation**	**Critical Effect(s):** Foliar damage in tomato plants
Long-Term Values	**Concentration**	**Notes**
^{chronic}ESL$_{threshold(nc)}$ (HQ = 0.3)	92 µg/m^3 (130 ppb) [b] **Long-Term ESL for Air Permit Reviews**	**Critical Effect:** Free-standing NOAEL for lack of significant differences in self-reported symptoms and/or measured lung function parameters in workers
^{chronic}ESL$_{threshold(c)}$ ^{chronic}ESL$_{nonthreshold(c)}$	---	Data are inadequate for an assessment of human carcinogenic potential
^{chronic}ESL$_{veg}$	**--**	Insufficient Data

[a] Based on the acute ReV of 590 µg/m^3 (830 ppb) multiplied by 0.3 to account for cumulative and aggregate risk during the air permit review.

[b] Based on the chronic ReV of 320 µg/m^3 (450 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	NH_3	ChemFinder (2008)
Chemical Structure		ChemFinder (2008)
Molecular Weight	17.03	Hazardous Substances Databank (HSDB) (1998)
Physical State at 25°C	Gas	HSDB (1998)
Color	Colorless	HSDB (1998)
Odor	Sharp, pungent, repellent	HSDB (1998)
CAS Registry Number	7664-41-7	HSDB (1998)
Synonyms	R 717, AM-Fol, ammonia gas, anhydrous ammonia, liquid ammonia, Nitro-sil, Spirit of hartshorn	HSDB (1998)
Solubility in water	482,000 mg/L at 25°C	HSDB (1998)
Log K_{ow}	0.23	HSDB (1998)
Vapor Pressure	7510 mm Hg at 25°C	HSDB (1998)
Relative Vapor Density (air = 1)	0.59	HSDB (1998)
Melting Point	-77.7°C	HSDB (1998)
Boiling Point	-33.3°C	HSDB (1998)
Conversion Factors	1 $\mu g/m^3$ = 1.414 ppb 1 ppb = 0.707 $\mu g/m^3$	USEPA (2012)

Chapter 2 Major Sources and Uses

Atmospheric ammonia is produced by both natural and anthropogenic sources. Natural, exogenous sources of ammonia in the environment include volatilization from the decomposition of organic matter and excreta by soil microbes and/or fungi, exhalation of endogenous ammonia, and volcanic eruptions. The National Atmospheric Deposition Program (NADP) estimates that approximately 85 percent of ammonia emissions in the United States was from livestock waste and commercial fertilizer application.

The majority (approximately 87%) of the over eight million metric tons of ammonia produced industrially in the United States in 2010 was used in fertilizer, but ammonia is also used in the manufacture of plastics, synthetic fibers, and explosives (USGS 2011). Ammonia is also a component of automobile exhaust and is a byproduct of three-way catalytic converters (Becker et al. 1999; Committee on the Environment and Natural Resources 2000). Anhydrous ammonia is used as a refrigerant in industrial applications. Therefore, potential sources of ammonia released to the environment can include deposition and/or run-off from usage of man-made fertilizer, accidental release during transport, or emissions and/or discharges from manufacturing facilities.

Sampling conducted in 2007 in the western New Mexico, western Colorado, and eastern Oklahoma areas indicated annual mean ambient air concentrations of ammonia range from 0.2 – 1.8 ppb, based on three-week integrated passive samples (Sather et al. 2008). Interestingly, Stilwell, Oklahoma (considered by the authors to be representative of rural, background levels) had the highest average concentration and second highest maximum concentration of the sampling locations, which included urban, power plant-impacted, oil/gas-impacted, and oil/gas/mobile-impacted representative areas. Currently, ammonia is not a targeted compound by the TCEQ's ambient air monitoring program, therefore, only ammonia data from targeted monitoring projects are available in Texas. There is one site of the NADP's ammonia gas monitoring network (AMoN), active since 2007, located in Randall County. Data from the AMoN are used to assess long-term national trends in ambient ammonia concentrations and to validate atmospheric models.

In the atmosphere, ammonia readily reacts with acidic compounds (sulfuric acid, nitric acid, nitrous acid, and hydrochloric acid) to form fine particulate ammonium salts (Krupa 2003). For this reason, ammonia is considered a fine particulate matter ($PM_{2.5}$) precursor. Ammonium salt formation is faster during the day and during the spring and summer months (Krupa 2003, Sather et al. 2008). The Agency for Toxic Substances and Disease Registry (ATSDR 2004) estimates that the half-life for gaseous ammonia in the air is a few days. The Ontario Ministry of the Environment (2001) indicated the estimated residence time is between 5 and 10 days, while a review by Krupa (2003) indicated the residence time was up to four days, depending on season.

Ammonia is one of the approximately 1000 volatile compounds that can be detected in human breath (Hibbard and Killard 2011). It is a product of amino acid and protein metabolism and as such is endogenously produced in humans and many other animals. In healthy human adults, an

average level of ammonia in breath ranges between approximately 265 ppb to 1 ppm (Hibbard and Killard 2011, Lewicki et al. 2005). However, with liver and/or kidney dysfunction, ammonia in blood may not be filtered properly and levels of ammonia in breath could be higher. The increased ammonia levels due to liver dysfunction may cause hyperammonemia (excess ammonia in the blood) to develop which could result in hepatic encephalopathy (symptoms may include confusion, drowsiness, and disorientation). With kidney dysfunction, conditions such as uremia, acidosis, and edema may develop. Any excess ammonia not filtered out of the body can diffuse into the lungs and be exhaled (Hibbard and Killard 2011). Thus, measurement of ammonia in breath can be a useful noninvasive diagnostic tool in detecting liver and/or kidney disease. Rapid and accurate methods for measuring ammonia in breath are being developed.

Although not significant to ambient levels, elevated personal exposures to ammonia can also occur in cigarette smoke and household cleaning solutions (ATSDR 2004; Fedoruk et al. 2005; Medina-Ramon 2005; WHO 1986; Willems et al. 2006). Ammonia has been measured inside beauty salons at concentrations ranging from 0.21 to 1.23 ppb with higher concentrations measured near the use of permanent wave solution (Oikawa et al. 2012)

Chapter 3 Acute Evaluation

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

The present evaluation of ammonia toxicity is based primarily on the Acute Exposure Guideline Levels (AEGL) assessment document (NRC 2008), ATSDR's toxicological profile (2004), and a review of scientific literature since 2000. The available studies (occupational and experimental) indicate that acute exposure to low to moderate concentrations of ammonia (less than 100 ppm) can cause sensory irritation (discomfort in the eyes and/or nose) in humans, but are not related to functional respiratory deficits. In general, the acute health effects reported in animals following short-term inhalation of ammonia include oral, nasal and eye irritation, respiratory tract irritation, decreased respiratory rate, increased respiratory depth, reduced body weight, and lethargy. In humans, the health effects of acute exposure are similar to those reported in animals and include oral, nasal and eye irritation, respiratory tract irritation, and increased respiratory depth (Alberta Environment 2004). Tissues and organs distant from the entry point do not experience toxic effects at levels < 150 ppm) because of the scrubbing mechanism of the nasopharyngeal region (Silverman et al. 1949). Ammonia is highly water soluble and as such readily dissolves in the mucous membrane layer of the cornea and upper airway. This "scrubbing" protects the lower respiratory tract and was shown to be concentration and time dependent (Silverman et al. 1949). Ninety one to 93% of ammonia at concentrations up to 429 ppm in humans exposed via inhalation in one breath was retained in the respiratory tract (Landahl and Herrmann 1950). However, if ammonia adsorbs to respirable dust (measured as particulate matter or PM), ammonia can penetrate deeper into the lungs (Alberta Environment 2004).

3.1.1 Physical/Chemical Properties

Ammonia is a colorless gas with a pungent, irritating odor. It is both highly water soluble and reactive. The main physical/chemical properties are summarized in Table 3.

3.1.2 Key and Supporting Studies

3.1.2.1 Human Studies

3.1.2.1.1 Key Study (Sundblad et al. 2004)

Sundblad et al. (2004) exposed 12 volunteers (seven women and five men aged 21-28 years) to either clean air, 5, or 25 ppm ammonia for 3 hours (h) in a 20-m^3 stainless steel exposure chamber. None of the volunteers reported a history of airway diseases. Exposure sessions included resting and bicycle exercising periods, which were rotated every 30 minutes (min) during the 3-h session. Exposure sessions were repeated on three occasions with a 1-week resting period between sessions.

Lung function was assessed by measuring vital capacity (VC) and forced expiratory volume in one second (FEV_1) one week prior to the first exposure and 7 h after exposure. Peak expiratory flow rate (PEFR) was also measured before exposure, immediately after exposure, and seven h after exposure. In addition, in order to determine whether exposure to ammonia altered bronchial responsiveness, volunteers were subjected to a methacholine provocation test. None of the lung function or bronchial responsiveness parameters from either of the exposed groups was statistically significantly different from the control group. Similarly, no treatment-related changes were noted in any of the assessments of inflammatory response (i.e., nasal lavage fluid, blood, and exhaled nitric oxide) collected approximately 30 min before exposure and seven h after exposure.

Volunteers were also given a standardized questionnaire to rate their level of discomfort (eye, nose, and throat or airway discomfort, difficulty breathing, solvent smell, headache, fatigue, nausea, dizziness, and feelings of intoxication) at regular intervals throughout the exposure session (immediately before exposure, during, and after exposure). Volunteers rated their discomfort on a Visual Analogue Scale, in which volunteers mark a vertical line on a 0 – 100 mm long horizontal line. The authors provided descriptors to marks on the scale for ease in evaluation, shown in Table 4.

Table 4 Visual Analogue Scale Ratings (Sundblad et al. 2004)

Visual Analogue Scale Rating (mm)	Description of Discomfort Level
0	Not at all
6	Hardly at all
26	Somewhat
48	Rather
72	Quite
90	Very
100	Almost unbearable

A statistically significant increase in symptom rating was identified for each of the ten symptoms at the 25 ppm ammonia exposure concentration as compared to the control group. Likewise, there was a statistically significant increase in symptom ratings for eye discomfort, solvent smell, headache, dizziness, and feelings of intoxication at the 5 ppm ammonia exposure concentration as compared to the control group. Irritation and central nervous system (CNS) symptoms during exposure did not exceed a "rather" rating on a scale of discomfort level. Some effects observed in this study could be odor-related as the the $^{acute}ESL_{odor}$ is 5.2 ppm (See Section 3.2.1). Based on the transient symptoms of eye discomfort, headache, dizziness, and feelings of intoxication, the 5 ppm dose was treated as a *minimal* lowest observable adverse effect level (LOAEL) in this analysis.

3.1.2.1.2 Supporting Study (Verberk 1977)

Verberk (1977) conducted an acute exposure study with 16 volunteers (eight volunteers knew the effects of ammonia from the literature (experts) and eight volunteers not familiar with ammonia (non-experts). All volunteers were exposed to 50, 80, 110, and 140 ppm gaseous ammonia in a resting state over a 2-h period in a 25-m^3 exposure chamber with a one-week recovery period between exposure sessions. No control group was used in this study. Subjective responses, such as smell, taste, eye irritation, nose irritation, throat irritation, chest irritation, urge to cough, headache, and general discomfort were recorded every 15 min throughout the exposure session. Lung function parameters (VC, FEV_1, and forced inspiratory volume in one second) were measured immediately before entering and after exiting the exposure chamber. Finally, 13 of the 16 volunteers participated in a histamine response experiment a few weeks after the ammonia exposure experiment to determine if the volunteers exhibited hypersensitivity to stimuli.

None of the lung function parameters were significantly depressed following exposure to any of the concentrations of ammonia used in this study. In addition, none of the tested volunteers exhibited any hyper-responsiveness to histamine. At the lowest concentration tested (50 ppm), half of the volunteers indicated subjective symptoms of irritation at or above a nuisance level.

Unfortunately, because no control group was used in this study and there was no statistical analysis of the subjective responses recorded by the volunteers during the exposure sessions, subjective responses can only be used qualitatively. Therefore, a LOAEL of 50 ppm for irritation was identified from this study. The authors noted that subjective responses were more pronounced in the non-expert group of volunteers than in the expert group. Verberk et al. (1977) was used by ATSDR for the derivation of the acute inhalation minimum risk level (ATSDR 2004).

3.1.2.1.3 Sigurdarson et al. (2004)

Sigurdarson et al. (2004) exposed six healthy volunteers and eight mild, intermittent asthmatics to 16 to 20 ppm ammonia and/or 4 mg/m3 grain dust aerosol for 30 min in an exposure chamber. Participants wore nose clips during exposures to ensure mouth breathing. Exposure to ammonia alone did not induce statistically or clinically significant changes in FEV1 or bronchial hyperreactivity in either the asthmatics or healthy volunteers. Exposure to grain dust induced changes in the asthmatics (transient decrease in FEV1 and increased bronchial hyperreactivity), but coexposure to ammonia did not enhance these effects.

3.1.2.1.4 Petrova et al. (2008)

Petrova et al. (2008) exposed 25 healthy volunteers and 15 mild to moderate asthmatics to one of 20 nominal ammonia concentrations of between 2 to 500 ppm via a nasal cannula and/or goggles for a maximum duration of five min. Participants were simultaneously exposed to clean air in one side of the cannula/goggles and the specified concentration of ammonia in the other and asked to identify which nostril/eye had been exposed to the ammonia. According to the authors, this lateralization method used to determine sensory irritation thresholds was designed because the trigeminal system in the eyes and nasal mucosa can provide spatial localization information, whereas the olfactory system cannot. Exposures lasted from 10 to 30 seconds, participants were given between 15 to 60 min rest in between exposures, and up to three exposures occurred in a single day. Ocular irritation thresholds for ammonia detection were 133 ppm (asthmatics) and 127 ppm (healthy controls). Nasal irritation thresholds for ammonia detection were 167 ppm (asthmatics) and 179 ppm (healthy controls).The authors concluded that the irritation thresholds did not differ between asthmatic and healthy volunteers in the ocular, nasal, or combined exposure conditions. In addition, asthmatics and healthy volunteers were statistically similar in their rating of odor, irritation, or annoyance to the ammonia exposures (all ratings were between weak and moderate). Finally, spirometry results retrieved during various parts of the study in asthmatics and a subset of healthy volunteers revealed no decreases greater than 5% in FEV1

3.1.2.1.5 Other Supporting Studies

An unpublished study conducted by MacEwen et al. (1970) has been used by NRC (2008) and California Environmental Protection Agency (CalEPA) (1999) to derive risk-based values (AEGL-1 for non-disabling effects and acute Reference Exposure Level (REL), respectively). In addition, CalEPA (1999) combined exposure concentrations adjusted for 1-hr exposure duration

from four studies using benchmark dose modeling. In addition to MacEwen et al. (1970), exposure concentrations from the Industrial Bio-Test Laboratories (1973) (unpublished), Silverman et al. (1949), and Verberk (1977) were used by CalEPA to derive the acute REL in 1999. The TCEQ was unable to obtain copies of MacEwen et al. (1970) and Industrial Bio-Test Laboratories (1973) and therefore did not include them in this derivation process. However, conclusions from these studies as cited in NRC (2008) are included below.

MacEwen et al. (1970) exposed six human volunteers (head only) to 30 and 50 ppm ammonia for 10 min. Volunteers were asked to subjectively rate odor and irritation to the nose and eyes on a five point scale. When exposed to 30 ppm, three volunteers reported that the odor was strong or highly penetrating and two volunteers reported the odor was easily noticeable or moderate. With regard to irritation, two volunteers reported faint irritation and three volunteers did not detect irritation. One volunteer did not respond. At 50 ppm, four volunteers indicated moderate irritation. One volunteer indicated faint or just perceptible irritation and one volunteer did not detect irritation. Odor was reported as strong or highly penetrating for all volunteers. Based on the discussion in NRC (2008) a control group was not used in this study. The LOAEL of 30 ppm was used for development of the AEGL-1.

The Industrial Bio-Test Laboratories (1973) exposed ten human volunteers to ammonia at 32, 50, 72, or 134 ppm for five min. Volunteers indicated whether they experienced nasal dryness, lacrimation, and irritation of the nose, eye, throat, and chest. The NRC (2008) summary indicated severity of effects was also documented, though this information was not detailed in the NRC document. One volunteer reported experiencing dryness of the nose at 32 ppm. Two volunteers reported experiencing nasal dryness at 50 ppm. At an exposure concentration of 72 ppm ammonia, two volunteers reported nasal irritation, three reported eye irritation, and three reported throat irritation. Nasal, eye, throat, and chest irritation and lacrimation was reported from several volunteers following exposure to 134 ppm. The CalEPA (1999) acute toxicity summary indicates that the authors "discounted the significance of nasal dryness reported at the two lowest levels," though this statement was not included in the NRC (2008) summary.

Ferguson et al. (1977) exposed six healthy, previously unaccustomed male and female workers to ammonia at 25, 50, and 100 ppm for 6 h per day, five days a week, over five weeks. Irritation, pulse, pulmonary function, and other biological responses were recorded twice daily by the workers and a physician. According to the authors, the physician noted less mild eye, nose, or throat irritation in the workers during the second week than the first week. In addition, the authors report that the workers "were not aware of the irritation [mild eye, nose, or throat irritation] noted by the physician and suffered no discomfort as a result of exposures up to 100 ppm after the first week." All other testing showed no significant differences between exposed volunteers and controls.

3.1.2.2 Animal Studies

3.1.2.2.1 Upper Respiratory Tract Studies

Studies in mice, rats, cats, pigs, and rabbits indicate that the upper respiratory tract is the target organ for short-term exposure to ammonia at concentrations below 1000 ppm (ATSDR 2004, NIWL 2005). However, animal studies were not considered for the derivation of the acute ReV and ^{acute}ESL because adequate human studies were available and are preferred over animal studies. Therefore, this document focuses on relevant human studies (see above). Please refer to ATSDR (2004) for a discussion of short-term animal inhalation studies.

3.1.2.2.1 Reproductive/Developmental Studies

Since ammonia is efficiently scrubbed in the upper airways, significant systemic accumulation does not occur. Minimal increases in blood ammonia concentration were observed after exposure to gaseous ammonia at concentrations up to 1000 ppm for 24 h in rats (Schaerdel et al., 1989 as cited in US EPA 1998). In addition, Silverman et al. (1949) calculated that seven humans exposed to 500 ppm ammonia (six for 30 min exposure and one for 15 min) had exhaled 70 to 80% of the ammonia (reported concentrations were between 350 and 400 ppm in breath) after reaching equilibrium within 30 min. After cessation of exposure, exhaled breath concentrations returned to pre-exposure concentrations within three to eight min. Therefore, because of the limited uptake in both humans and animals, developmental effects would not be expected to occur.

No statistically significant differences were noted in ovarian or uterine weights of pigs exposed to about 7 or 35 ppm ammonia for 6 weeks (Diekman et al. 1993, as cited in ATSDR 2007). Female pigs that were continuously exposed to about 35 ppm ammonia from 6 weeks before breeding until day 30 of gestation had no statistically significant differences in age at puberty, number of live fetuses, or fetus-to-corpus luteum ratio compared to pigs exposed to only about 7 ppm (Diekman et al. 1993). (ATSDR 2007)

3.1.3 Mode of Action (MOA) and Dose Metric

Because of its high reactivity and water solubility, ammonia is an upper respiratory irritant at lower concentrations, but may cause severe lower respiratory effects at higher concentrations, such as those that occur in occupational accidents, when the scrubbing mechanism of the nasopharyngeal region is saturated. Injury to respiratory tissues is primarily due to ammonia's alkaline (i.e., caustic) properties and it will form ammonium ion (NH^{4+}) and/or ammonium hydroxide (NH_4OH) upon contact with water or mucosa, often resulting in thermal and/or chemical burns of the epithelial tissue of the eyes, mouth, and respiratory tract. Ammonia directly denatures tissue proteins and causes saponification of cell membrane lipids, which leads to cell disruption and death (EPA 2012). The breakdown of proteins in turn results in an inflammatory response which further damages surrounding tissue (EPA 2012).

Ammonia concentrations in the blood remain stable after inhalation exposure in humans to very high concentrations of ammonia, indicating a lack of absorption from the respiratory tract (NRC 2008). Animal studies have shown that inhalation of ammonia increases the level of ammonia in blood (NRC 2008). Studies by Sigurdarson et al. (2004) and Petrova et al. (2008) collectively indicate that asthmatics are not more sensitive to the irritant effect of ammonia.

Because adverse effects due to ammonia exposure (e.g., ammonia-induced irritation effects) are typically concentration-dependent, air ammonia concentration will be used as the dose metric.

3.1.4 Point of Departure (POD) for Key Study and Critical Effect

The LOAELs for the key Sundblad et al. (2004) study and supporting Verberk (1977) study are 5 ppm and 50 ppm, respectively, with the LOAEL of 5 ppm from the key study conservatively selected as the POD. The critical effects observed at the LOAEL of 5 ppm were eye discomfort, solvent smell, headache, dizziness, and feelings of intoxication. Since Sundblad et al. (2004) is a human study, the POD of 5 ppm is the same as the POD_{HEC}.

3.1.5 Dosimetric Adjustments

Exposure concentration, and not exposure duration, appears to determine ammonia's acute local irritation effects (NRC 2008; ATSDR 2004). Therefore, no exposure duration adjustment was deemed necessary. The adjusted point of departure ($POD_{HEC\text{-}ADJ}$) for the key study is 5 ppm.

3.1.6 Adjustments of the POD_{HEC}

Due to ammonia's nonlinear MOA, uncertainty factors (UFs) were applied to the POD for the key study consistent with TCEQ guidance (TCEQ 2012). UFs for intrahuman variability (UF_H), LOAEL-to-NOAEL uncertainty (UF_L), and database uncertainty (UF_D) applied to the POD_{HEC} from the key study are described below.

- A UF_H of 3 was applied to account for sensitive members of the population. A higher UF_H was not applied because short-term studies indicate that asthmatics, have similar sensitivities to the irritant effects of ammonia as healthy individuals (Sigurdarson et al. 2004 and Petrova et al. 2008).
- Because the key study involved human subjects, a UF_A was not applicable.
- A UF_L of 2 was applied because the effects experienced by exercising human volunteers in this study were mild and transient local irritant effects and the minimal LOAEL selected was well below that identified in other similar studies.
- A UF_D of 1 was applied because there was high database confidence. Although data on systemic endpoints, including reproductive and developmental data, are minimal, the UF_D is not higher because ammonia is efficiently removed by the upper airway at lower and closer to more environmentally relevant concentrations (e.g., minimal increases in blood ammonia concentration were observed after exposure to gaseous ammonia at

concentrations up to 1,000 ppm for 24 h in rats (Schaerdel et al. 1989) and humans exhaled between 350 to 400 ppm of the inhaled 500 ppm exposure concentration in breath after 30 min of exposure (Silverman et al. 1949)).

The UFs were applied to the POD from the key study to calculate the acute ReV (Table 5).

$$\text{acute ReV} = POD_{HEC} / (UF_H \times UF_L \times UF_D)$$
$$= 5 \text{ ppm} / (3 \times 2 \times 1)$$
$$= 5 \text{ ppm} / 6$$
$$= 0.833 \text{ ppm}$$

Once the ReV was calculated, it was rounded to two significant figures to result in an acute ReV of 830 ppb (590 µg/m^3).

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

The acute ReV of 830 ppb from the key study was multiplied by the target hazard quotient of 0.3 to produce the ^{acute}ESL of 250 ppb (180 µg/m^3) (Table 5).

Table 5 Derivation of the Acute ReV and ^{acute}ESL

Parameter	**Values and Descriptions**
Study	Sundblad et al. (2004)
Study Population	12 healthy volunteers (seven women and five men) in 30-min alternating exercising and resting states
Study Quality	Medium
Exposure Methods	3-h inhalation exposure in a 20-m^3 stainless steel exposure chamber to 0, 5, or 25 ppm ammonia
POD_{HEC}	5 ppm (minimal LOAEL)
Critical Effects	Mild, transient upper respiratory symptoms and CNS effects (eye discomfort, smell, headache, dizziness, and feelings of intoxication)
Exposure Duration	3 h
Extrapolation to 1 h	No adjustment made; effects are concentration-dependent
$POD_{HEC\ ADJ}$ (1 h)	5 ppm
Total UFs	6
Interspecies UF	NA
Intraspecies UF	3
LOAEL UF	2
Incomplete Database UF *Database Quality*	1 High
acute ReV [1 h] (HQ = 1)	**590 µg/m^3 (830 ppb)**
^{acute}ESL [1 h] (HQ = 0.3)	**180 µg/m^3 (250 ppb)**

3.2. Welfare-Based Acute ESLs

3.2.1 Odor Perception

Ammonia has a pungent, irritating odor with a wide odor detection threshold range of 43 to 53,000 ppb. Leonardos et al. (1969) reported a 100% odor detection threshold of 46,800 ppb ammonia. Smeets et al. (2007) reported a mean odor detection threshold of 2600 ppb ammonia in female volunteers using the European standard CEN 13725 dynamic olfactometry. Nagata

(2003) reported a 50% odor detection threshold of 1500 ppb using the triangular bag method. Van Doorn (2002) reported odor thresholds using three different methods: the NVN2820 compatible method (1590 ppb), the 1988 TNO method from the Netherlands (1070 ppb), and the Japan method (150 ppb). Additionally, the American Industrial Hygiene Association (AIHA 1989) reported the geometric mean of the range of reported values to be 17,000 ppb ammonia.

Based on an evidence integration approach and historical information, the $^{acute}ESL_{odor}$ is 3600 $\mu g/m^3$ (5200 ppb) (TCEQ 2015). 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 Vegetative Effects

Ammonia is naturally-occurring in the atmosphere and is used by plants as a source of nitrogen. Depending on the ambient air concentration of ammonia, plants can either absorb ammonia or be an emitter of ammonia. Farquhar et al. (1980) determined that young plants emit ammonia below ambient concentrations of between 1 – 4 $\mu g/m^3$ and will absorb ammonia when ambient concentrations rise above 4 $\mu g/m^3$. Atmospheric ammonia enters the plant almost exclusively through the stomata of the leaves (Van Hove et al., 1987a, as cited in Krupa 2003). It is quickly dissolved and converted to ammonium (NH_4^+) in the plant.

Krupa (2003) conducted an extensive literature review of plant toxicity studies which serves as the basis for the following evaluation. At very high concentrations, ammonia can cause direct toxic effects on plants by leaf etching. Several European studies have documented foliar damage in trees, including yellowing needles and needle necrosis in conifers, near large livestock farms. However, because gaseous ammonia can provide nitrogen that is necessary for plant growth, studies have shown enhanced growth after exposure to lower concentrations. Indeed, it is only after the plant's ability to assimilate ammonia into organic nitrogen compounds has been overwhelmed that plant toxicity is evident. The point at which the assimilation capacity of the plant is overwhelmed can fluctuate based on several internal and external factors, including seasonal changes in availability of light and temperature. Krupa (2003) noted that, in general, native vegetation, including mosses, lichens, mountain tobacco and some flowering plants (petunias), are more sensitive to the effects of ammonia than forests, which are more sensitive than agricultural plants. However, according to the TCEQ (2012) Guidelines, evaluation of adverse vegetative effects for the purpose of this DSD should be focused on native plants and/or plants of agricultural importance grown in Texas.

Therefore, the key study for the derivation of a short-term vegetative-based ESL was Van der Eerden (1982). Tomato plants (*Lycopersicon esculentum*) were exposed to 2800 ppb (2000 $\mu g/m^3$) ammonia for 24 h in indoor controlled environmental chambers. Tomatoes that were exposed to ammonia in the dark (thus limiting photosynthetic ability) displayed increased foliar injury to ammonia than plants that were exposed to ammonia in the presence of light. The author determined that ammonia inhibited photosynthetic phosphorylation, which decreased

carbohydrate production and growth. This was compounded by the lack of photosynthesis due to the dark fumigation conditions.

The key study is supported by subacute studies conducted by Hulsenberg (1990), as cited in Krupa (2003). Hulsenberg (1990) noted that cucumbers (*Cucumis sativus*) exposed to 2800 ppb (2000 µg/m^3) ammonia for 30 days in closed field chambers exhibited over 50% more brownish discoloration in the leaves than controls. In addition, both lettuce (*Lactuca sativa var. capitata*) and spinach (*Spinacia oleracea*) exposed in closed field containers to 7100 ppb (5000 µg/m^3) ammonia for 14 days exhibited over 50% more chlorotic leaves than controls.

According to the TCEQ Guidelines, $^{acute}ESL_{veg}$ is set at a threshold concentration for adverse effects (TCEQ 2012). Therefore, the $^{acute}ESL_{veg}$ is set at 2800 ppb, a lowest-observed-effect-level (LOEL) identified by Van der Eerden (1982) for tomato plants.

3.3. Short-Term ESL and Values for Air Monitoring Evaluation

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

acute ReV = 590 µg/m^3 (830 ppb)
$^{acute}ESL$ = 180 µg/m^3 (250 ppb)
$^{acute}ESL_{odor}$ = 3600 µg/m^3 (5200 ppb)
$^{acute}ESL_{veg}$ = 2000 µg/m^3 (2800 ppb)

The short-term ESL for air permit evaluations is the $^{acute}ESL$ of 180 µg/m^3 (250 ppb) (Table 2). Although we do not currently monitor for ammonia, the ReV of 590 µg/m^3 (830 ppb) is lower than both the $^{acute}ESL_{odor}$ of 3600 µg/m^3 (5200 ppb) and the $^{acute}ESL_{veg}$ of 2000 µg/m^3 (2800 ppb) (Table 1).

3.3 Acute Inhalation Observed Adverse Effect Levels (OAELs)

In regard to acute inhalation OAELs in Section 3.13 of TCEQ's Guidelines to Develop Toxicity Factors (2012), as the lowest human LOAEL for minimal effects including mild, transient upper respiratory symptoms and central nervous system (CNS) effects (eye discomfort, smell, headache, dizziness, and feelings of intoxication) was 5 ppm at an exposure duration of 3 h. This level is the considered the lowest concentration where such effects could be expected to occur in some members of the population exposed for a sufficient duration. In the supporting study, eye, nose, and throat irritation was reported in human volunteers exposed to 50 ppm for 2 h. Adverse effects are not a certainty at this concentration and duration, although depending upon the sensitivities of the study population relative to those exposed environmentally, other subpopulations could be more sensitive.

Chapter 4 Chronic Evaluation

4.1 Noncarcinogenic Potential

Few studies have been conducted on the effect of long-term exposure to ammonia at low concentrations. Ammonia is an upper respiratory tract irritant in humans. Symptoms including cough, chest tightness, stuffy/runny nose, sneezing, phlegm, wheezing, dyspnea, chronic bronchitis, and asthma, have been reported in studies of workers exposed to ammonia (Rahman et al. 2007, Ballal et al. 1998). Several studies were identified which noted various respiratory illnesses (e.g., restrictive lung disease, chronic obstructive pulmonary disease, bronchiectasis) as sequelae following acute exposures to very high concentrations of ammonia, typically in occupational or industrial accidents (Brautbar et al. 2003; de la Hoz et al. 1996; NRC 2008). Animal studies also show that repeated exposure to ammonia can affect the respiratory tract.

In addition to irritation effects noted as a result of both short- and long-term ammonia exposure, studies have shown acclimation effects in humans exposed to ammonia. Ferguson et al. (1977) exposed six healthy, previously unaccustomed male and female workers to ammonia at 25, 50, and 100 ppm for 6 h per day, five days a week, over five weeks. Irritation, pulse, pulmonary function, and other biological responses were recorded twice daily by the workers and a physician. According to the authors, the physician noted less mild eye, nose, or throat irritation in the workers during the second week and subsequent weeks, than the first week.

Similarly, Ihrig et al. (2006) exposed 43 healthy male volunteers (10 previously exposed to ammonia and 33 naïve workers) to 0, 10, 20, 20 with two 30-min peak exposures of 40 and 50 ppm ammonia for 4 h over five consecutive days in an exposure chamber. In general, previously exposed workers reported fewer symptoms than the naïve workers. The differences between previously exposed and naïve workers were only statistically significant with regard to olfactory symptoms, not respiratory or irritant symptoms.

Due to the decrease in awareness of irritation following acclimation to the irritant effects of ammonia, it is possible that acclimatized individuals would be more susceptible to pulmonary disease. However, because a study of sufficient quality in occupationally exposed workers is available and the study provides a NOAEL, the added susceptibility of acclimatized persons is most likely accounted for in the derivation of the chronic ReV by the application of the intra-human, UF_H. This is also supported by occupational studies discussed in Section 4.1.1.3.

4.1.1 Physical/Chemical Properties and Key Studies

4.1.1.1 Physical/Chemical Properties

Physical/chemical properties of ammonia are discussed in Chapter 3. Because of ammonia's high reactivity and water solubility, it is anticipated to primarily cause portal-of-entry respiratory effects.

4.1.1.2 Key Study (Holness et al. 1989)

Holness et al. (1989) conducted a cross-sectional occupational exposure study to determine effects of ammonia on 58 workers who had chronic exposure to ammonia compared with 31 control workers (from stores and office areas of the plant) in a soda ash plant in Canada. All workers were male and were exposed to ammonia in the production of sodium carbonate (soda ash). Study participants had an average of 12.2 years of exposure. Air samples collected near the worker's collar over an average period of 8.4 h (one work shift) demonstrated a mean time weighted average (TWA) of 9.2 ppm ammonia in the exposed group and 0.3 ppm ammonia in the control group. The exposed workers were also grouped into three exposure categories of high (≥12.5 ppm), medium (6.25-12.5 ppm), and low (<6.25 ppm). The authors stated that it was not possible to estimate each individual's exposure over his working lifetime. Instead, they created an exposure index by multiplying personal ammonia results obtained by the authors by years of exposure. The resulting exposure index was used in a regression analysis with baseline lung function parameters.

Each volunteer was given a questionnaire to determine work and medical history. No statistically significant difference in age, height, weight, years at the plant, cigarette smoking habits, or self-reported medical symptoms (e.g., flu, cough, sputum, chronic bronchitis, wheeze, chest tightness, dyspnea, chest pain, rhinitis, eye complaints, throat, or skin rash) was evident between the exposed and control volunteers. Though not statistically significant, workers in the exposed group reported exacerbated symptoms, including cough, wheeze, nasal complaints, eye irritation, and throat discomfort, due to working in the plant. Forced vital capacity (FVC), FEV_1, and forced expiratory flow rates at 50% and 75% of the vital capacity were measured by spirometry on the first and last day of the worker's work week. There was no statistically significant difference in lung function parameters before and after the work shift of the exposure group. Similarly, no dose-dependent trend was evident when comparing the control group to the exposure group. The workers, grouped into three exposure categories, experienced no exposure-related differences, including symptoms, decline in baseline lung function, or increasing declines in lung function over the work shift. No relationship between chronic exposure and lung function parameters was demonstrated.

Because no significant relationship was determined between ammonia exposure and self-reported symptoms and/or the measured lung function parameters, a free-standing NOAEL of 12.5 ppm from the high exposure group (8.8 mg/m^3) was identified for this study. A LOAEL was not identified for this study. Holness et al. (1989) was also used as the key study in the derivation of the USEPA's recent draft chronic inhalation reference value and Ontario Ministry of the Environment's 24-h air quality standard (USEPA 2012 and OMOE 2001).

4.1.1.3 Other Studies

Other limited occupational exposure studies are available, but are not of sufficient quality to use in the derivation of the chronic ReV. These studies are included as a qualitative comparison to the key study.

Ballal et al. (1998) examined the prevalence of respiratory symptoms and disease in 161 male workers and 355 control male workers in two urea fertilizer factories in Saudi Arabia. Volunteers completed a respiratory symptom questionnaire based on a British Medical Research Council questionnaire. The geometric mean of three 8-h air samples collected close to the workers' stations in Factories A and B (a total of 97 air samples from both facilities) was considered representative of concentrations since production at the facilities began in 1983 (Factory A) and 1988 (Factory B). Ammonia concentrations ranged from 2.0 – 130.4 mg/m^3 (2.8 – 184.1 ppm) in Factory A and from 0.02 – 7.0 mg/m^3 (0.03 – 9.9 ppm) in Factory B. The highest geometric mean ammonia concentrations (115.1 mg/m^3 and 18.6 mg/m^3 or 162.5 ppm and 26.3 ppm) were noted in the urea store and packing area of Factory A, respectively. The authors noted that workers in these areas were required to have "full protective clothing," but it was not made clear what impact this clothing would have on their actual exposure. Taking into account smoking habits, none of the relative risks for respiratory symptoms (cough, phlegm, wheezing, dyspnea) were statistically significantly different from controls for Factory B workers. Hemoptysis (coughing up blood) was only noted in workers where ammonia levels were high (concentrations not provided) and there was a higher prevalence rate in Factory A workers than in Factory B workers. Analysis of the calculated cumulative ammonia concentration (mg/m^3-years) indicated significant relative risks for cough, phlegm, wheezing, dyspnea, chronic bronchitis, and bronchial asthma for those workers exposed to concentrations above 18 mg/m^3 (the ACGIH TLV). In addition, a cumulative ammonia concentration of more than 50 mg/m^3-years was associated with significant relative risks for all respiratory symptoms, including bronchial asthma and chronic bronchitis.

The authors also noted that current smokers in Factory A were significantly more frequently diagnosed with chronic bronchitis or bronchial asthma than controls, suggesting a possible interaction between cigarette smoke and ammonia exposure. Logistic regression analysis indicated ammonia concentration was significantly related to cough, phlegm, wheezing with or without shortness of breath, and asthma. Because exposures to ammonia and coexposures to cigarette smoking and other pollutants were not fully characterized, this study was not used for derivation of the chronic ReV. However, the NOAEL identified from the Holness et al. (1989) study is much lower than the levels discussed in Ballal et al. (1998). Inadequate reporting of exposure concentrations precludes the identification of NOAEL or LOAEL values. It is believed that values identified from the key study will be protective of potential adverse effects suggested by this study.

Rahman et al. (2007) conducted a cross-sectional study of 88 workers in two fertilizer factories in Bangladesh. Twenty-five staff from the administration building were used as the subjects for the control group. Because one objective of the study was to determine the best method for monitoring ammonia, two types of personal samplers were attached to workers' breathing zones during the day shift to measure ammonia concentrations. Average ammonia concentrations for a shift were driven by short peaks of up to 200 ppm, which tended to skew the results. The authors concluded that the exposure methods could not be validated and should be used with caution.

Participants completed two questionnaires, which documented complaints of respiratory disease, occupational history, smoking status, demographic data, and use of protective devices. In addition, lung function via forced vital capacity (FVC), forced expiratory volume at timed intervals of 1 sec (FEV_1), and peak expiratory flow rate (PEFR) were recorded before and after the shift in exposed workers (controls were not tested). The authors noted that chest tightness was significantly higher among workers in the urea plant than in administration workers, even when current smokers and workers with previous respiratory diseases were excluded from the analysis. The authors also noted that each year of work in a production section was associated with a decrease in cross-shift change in FEV_1 of 0.6%. Because of difficulties in determining exposure concentrations, a clear dose-response, or chronic reports of health symptoms other than pulmonary effects which are likely not the most sensitive endpoint, the Rhaman et al. (2007) study was not used in the derivation of the chronic ReV. Values derived using the Holness et al. (1989) study are anticipated to be protective of symptoms identified in Rahman et al. (2007) because the exposure concentrations and POD from the Holness study were much lower.

4.1.2 MOA and Dose Metric

Limited data exist to establish the MOA by which ammonia may produce noncarcinogenic effects (e.g., change in lung function parameters) following chronic exposure. However, the MOA can be anticipated to be similar to the acute MOA discussed in Section 3.1.3. and portal of entry irritation effects, followed by tracheobronchial and pulmonary effects once the scrubbing mechanism has been overwhelmed (NRC 2008).

For the key study, data on ammonia air concentrations for occupationally exposed workers are available and, therefore, are the most appropriate (and only) dose metric for the chronic noncarcinogenic evaluation.

4.1.3 POD for Key Study and Critical Effect

The POD for the Holness et al. (1989) key study is the NOAEL of 12500 ppb (8837.5 µg/m^3). Since this study is an occupational study, the POD is the POD_{HEC}. The critical effect was the absence of exposure-related differences in lung function.

4.1.4 Dosimetric Adjustment

The TCEQ adjusted the noncontinuous occupational exposure in the key study to account for continuous chronic exposure using the following default equation.

$$POD_{HEC\text{-}ADJ} = POD_{OC} \times (VE_{HO}/VE_H) \times [(days/week_{OC}) / (days/week_{res})]$$

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)

$POD_{HEC-ADJ}$ = 12500 ppb x [10 m^3/day/20 m^3/day] x [5 day/7 day] = 4464 ppb

4.1.5 Adjustments of the POD_{HEC}

Respiratory effects in humans caused by ammonia are considered to have a threshold (i.e., a nonlinear MOA). Therefore, UFs were applied to the $POD_{HEC-ADJ}$ of the key study. UFs for UF_H, UF_A, UF_L, subchronic-to chronic (UF_{Sub}) and UF_D that are applied are described below.

- A UF_H of 10 was applied to account for members of the population that may be sensitive to respiratory effects or have preexisting respiratory disease. In addition, people with liver or kidney disease or other conditions that result in hyperammonemia (increased ammonia levels) may be more susceptible to external ammonia exposure , although there no studies were located that examine that hypothesis (EPA 2012).
- A UF_A was not applicable because the key study involved human subjects.
- A UF_L was not applicable because a free-standing NOAEL was identified in the study.
- A UF_{Sub} was not applicable because workers were exposed to ammonia for 12 years, which is greater than 10% of the default lifetime exposure duration of 70 years.
- A UF_D of 1 was applied as the database on ammonia is extensive. Epidemiological studies on ammonia include industrial worker populations, cross sectional studies in livestock farmers exposed to inhaled ammonia and other chemicals, and controlled exposure studies. Subchronic animal studies, conducted in a number of species, including rats, guinea pigs, and pigs, examined respiratory and other systemic effects of ammonia. Other animal studies include several immunotoxicty studies and one limited, reproductive toxicity study in young female pigs. While the database lacks multigeneration reproductive and developmental toxicity studies, these studies would not be expected to impact the determination of ammonia toxicity at the POD. Ammonia is endogenously produced and homeostatically regulated in humans and animals during fetal and adult life. Evidence in animals suggests that exposure to ammonia at concentrations up to 1000 ppm does not alter blood ammonia levels (Schaerdel et al. 1989). The concentrations of ammonia at the POD for the ReV would not be expected to result in systemic toxicity, including reproductive or developmental toxicity.

The UFs were applied to the $POD_{HEC-ADJ}$ from the key study to calculate the chronic ReV (Table 6). The chronic ReV was calculated as follows:

chronic ReV = $POD_{HEC-ADJ}$ / (UF_H x UF_A x A UF_L x UF_{Sub} x UF_D)
= 4464 ppb / (10 x 1 x 1 x 1 x 1)
= 446.4 ppb
= 450 ppb (rounded to two significant figures)

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

The chronic ReV of 446.4 ppb from the key study was rounded to two significant figures at the end of all calculations, yielding a chronic ReV of 450 ppb (320 µg/m^3) (Table 6). The rounded chronic ReV was multiplied by the target hazard quotient of 0.3 to produce the $^{chronic}ESL_{threshold(nc)}$ of 130 ppb (92 µg/m^3).

Table 6 Derivation of the Chronic ReV and $^{chronic}ESL_{threshold(nc)}$

Parameter	**Values and Descriptions**
Study	Holness et al. (1989)
Study Population	58 occupationally-exposed healthy male workers in a soda ash plant (31 control workers)
Study Quality	Medium
Exposure Method	High exposure group of 12.5 ppm, as determined by personal sampler tubes worn for the duration of the work shift
Critical Effects	Free-standing NOAEL for lack of significant differences in self-reported symptoms and/or measured lung function parameters
POD_{HEC}	12500 ppb (free-standing NOAEL)
Exposure Duration	8.4 h (average) for 12.2 years (average)
Extrapolation to continuous exposure ($POD_{ADJ\text{-}HEC}$)	4464 ppb
Total UFs	10
Interspecies UF	10
Intraspecies UF	NA
LOAEL UF	NA
Subchronic to chronic UF	NA
Incomplete Database UF *Database Quality*	1 High
Chronic ReV (HQ = 1)	**320 µg/m^3 (450 ppb)**
$^{chronic}ESL_{threshold(nc)}$ (HQ = 0.3)	**92 µg/m^3 (130 ppb)**

4.1.7 Comparison of Various Chronic Toxicity Values

Table 7 is a comparison of the toxicity values derived by other federal and state agencies.

Table 7 Comparison of Ammonia Chronic Toxicity Values

Toxicity Value and Agency	Chronic Toxicity Value	Point of Departure	Total Uncertainty Factors	Key Study
Draft RfC USEPA (USEPA 2012)	420 ppb (300 µg/m^3)	12500 ppb (NOAEL)	10	Holness et al. (1989)
REL California Environmental Protection Agency (California EPA 1999)	300 ppb (200 µg/m^3)	9200 ppb (NOAEL)	10	Holness et al. (1989), supported by Broderson et al. (1976)
Inhalation MRL ATSDR (ATSDR 2004)	100 ppb (70 µg/m^3)	9200 ppb (NOAEL)	30 (uncertainty factor of 10 and modifying factor of 3)	Holness et al. (1989)
ReV TCEQ	450 ppb (320 µg/m^3)	12500 ppb (NOAEL)	10	Holness et al. (1989)

4.2 Carcinogenic Potential

Data are inadequate for an assessment of human carcinogenic potential of ammonia via the inhalation route. Ammonia has not been evaluated for its carcinogenic potential by the International Agency for Research on Cancer. The USEPA states that under their Guidelines for Carcinogen Risk Assessment, there is "inadequate information to assess carcinogenic potential" of ammonia (USEPA 2012). According to ATSDR (2004), there is no evidence that ammonia causes cancer.

4.3 Welfare-Based Chronic ESL

Scant information on the long-term effects of ambient concentrations of ammonia on vegetation was available in the reviewed literature. Field observations have noted foliar damage in trees and reduced forest vitality in areas near large sources of ammonia, such as agricultural activities and intensive livestock operations (Krupa 2003; Dueck et al. 1990. Van der Eerden et al. (1991) state

that generally concentrations of ammonia less than 100 µg/m^3 result in plant growth stimulation, rather than adverse vegetation effects. A $^{chronic}ESL_{veg}$ was not developed due to limitations and effects in species not grown in Texas (TCEQ 2012) discussed below.

Van der Eerden et al. (1991) evaluated a series of ammonia exposure experiments in heathland vegetation. In one experiment, European mountain tobacco (*Arnica montana*) was exposed in open-top chambers to 3, 6, 35, 53, or 105 µg/m^3 ammonia or a combination of 53 µg/m^3 ammonia and 90 µg/m^3 sulfur dioxide for 16 months. Approximately 60% of the plants at the 6 µg/m^3 ammonia exposure level survived and approximately 40% of these plants produced flowers. A LOEL of 6 µg/m^3 for mountain tobacco was identified from this study. It should be noted that two grasses in the experiment (*Deschampsia flexuosa* and *Molinia cearulea*) showed no reduction in survival under the same conditions. The authors also note that heathland vegetation is relatively sensitive to the effects of ammonia. Since mountain tobacco is not grown in or of agricultural importance to Texas, the LOEL of 6 µg/m^3 identified by Van der Eerden et al. (1991) was not used to set an $^{chronic}ESL_{veg.}$

Van Hove et al. (1991) fumigated poplar (*Populus euramericana* L. cv. Flevo) shoots with 64 µg/m^3 ammonia or 69 µg/m^3 ammonia in conjunction with 46 µg/m^3 sulfur dioxide for seven weeks. The authors noted no injury to the leaf cuticle and instead noted a positive effect of ammonia exposure on carbon dioxide assimilation, stomatal conductance, and ammonia uptake into leaves. According to the authors, "It seems that the NH_3 concentration in the atmosphere counteracts the negative effect of SO_2 on the CO_2 assimilation of leaves."

Dueck et al. (1990) showed increased injury to Scots pine trees (*Pinus sylvestris*); however, the study was not deemed of sufficient quality to derive the ESL. In the first experiment, 12 three year-old trees were fumigated in open-top chambers to 53 or 105 µg/m^3 of ammonia or a mixture of 53 µg/m^3 ammonia and 92 µg/m^3 sulfur dioxide for five months. The authors only noted needle injury in the presence of both ammonia and sulfur dioxide. In the second experiment, ten trees were fumigated in open-top containers to filtered air, ambient air, or ammonia-amended ambient air at 25, 53, or 105 µg/m^3 for ten months and the trees' frost hardiness, as measured by rate of electrolyte leakage in needles, and drought hardiness was determined. The authors noted some evidence of increased frost sensitivity at the 105 µg/m^3 exposure level, but only at temperatures below -10 °C (14 °F). The authors also noted that drought hardiness was affected by increasing ammonia concentrations, but statistical analysis of the data was not provided. Similarly, although the authors noted decreased bud bursts with increasing ammonia concentrations, statistical analyses of the data were not provided. In addition, the authors noted that they were unsure how severe of a detriment the observed bud mortality and reduced shoot length would be to the overall productivity of the plant, as the tree may be able to recover. Because the experimental temperatures are not common to Texas and sustained temperatures at these levels are even less common, the study's evaluation of frost hardiness was not considered applicable to Texas. In addition, because of the lack of statistical analyses for drought tolerance

and data on bud mortality was not provided and difficult to interpret, the study was not considered of sufficient quality for derivation of the $^{chronic}ESL_{veg}$.

4.4 Long-Term ESL and Values for Air Monitoring Evaluation

The chronic evaluation resulted in the derivation of the following values (see Table 6):

Chronic ReV = 320 µg/m^3 (450 ppb)
$^{chronic}ESL_{threhsold\ (nc)}$ = 92 µg/m^3 (130 ppb)

The long-term ESL for air permit evaluations is the $^{chronic}ESL_{threshold(nc)}$ of 130 ppb (92 µg/m^3) (Table 2). Although we do not currently monitor for ammonia, the chronic ReV of 450 ppb (320 µg/m^3) would be used to evaluate monitoring data (Table 1). The $^{chronic}ESL_{threshold\ (nc)}$ is not used to evaluate ambient air monitoring data.

4.5 Chronic Inhalation OAEL

In regard to the lowest chronic concentrations producing respiratory symptoms in humans, a concentration of 18 mg/m^3 (25 ppm) was associated with significant relative risks for cough, phlegm, wheezing, dyspnea, chronic bronchitis, and bronchial asthma in workers (exposure duration not reported). Since the chronic ReV is based on a NOAEL, the concentration of 18 mg/m^3 (25 ppm) is selected as the chronic OAEL (Ballal et al. 1998). This concentration is higher than the acute OAEL of 5 ppm, but in the range of other acute concentrations causing eye, nose, throat, and respiratory irritation. Adverse effects are not a certainty at that concentration. 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. Depending on the sensitivity of the study population (male workers in two Saudi Arabian urea fertilizer plants) to those exposed environmentally, other subpopulations could be more sensitive.

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