ACUTE EXPOSURE GUIDELINE LEVELS (AEGLs)
FOR
THIONYL CHLORIDE
7719-09-7

$SOCl_2$

INTERIM

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PREFACE

Under the authority of the Federal Advisory Committee Act (FACA) P. L. 92-463 of 1972, the National Advisory Committee for Acute Exposure Guideline Levels for Hazardous Substances (NAC/AEGL Committee) has been established to identify, review and interpret relevant toxicologic and other scientific data and develop AEGLs for high priority, acutely toxic chemicals.

AEGLs represent threshold exposure limits for the general public and are applicable to emergency exposure periods ranging from 10 minutes to 8 hours. Three levels — AEGL-1, AEGL-2 and AEGL-3 — are developed for each of five exposure periods (10 and 30 minutes, 1 hour, 4 hours, and 8 hours) and are distinguished by varying degrees of severity of toxic effects. The three AEGLs are defined as follows:

AEGL-1 is the airborne concentration (expressed as parts per million or milligrams per cubic meter [ppm or mg/m3]) of a substance above which it is predicted that the general population, including susceptible individuals, could experience notable discomfort, irritation, or certain asymptomatic, non-sensory effects. However, the effects are not disabling and are transient and reversible upon cessation of exposure.

AEGL-2 is the airborne concentration (expressed as ppm or mg/m3) of a substance above which it is predicted that the general population, including susceptible individuals, could experience irreversible or other serious, long-lasting adverse health effects or an impaired ability to escape.

AEGL-3 is the airborne concentration (expressed as ppm or mg/m3) of a substance above which it is predicted that the general population, including susceptible individuals, could experience life-threatening health effects or death.

Airborne concentrations below the AEGL-1 represent exposure levels that could produce mild and progressively increasing but transient and nondisabling odor, taste, and sensory irritation or certain asymptomatic, non-sensory effects. With increasing airborne concentrations above each AEGL, there is a progressive increase in the likelihood of occurrence and the severity of effects described for each corresponding AEGL. Although the AEGL values represent threshold levels for the general public, including susceptible subpopulations, such as infants, children, the elderly, persons with asthma, and those with other illnesses, it is recognized that individuals, subject to unique or idiosyncratic responses, could experience the effects described at concentrations below the corresponding AEGL

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EXECUTIVE SUMMARY

Thionyl chloride is a colorless to pale yellow liquid used in the production of batteries. It is also used during synthesis of drugs, vitamins, and herbicides. It is commercially available and used in industrial chemical reactions.

Thionyl chloride is a respiratory irritant causing bronchoconstriction, and can cause death from pulmonary edema caused by the hydrolysis products, sulfur dioxide and hydrogen chloride. Few human case reports are available, and they lack quantitative exposure data. The reports confirm respiratory irritation in humans.

Exposure-response data from rat studies are used to derive acute exposure guideline level (AEGL) values for thionyl chloride due to lack of quantitative data from human case reports. The AEGL values for the exposure periods of concern were scaled from the experimental exposure duration using exponential scaling ($C^n \times t = k$, where C= exposure concentration, t= exposure duration, and k= a constant). Data are unavailable to empirically derive a scaling factor (n) for thionyl chloride. The concentration-exposure time relationship for many irritant and systemically acting vapors and gases may be described by $C^n \times t = k$, where the exponent n ranges from 0.8 to 3.5 (ten Berge et al. 1986). Temporal scaling was performed using n = 3, when extrapolating to shorter time points and n = 1 when extrapolating to longer time points for AEGL values (NRC 2001).

Data are not available from human or animal studies to derive AEGL-1 values. Therefore, AEGL-1 values are not recommended.

Rats exposed to 71 ppm thionyl chloride for one hour experienced swollen noses and dyspnea (Pauluhn 1987). These are toxic reponses but not irreversible or incapacitating effects and will not impair ability to escape. The AEGL-2 values are derived from this data. A total uncertainty factor of 30 was applied. A similar mechanism of action would be expected across species, therefore, an uncertainty factor of 3 was used for interspecies variability while a factor of 10 was used for intraspecies variability to account for sensitive populations. Thionyl chloride hydrolyzes into sulfur dioxide and hydrogen chloride. Asthmatics are more sensitive than healthy people to the effects of sulfur dioxide.

The AEGL-3 values were based upon the highest concentration causing no lethality in rats exposed to thionyl chloride for one hour (Pauluhn 1987 and Nachreiner 1993). A one hour exposure to 593 ppm produced 58% mortality (Nachreiner 1993). In Pauluhn (1987), the next lowest experimental level, 407 ppm, did not cause lethality. This was used as the point of departure. This concentration is only slightly higher than the lethality threshold (371 ppm) reported in Nachreiner (1993). The same uncertainty factors and rationale used for AEGL-2 were applied to AEGL-3 calculations.

The calculated values are listed in Table 1.

TABLE 1. Summary of AEGL Values for Thionyl Chloride

Classification	10-minute	30-minute	1-hour	4-hour	8-hour	Endpoint (Reference)
AEGL–1 (Notable discomfort)	NR	NR	NR	NR	NR	
AEGL–2 (Disabling)	4.3 ppm (21 mg/m^3)	3.0 ppm (15 mg/m^3)	2.4 ppm (12 mg/m^3)	0.59 ppm (2.9 mg/m^3)	0.30 ppm (1.5 mg/m^3)	Dyspnea (not incapaciting or irreversible) (Pauluhn 1987)
AEGL–3 (Lethal)	25 ppm (120 mg/m^3)	17 ppm (83 mg/m^3)	14 ppm (68 mg/m^3)	3.4 ppm (17 mg/m^3)	1.7 ppm (8.3 mg/m^3)	Threshold of lethality (Pauluhn 1987; Nachreiner 1993)

NR-Not recommended. Numeric values for AEGL-1 are not recommended because of insufficient data. Absence of an AEGL-1 value does not imply that exposure below the AEGL-2 concentration is without adverse effects.

1. INTRODUCTION

Thionyl chloride is an industrially produced liquid used to make acyl chlorides and to synthesize pharmaceuticals including drugs and vitamins. It is used to make dyes, to prepare organic chlorine compounds, as a solvent in the production of herbicides, and as an electrolyte in lithium batteries. Thionyl chloride is also used to prepare polyarylate-type engineering thermoplastics made from iso- and tere-phthaloyl chlorides. The production is monitored and controlled by the Chemical Weapons Convention under Schedule 3 because of the potential for it to be used as a toxic chemical weapon and its widespread industrial use.

Thionyl chloride is a respiratory and skin irritant. Symptoms of exposure range from mild irritation to death and include dyspnea, burns, pulmonary edema, and inflammation. When exposed to water or water vapor, one mole of thionyl chloride produces one mole of sulfur dioxide and two moles of hydrogen chloride very rapidly. Its hydrolysis occurs faster than that of phosgene due to a pair of lone electrons in the S center of its pyramidal molecule.

TABLE 2. Chemical and Physical Properties

Parameter	Value	References
Synonyms	Sulfurous oxychloride, sulfinyl chloride, sulfur chloride oxide, sulfurous dichloride, thionyl dichloride	O'Neil et al. 2001, RTECS 2006
Chemical formula	$SOCl_2$	O'Neil et al. 2001
Molecular weight	118.98	O'Neil et al. 2001
CAS Reg. No.	7719-09-7	O'Neil et al. 2001
Physical state	Liquid- colorless, pale yellow, or red	O'Neil et al. 2001
Solubility in water	Reacts with H_2O to form SO_2 and HCl, miscible with benzene, chloroform, and carbon tetrachloride	O'Neil et al. 2001
Vapor pressure	11.6 kPa at 20ºC	AIHA 2002
Vapor density (air =1)	4.1 at 760 mmHg and 25ºC	AIHA 2002
Melting point	104.5ºC	O'Neil et al. 2001
Boiling point	75.6ºC at 760 mmHg	O'Neil et al. 2001
Flammability limits	Nonflammable	O'Neil et al. 2001
Conversion factors	1 ppm= 4.87 mg/m^3, 1 mg/m^3= 0.206 ppm	AIHA 2002

2. HUMAN TOXICITY DATA

2.1. Acute Lethality

There are very few data on fatalities caused by acute thionyl chloride exposure. One case report is noted below.

2.1.1. Case Reports

Ducatmen et al. (1988) reported on a worker exposed to an unknown concentration of thionyl chloride for an estimated six minutes following a lithium thionyl chloride battery cell explosion. The worker developed severe respiratory distress and fell unconscious. He also suffered chemical burns and fractures from the exploding battery. Fatal pulmonary edema from inhalation of SO_2 and HCl mist, products of thionyl chloride and water, occurred three hours after exposure. Estimates of sulfur dioxide concentration in the room were calculated to be below 17,000 ppm.

2.2. Nonlethal Toxicity

Humans have been exposed to unknown amounts of thionyl chloride through their occupations. Most data on nonlethal effects of thionyl chloride in humans are case reports of accidental occupational exposures.

2.2.1. Odor Threshold/Odor Awareness

Thionyl chloride has a suffocating or pungent odor, but there is currently no odor threshold reported.

2.2.2. Case Reports

Few cases of thionyl chloride poisoning have been reported. These reports lack exposure and duration data and are described below. They do not provide quantitative data suitable for deriving AEGL values, but provide insight on human poisoning.

Grieco (1962) reported a case of a pharmaceutical production plant worker exposed for two minutes to an unknown amount of thionyl chloride vapor during repair of a vent pipe. The worker experienced burning of the eyes, upper airway, and chest followed by feelings of suffocation. He began coughing with expulsion of blood. He was hospitalized in June with cough, sero-mucosal excretion, pharyngeal and chest burning. His respiratory function test showed insufficient ventilation and examination revealed vesicular murmur with wheezing at end of expiration. He was diagnosed with acute asthmatic tracheal bronchitis, was treated with bronchodilators and antibiotics, and recovered.

Two cases were reported by Konichezky et al. (1993) of accidental inhalation in a battery plant by non-smoking employees. Exposure for one 30 year old employee occurred when a thionyl chloride tank burst in an open space. Immediately following exposure, he had no symptoms. Over a two week period, dyspnea developed and he was found to have mild hypocarbia (lower than normal levels of blood carbon dioxide) and moderate restrictive dysfunction in lung function tests. Treatment with salbutamol, oral aminophylline, and prednisone was successful after a six month period. The employee was accidentally exposed eight months later and suffered similar symptoms as before. Corticosteriod therapy over a six month period successfully returned the employee to normal health. The second employee was a 23 year old male exposed to thionyl chloride fumes through a similar accident with the exception that the tank burst occurred in a closed space. He was washed with tap water and admitted to the emergency department. He suffered chemical burns on various parts of his body including corneas, tongue, and nasal septum. He was treated with hydrocortisone and prednisone. He returned to the hospital 18 days later with shortness of breath and had hyperinflated and hyperlucent lungs. He was admitted to the intensive respiratory care unit and exhibited signs of dyspnea and sinus tachycardia. The employee continued to be ill and was diagnosed with end-stage lung disease 74 days post exposure. Eventually his respiratory condition improved somewhat, and he was able to perform minimal tasks for short periods of time without breathlessness. However, he was listed as permanently disabled (Konichezky et al. 1993).

A case report was submitted to the U.S. Environmental Protection Agency (USEPA/OPPT 2000). The employee suffered CNS effects after an acute exposure to an unknown concentration of what was believed to be thionyl chloride. The employee was not wearing any respiratory protection, inhaled 2-3 breaths of thionyl chloride vapor, and began suffering from rhinitis, lacrimation, sore throat, and coughing. The employee also exhibited signs of impaired hand-eye coordination, memory, judgment, and slurred speech. These clinical signs had improved six hours post exposure and no symptoms were present 72 hours post exposure.

2.2.3. Epidemiologic Studies

No epidemiological studies have been found in the available literature.

2.3. Neurotoxicity

No neurotoxicity studies were located; however neurotoxic effects were noted in the case report submitted to the U.S. Environmental Protection Agency (2000). A worker exposed to 2-3 breaths of an unknown concentration of thionyl chloride displayed impaired cerebellar function and ataxia. Normal cerebellar function returned twenty-four hours post exposure.

2.4. Developmental/Reproductive Toxicity

No data were available regarding the potential reproductive and developmental toxicity of thionyl chloride.

2.5. Genotoxicity

There are no data relevant to the derivation of AEGLs for thionyl chloride.

2.6. Carcinogenicity

No information was found regarding the carcinogenicity of thionyl chloride.

2.7. Summary

There is a lack of exposure and duration data regarding lethal and nonlethal human exposures to thionyl chloride. The case reports provide good qualitative data about health effects resulting from exposure. Signs of exposure include burning and watering of the eyes, difficulty breathing, coughing, and pulmonary edema.

3. ANIMAL TOXICITY DATA

3.1. Acute Lethality

Acute lethality data on thionyl chloride in laboratory animals are summarized in the following section and listed in Table 3. Benchmark concentrations (BMC) were calculated for mortality in the following studies.

3.1.1. Rats

Kinkead and Einhaus (1984) exposed male Fischer 344 rats to 99% pure thionyl chloride in a 60-liter whole-body inhalation chamber for one hour and observed the animals for at least two weeks post exposure. Analytical concentrations were measured by IR analysis. Moisture from the rats increased the humidity of the chamber to around 50% and caused almost complete hydrolysis of thionyl chloride to a mixture of sulfur dioxide and hydrogen chloride, and rats were exposed to this mixture more than to thionyl chloride. Exposure concentrations were reported as the mixture of sulfur dioxide and hydrogen chloride concentrations (906, 1080, 1239, 1509, or 1983 ppm). Five animals were exposed per group and no deaths were reported at 906 or 1080 ppm of the mixture. Two of five males died at 1239 ppm, three of five died at 1509 ppm, and four of five died at 1989 ppm of the mixture. All deaths occurred within 48 hours of exposure.

Examination of the animals revealed mild to moderate multifocal congestion and alveolar damage. Severe lung irritation and edema were reported as the cause of death. The $BMCL_{05}$ and BMC_{01} were 663 and 830 ppm, respectively.

Pauluhn (1987) exposed five male and five female Wistar rats in an OECD Guideline study to 71, 407, 769, 2121, or 3441 ppm of thionyl chloride vapor for one hour and observed the animals for 14 days post exposure. The thionyl chloride used for the study was reported to be 99.8% pure, and rats were exposed head/nose only in a chamber 30 X 28 cm that prevented expired air from mixing with test atmosphere. Analytical concentration was determined using spectrophotometry. The LC_{50} was calculated to be 1277 ppm. Four of five males and four of five females died at 2121 ppm, and five of five males and four of five females died at 3441 ppm prior to sacrifice. Prior to death, labored breathing was observed in the animals. The author noted opacity of cornea, lung distention, necrotic changes in the nose, and pulmonary edema in the animals that died. The $BMCL_{05}$ and BMC_{01} were 507 and 671 ppm, respectively.

Nachreiner (1993) exposed 6 male and 6 female Wistar rats to 196, 371, 593, 954, or 1241 ppm to 99.9% pure (a.i.) thionyl chloride vapor in a nose-only chamber for one hour and observed the animals 14 days post exposure. Gas chromatography was used to analyze thionyl chloride during exposure. The LC_{50} was 736 ppm for males and females combined. No deaths were recorded in the 196 or 371 ppm exposure groups. Five of six males and two of six females died at 593 ppm. Five of six males and two of six females died at 954 ppm. Six of six males and four of six females died at 1241 ppm. Prior to death, audible respiration was observed. Hyperinflation of the lungs, perinasal and periocular encrustation were noted in some of the animals that died in the 954 and 1241 ppm exposure groups. One control male rat died during exposure and it was thought to be due to incorrect positioning in the chamber. The $BMCL_{05}$ and BMC_{01} were 193 and 222 ppm, respectively.

The variability of the lowest levels causing lethality among the three studies could possibly be explained by the different exposure conditions of three studies. The rats in Kinkead and Einhaus (1984) were exposed whole body to sulfur dioxide and hydrogen chloride produced by thionyl chloride in 39% to 58% relative humidity. Pauluhn (1987) exposed rats head/nose only and the input air had a relative humidity range from 29% to 51%. Although the chamber design prevented moisture from rat expiration from mixing with thionyl chloride and forming hydrolysates, it is possible that the humidity of the input air caused thionyl chloride hydrolysis before inhalation by the rats. Nachreiner (1993) exposed rats using compressed air at 11% relative humidity in a nose only chamber which greatly reduced the formation of thionyl chloride hydrolysates in the chamber. The nose only route allowed for inhalation of thionyl chloride only and the formation of hydrolysis products (sulfur dioxide and hydrogen chloride) within the respiratory tract. Nachreiner (1993) estimated the half-life of thionyl chloride at 53% relative humidity to be five minutes.

TABLE 3. Inhalation Data on Rats Exposed to Thionyl Chloride

Inhalation	Concentration (ppm)	Duration (min)	Effect	Reference
Head/Nose Only	71	60	Reddened, swollen noses, slight dyspnea, slight piloerection, 0% mortality	Pauluhn 1987
Nose Only	196	60	Color change in lungs, 0% mortality	Nachreiner, 1993
Nose Only	371	60	Color change in lungs, 0% mortality	Nachreiner, 1993
Head/Nose Only	407	60	Reddened, swollen noses, moderate dyspnea, moderate piloerection, 0% mortality	Pauluhn 1987
Nose Only	593	60	Color change in lungs, audible respiration, 58% mortality	Nachreiner, 1993
Head/Nose Only	769	60	Necrotic changes in nasal speculum, lung distention, wheezing sounds, 0% mortality	Pauluhn 1987
Whole Body	906	60	Eye irritation, shallow breathing and gasping, 0% mortality	Kinkead and Einhaus, 1984
Nose Only	954	60	Hyperinflation of the lungs, perinasal and periocular encrustation, 58% mortality	Nachreiner, 1993
Whole Body	1080	60	Eye irritation, shallow breathing and gasping, 0% mortality	Kinkead and Einhaus, 1984
Whole Body	1239	60	Pulmonary edema, 40% mortality	Kinkead and Einhaus, 1984
Nose Only	1241	60	Hyperinflation of the lungs, perinasal and periocular encrustation, 83% mortality	Nachreiner, 1993
Whole Body	1509	60	Severe lung irritation, pulmonary edema, 60% mortality	Kinkead and Einhaus, 1984
Whole Body	1983	60	Severe lung irritation, pulmonary edema, 80% mortality	Kinkead and Einhaus, 1984
Head/Nose Only	2121	60	Severe dyspnea, reduced motility, complete cornea opacity, pulmonary edema, 80% mortality	Pauluhn 1987
Head/Nose Only	3441	60	Pulmonary edema, cornea opacity, 90% mortality	Pauluhn 1987

3.2. Nonlethal Toxicity

The three studies reporting lethal toxicity effects of thionyl chloride also described nonlethal toxicity and are listed in Table 3. A summary of each study is given below.

3.2.1. Rats

Kinkead and Einhaus (1984) exposed male Fischer 344 rats to thionyl chloride in an

inhalation chamber for one hour. Moisture from the rats caused decomposition of thionyl chloride to a mixture of sulfur dioxide and hydrogen chloride (906, 1080, 1239, 1509, or 1983 ppm). Five animals were exposed per group and no deaths were reported at 906 or 1080 ppm of the mixture. Animals were reported to have eye and respiratory irritation. Shallow breathing and gasping were also observed in these animals during the exposure. Animals died at the higher concentrations.

Pauluhn (1987) exposed male and female Wistar rats for one hour to 71, 407, 769, 2121, or 3441 ppm of thionyl chloride. Both genders exhibited swollen noses and dyspnea at 71 and 407 ppm. Symptoms were slight at 71 ppm and moderate at 407 ppm. Wheezing and necrotic changes in the nose were observed at 769 ppm as well as moderate dyspnea and swollen noses. One female rat from 769 ppm was observed to determine the duration of the symptoms. From day 7 to 14, the rat was found to be apathetic. The dyspnea in the rat was non-reversible within the post-treatment observation period. Some rats from all groups mentioned above had distended lungs at necropsy. Mortality was noted at the higher concentrations.

Nachreiner (1993) exposed male and female Wistar rats to 196, 371, 593, 954, or 1241 ppm to thionyl chloride vapor in a nose-only chamber for one hour and observed the animals 14 days post exposure. All animals exposed to thionyl chloride were observed using mouth breathing. No other outward clinical signs attributed to treatment were observed in the 196 and 371 ppm exposed animals. Histopathology revealed color changes in the lungs of males and females starting at the lowest dose. Higher concentrations led to death.

3.3. Developmental/Reproductive Toxicity

There are currently no studies on the developmental/reproductive toxicity of thionyl chloride.

3.4. Genotoxicity

There are no genotoxicity studies with thionyl chloride.

3.5. Carcinogenicity

There are no data to suggest that thionyl chloride is a carcinogen.

3.6. Summary

The effects of acute inhalation exposure of rats to thionyl chloride are noted in the above section. Effects consisted of ocular and respiratory irritation, lung discoloration, and/or death. Death appeared to be caused by lung irritation and pulmonary edema. LC_{50} values for the two of the three rat studies were 1277 ppm (Pauluhn 1987), and 736 ppm (Nachreiner 1993). Data from the Kinkead and Einhaus study (1984) suggested lethality values much higher than Nachreiner (1993) and Pauluhn (1987), but due to the study design, were not considered useful.

4. SPECIAL CONSIDERATIONS

4.1. Metabolism and Disposition

Thionyl chloride is rapidly hydrolyzed to sulfur dioxide and hydrogen chloride and the metabolism and disposition follow those two compounds. Following inhalation, sulfur dioxide is distributed throughout the body after dissolving into surface fluid. Some remains in the respiratory system for a week or more following exposure. Urinary excretion clears it from the body (Costa 2001). Hydrogen chloride dissolves in the nasal passages. Hydrogen chloride is not metabolized; however, hydrogen and chloride ions resulting from adsorption in the respiratory tract may be distributed throughout the body (NRC, 2000).

4.2. Mechanism of Toxicity

Sulfur dioxide acts on the respiratory system via stimulation of bronchoconstriction and mucus secretion in the upper airways. It injures cells lining the airway passages and causes mucus-secreting goblet cells to proliferate. These two events result in airway narrowing and increased airflow resistance (Costa 2001). Inhaled hydrogen chloride irritates the respiratory tract following a latency period of several hours. Following exposure, the epithelial barrier in the alveolar zone breaks down and begins to leak, flooding the alveoli and causing pulmonary edema (Witschi and Last 2001).

4.3. Structure Activity Relationships

There are no structure-activity relationships applicable for estimating acute exposure limits for thionyl chloride.

4.4. Other Relevant Information

4.4.1. Susceptible Populations

Asthmatics have been shown to be sensitive to respiratory effects caused by sulfur dioxide exposure. As noted above, sulfur dioxide stimulates bronchoconstriction and increases airflow resistance. Response to inhalation of sulfur dioxide is enhanced with moderate exertion and/or mouth breathing and can lead to decreased forced expiratory volume (Koren 1995). Exercise exacerbates the respiratory effects of sulfur dioxide in both healthy and asthmatic subjects (Kulle et al. 1984; Horstman et al. 1988). Exercising is also known to increase hydrogen chloride intake and exacerbate respiratory effects.

5. DATA ANALYSIS FOR AEGL-1

5.1. Summary of Human Data Relevant to AEGL-1

Human data were not available for deriving an AEGL.

5.2. Summary of Animal Data Relevant to AEGL-1

Nonlethal toxicity data in animals consistent with AEGL-1 effects were not available.

5.3. Derivation of AEGL-1 Values

No AEGL-1 values were derived because of insufficient data.

TABLE 4. AEGL-1 Values for Thionyl Chloride

10-minute	30-minute	1-hour	4-hour	8-hour
NR	NR	NR	NR	NR

NR-Not recommended. Numeric values for AEGL-1 are not recommended because of insufficient data. Absence of an AEGL-1 value does not imply that exposure below the AEGL-2 concentration is without adverse effects.

6. DATA ANALYSIS FOR AEGL-2

6.1. Summary of Human Data Relevant to AEGL-2

Human data were not available for deriving an AEGL based upon non-lethal, irreversible effects of thionyl chloride exposure.

6.2. Summary of Animal Data Relevant to AEGL-2

Exposure to 71 and 407 ppm produced dyspnea in male and female rats (Pauluhn 1987). Nachreiner (1993) noted lung discoloration at 196 and 371 ppm. It is unknown if discoloration of the organs was reversible.

6.3. Derivation of AEGL-2

The one hour exposure data (71 ppm) from the study by Pauluhn 1987 were selected to derive AEGL-2 values as there was an effect level for a toxic response that was not incapacitating or irreversible. One hour exposures to 71 ppm produced slight dyspnea and nasal irritation in rats. The next higher concentration (407 ppm) caused moderate dyspnea and nasal irritation. A total uncertainty factor of 30 was applied to account for interspecies extrapolation (3) and intraspecies variability (10). An appropriate animal model was used and, the mechanism of action (bronchoconstriction, irritation of the epithelial lining, and increased mucus production via goblet cell proliferation) would not differ across species. Although human data did not provide quantitative information, there was qualitative data that showed similarities to rat thionyl chloride effects; irritation and hyperinflation of the lungs and pulmonary edema. An uncertainty factor of 10 was used for intraspecies variability due to the wide variability in response to sulfur dioxide exposure between healthy and asthmatic humans. Although data on a sensitive subpopulation are lacking for thionyl chloride, it is known that asthmatics are more sensitive than healthy humans to sulfur dioxide, one of thionyl chloride's hydrolysis products. It is believed that the intraspecies uncertainty factor of 10 is protective of asthmatics.

The concentration exposure time relationship for many irritant and systemically acting vapors and gases may be described by $C^n \times t = k$, where the exponent ranges from 0.8 to 3.5 (ten Berge et al. 1986). In lieu of a definitive data set allowing empirical derivation of the exponent n, temporal scaling was performed, using n = 3 when extrapolating to shorter time points and n =

1 when extrapolating to longer time points using the $C^n \times t = k$ equation (NRC 2001).

TABLE 5. AEGL-2 Values for Thionyl Chloride

10-minute	30-minute	1-hour	4-hour	8-hour
4.3 ppm (21 mg/m^3)	3.0 ppm (15 mg/m^3)	2.4 ppm (12 mg/m^3)	0.59 ppm (2.9 mg/m^3)	0.30 ppm (1.5 mg/m^3)

7. DATA ANALYSIS FOR AEGL-3

7.1. Summary of Human Data Relevant to AEGL-3

Human data were not available for deriving thionyl chloride AEGL-3 values based upon lethality.

7.2. Summary of Animal Data Relevant to AEGL-3

Lethality data were available for rats. Exposures producing lethality range from 593 to 3441 ppm, with all values representing a one hour exposure. Rats exposed to a mixture of the hydrolysis products of thionyl chloride at concentrations at or lower than 1080 ppm survived. A $BMCL_{05}$ of 663 ppm and BMC_{01} of 830 were calculated from this study (Kinkead and Einhaus 1984). No deaths occurred in rats exposed to 769 ppm thionyl chloride; an LC_{50} of 1277 ppm; and $BMCL_{05}$ of 507 ppm and BMC_{01} of 671 ppm were also calculated from the same study (Pauluhn 1987). In the report from Nachreiner (1993) no animals died at or below exposures of 371 ppm; the LC_{50} was 736 ppm, and the $BMCL_{05}$ and BMC_{01} were calculated at 193 and 222 ppm, respectively.

7.3. Derivation of AEGL-3

The data sets for deriving AEGL-3 values are that of Pauluhn (1987) and Nachreiner (1993). Both provide exposure response data for rats exposed to thionyl chloride for one hour at concentrations of 71, 407, 769, 2121, or 3441 ppm (Pauluhn 1987) and 196, 371, 593, 954, and 1241 ppm (Nachreiner 1993). There was 80% mortality at 2121 and 91% mortality at 3441 ppm. No mortality was observed in the 769 ppm exposure group, but wheezing and necrotic changes in the nasal speculum were noted in these animals. At 407 ppm, the animals displayed moderate dyspnea and reddened and swollen noses, but there was no mortality (Pauluhn 1984). There was 58% mortality at 593 and 954 ppm and 83% mortality at 1241 ppm (Nachreiner 1987). No mortality was observed in the 371 ppm exposure group, but lung discoloration was noted in these animals. These data provide a basis for a lethality threshold. A benchmark dose concentration was calculated from the combined data of the Pauluhn (1984) and Nachreiner (1993) studies. However, the p value of the fitted model for the benchmark analysis was too low ($p= 0.0022$), indicating that the model did not fit the combined data set, and the combined benchmark value could not be used. (A p value greater than 0.1 indicates that the model fits the data.) The calculated benchmark dose concentration for either study was not used to derive AEGL-3 values because of the high variability between the two. In the absence of knowledge of which value is "more accurate", 407 ppm was chosen as the point of departure.

The one hour inhalation study by Pauluhn (1987) supported by Nachreiner (1993) provided the most sound basis and were selected to derive AEGL-3 values as it had the highest experimental concentration at which no mortality was observed (407 ppm). A total uncertainty factor of 30 was applied to account for interspecies extrapolation (3) and intraspecies variability (10). A factor of 3 was applied for interspecies variability since an appropriate animal model was used and, the mechanism of action (bronchoconstriction, irritation of the epithelial lining, and increased mucus production via goblet cell proliferation) would not differ across species. Although human data did not provide quantitative exposure information, they described effects similar to those seen in rats; irritation and hyperinflation of the lungs and pulmonary edema. An uncertainty factor of 10 was used for intraspecies variability due to the wide variability in response to sulfur dioxide exposure between healthy and asthmatic humans. Although data on sensitive subpopulations are lacking for thionyl chloride, it is known that asthmatics are more sensitive than healthy humans to sulfur dioxide, one of thionyl chloride's hydrolysis products. It is believed that the intraspecies uncertainty factor of 10 is protective of asthmatics.

The concentration exposure time relationship for many irritant and systemically acting vapors and gases may be described by $C^n \times t = k$, where the exponent ranges from 0.8 to 3.5 (ten Berge et al. 1986). In lieu of a definitive data set allowing empirical derivation of the exponent n, temporal scaling was performed, using n = 3 when extrapolating to shorter time points and n = 1 when extrapolating to longer time points using the $C^n \times t = k$ equation (NRC 2001).

TABLE 6. AEGL-3 Values for Thionyl Chloride

10-minute	30-minute	1-hour	4-hour	8-hour
25 ppm (120 mg/m^3)	17 ppm (83 mg/m^3)	14 ppm (68 mg/m^3)	3.4 ppm (17 mg/m^3)	1.7 ppm (8.3 mg/m^3)

8. SUMMARY OF AEGLS

8.1. AEGL Values and Toxicity Endpoints

Data consistent with the AEGL-1 effects are not available. Therefore, AEGL-1 values are not recommended. AEGL-2 values are based on experimental concentrations that were neither incapacitating nor irreversible in rats (71 ppm). AEGL-3 values are based on the highest experimental concentration that did not produce lethality. AEGL values for thionyl chloride are listed in Table 7.

TABLE 7. Summary of AEGL Values

Classification	Exposure Duration				
	10-minute	30-minute	1-hour	4-hour	8-hour
AEGL-1 (Notable discomfort)	NR	NR	NR	NR	NR
AEGL-2 (Disabling)	4.3 ppm	3.0 ppm	2.4 ppm	0.59 ppm	0.30 ppm
AEGL-3 (Lethal)	25 ppm	17 ppm	14 ppm	3.4 ppm	1.7 ppm

NR-Not recommended. Numeric values for AEGL-1 are not recommended because of insufficient data. Absence of an AEGL-1 value does not imply that exposure below the AEGL-2 concentration is without adverse effects.

8.2. Comparison with Other Standards and Guidelines

All currently available standards and guidelines are shown in Table 8. Emergency response planning guideline (ERPG) values and Dutch maximum allowable concentration (MAC) values have been published. The National Institute of Occupational Safety and Health (NIOSH) recommended exposure limits-short term exposure (REL-STEL) and American Conference of Governmental Industrial Hygienists (ACGIH) threshold limit value-short term exposure limits (TLV-STEL) both have ceiling values. The derived AEGL values are consistent with current standards and guidelines.

Thionyl chloride hydrolyzes into sulfur dioxide and hydrogen chloride. Kinkead and Einhaus (1984) suggest that the toxicity of thionyl chloride is greater than the simple additivity of its hydrolysis products, and this concept was incorporated into ERPG recommendations (AIHA 2002). AEGL values have been recommended for sulfur dioxide (USEPA 2006) and hydrogen chloride (NRC 2004) and are listed in Table 8. A weight of evidence approach using data from exercising asthmatics was used to derive AEGL-2 values for sulfur dioxide. Sulfur dioxide AEGL3 values were derived from the calculated $BMCL_{05}$ in rats following a 4 hour exposure. Compared to sulfur dioxide, derived AEGL-2 thionyl chloride values are based on animal studies and are greater at timepoints of 1 hour or less. The AEGL-3 values for thionyl chloride are lower than the same values for sulfur dioxide and are expected to be protective. Hydrogen chloride AEGL-2 values were based on histopathology and the mouse RD_{50}, and AEGL-3 values were derived from the estimated NOEL for death from the one hour rat LC_{50}. Hydrogen chloride is well scrubbed by the upper respiratory tract and would require higher concentrations to cause adverse effects. The derived thionyl chloride AEGL values are lower than both of the hydrogen chloride values and would be expected to be protective of individuals exposed. No other standards and guidelines are available for thionyl chloride.

TABLE 8. Extant Standards and Guidelines for Thionyl Chloride

Guideline	Exposure Duration				
	10 minute	30 minute	1 hour	4 hour	8 hour
AEGL-1	NR	NR	NR	NR	NR
AEGL-2	4.3 ppm	3.0 ppm	2.4 ppm	0.59 ppm	0.30 ppm
AEGL-3	25 ppm	17 ppm	14 ppm	3.4 ppm	1.7 ppm
AEGL-1 SO_2	0.20 ppm	0.20 ppm	0.20 ppm	0.20 ppm	0.20 ppm
AEGL-2 SO_2	0.75 ppm	0.75 ppm	0.75 ppm	0.75 ppm	0.75 ppm
AEGL-3 SO_2*	30 ppm	30 ppm	30 ppm	19 ppm	9.6 ppm
AEGL-1 HCl	1.8 ppm	1.8 ppm	1.8 ppm	1.8 ppm	1.8 ppm
AEGL-2 HCl	100 ppm	43 ppm	22 ppm	11 ppm	11 ppm
AEGL-3 HCl	620 ppm	210 ppm	100 ppm	26 ppm	26 ppm
ERPG-1 (AIHA)[a]			0.2 ppm		
ERPG-2 (AIHA) [a]			2 ppm		
ERPG-3 (AIHA) [a]			10 ppm		
REL-STEL (NIOSH)[b]					1 ppm ceiling
TLV-STEL (ACGIH)[c]					1 ppm ceiling
MAC (The Netherlands)[d]					1 ppm

NR-Not recommended. Numeric values for AEGL-1 are not recommended because of insufficient data. Absence of an AEGL-1 value does not imply that exposure below the AEGL-2 concentration is without adverse effects.
*Proposed AEGL-3 values adopted at the NAC-41 meeting.

[a]ERPG (Emergency Response Planning Guidelines, American Industrial Hygiene Association (AIHA 2006)

- The ERPG-1 is the maximum airborne concentration below which it is believed nearly all individuals could be exposed for up to one hour without experiencing other than mild, transient adverse health effects or without perceiving a clearly defined objectionable odor. The ERPG-1 is based on increased airway resistance in exercising asthmatics exposed to sulfur dioxide.
- The ERPG-2 is the maximum airborne concentration below which it is believed nearly all individuals could be exposed for up to one hour without experiencing or developing irreversible or other serious health effects or symptoms that could impair an individual's ability to take protective action. The ERPG-2 is based on bronchoconstriction in resting asthmatics exposed to 5 ppm of sulfur dioxide.
- The ERPG-3 is the maximum airborne concentration below which it is believed nearly all individuals could be exposed for up to one hour without experiencing or developing life-threatening health effects. The ERPG-3 is based on the toxicity of sulfur dioxide with an additional safety factor because the mixture of sulfur dioxide and hydrogen chloride is more toxic than simple additivition of the two compounds would indicate.

[b]NIOSH REL-STEL (Recommended Exposure Limits - Short Term Exposure Limit) (NIOSH 2005) is defined analogous to the ACGIH TLV-STEL.

[c]ACGIH TLV-STEL (Threshold Limit Value - Short Term Exposure Limit) (ACGIH 2006)

is defined as a 15-minute TWA exposure which should not be exceeded at any time during the workday even if the 8-hour TWA is within the TLV-TWA. Exposures above the TLV-TWA up to the STEL should not be longer than 15 minutes and should not occur more than 4 times per day. There should be at least 60 minutes between successive exposures in this range.

[d]MAC Ministry of Social Affairs and Employment (SDU Uitgevers (Maximaal Aanvaaarde Concentratie [Maximal Accepted Concentration]), The Hague, The Netherlands 2000) is defined analogous to the ACGIH-TLV-TWA.

8.3. Data Adequacy and Research Needs

The data reported for human exposure to thionyl chloride are qualitative only and do not contain actual concentration and /or duration parameters. The absence of exposure concentrations for humans is one key area where data are lacking. However, the data confirm the respiratory effects of thionyl chloride exposure, and add support to the toxicological endpoints of the animal data. Quantitative animal data are available from three studies that demonstrate a respiratory response similar to that observed in humans. The animal data are sufficient for showing lethality and non-incapacitating exposures. Additional data providing information at concentrations below 71ppm (dyspnea in rats) would be useful to determine a NOAEL or reversible mild irritation level in rats to derive AEGL-1 values. There are no data for addressing exposure concentration-duration relationships as all available studies exposed the animals for only one hour. Data on more exposure durations would be useful in the development of a more precise temporal extrapolation for the development of AEGL values of varying exposure time durations.

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APPENDIX A: Derivation of AEGL Values

Derivation of AEGL-1
No AEGL-1 values were derived due to insufficient data.

Key Study:

Toxicity endpoint:

Time scaling:

Uncertainty factors:

Modifying factor:

Calculations:

10-minute AEGL-1

30-minute AEGL-1

1-hour AEGL-1

4-hour AEGL-1

8-hour AEGL-1

Derivation of AEGL-2 Values

Key Study: Pauluhn (1987), based upon slight dyspnea and reddened and swollen noses at 71 ppm for one hour.

Toxicity endpoint: Slight dyspnea.

Time scaling: The concentration exposure time relationship for many irritant and systemically acting vapors and gases may be described by $C^n \times t = k$, where the exponent ranges from 0.8 to 3.5 (ten Berge et al. 1986). In lieu of a definitive data set allowing empirical derivation of the exponent n, temporal scaling was performed, using n = 3 when extrapolating to shorter time points and n = 1 when extrapolating to longer time points using the $C^n \times t = k$ equation (NRC 2001).

Uncertainty factors: A total uncertainty factor of 30 was applied. A factor of 3 was applied for interspecies variability. An appropriate animal model was used and, the mechanism of action (bronchoconstriction, irritation of the epithelial lining, and increased mucus production via goblet cell proliferation) would not differ across species. Although human data did not provide quantitative exposure data, they did show similar effects; irritation and hyperinflation of the lungs and pulmonary edema. An uncertainty factor of 10 was used for intraspecies variability. Although data on a sensitive subpopulation are lacking for thionyl chloride, it is known that asthmatics are more sensitive than healthy humans to sulfur dioxide, one of thionyl chloride's hydrolysis products. It is believed that the intraspecies uncertainty factor of 10 is protective of asthmatics.

Modifying factor: None

Calculations: 71 ppm/30 = 2.37 ppm

$C^3 \times t = k$

$(2.37\ ppm)^3 \times 60\ min = 798.7\ ppm^3 \cdot min$

$C^1 \times t = k$

$2.37\ ppm \times 60\ min = 142.2\ ppm\ min$

10-minute AEGL-2 $C^3 \times 10\ min = 798.7\ pm^3 \cdot min$

$C = 4.3\ ppm$

30-minute AEGL-2 $C^3 \times 30\ min = 798.7\ ppm^3 \cdot min$

$C = 3.0\ ppm$

1-hour AEGL-2 $C^3 \times 60\ min = 798.7\ ppm^3 \cdot min$

$C = 2.4\ ppm$

4-hour AEGL-2 $C^1 \times 240\ min = 142.2\ ppm \cdot min$

$C = 0.59\ ppm$

8-hour AEGL-2 $C^1 \times 480\ min = 142.2\ ppm \cdot min$

$C = 0.30\ ppm$

Derivation of AEGL-3 Values

Key Studies: Paulunhn (1987) and Nachreiner (1993), based upon an estimate of a lethality threshold experimental concentration of 407 ppm. Experimental concentrations greater than 407 ppm produced mortality.

Toxicity endpoint: Threshold for lethality (407 ppm)

Time scaling: $C^n \times t = k$, temporal scaling, using n = 3 when extrapolation to shorter time points and n = 1 when extrapolating to longer time points due to lack of data to derive the value of n (NRC 2001).

Uncertainty factors: A total uncertainty factor of 30 was applied to account for interspecies extrapolation. A factor of 3 was applied for interspecies variability. An appropriate animal model was used and, the mechanism of action (bronchoconstriction, irritation of the epithelial lining, and increased mucus production via goblet cell proliferation) would not differ across species. Although human data did show similar effects; irritation and hyperinflation of the lungs and pulmonary edema. An uncertainty factor of 10 was used for intraspecies variability. Although data on a sensitive subpopulation are lacking for thionyl chloride, it is known that asthmatics are more sensitive than healthy humans to sulfur dioxide, one of thionyl chloride's hydrolysis products. It is believed that the intraspecies uncertainty factor of 10 is protective of asthmatics.

Modifying factor: None

Calculations: 407 ppm/30 = 13.57 ppm

$C^3 \times t = k$

$(13.57 \text{ ppm})^3 \times 60 \text{ min} = 149930 \text{ ppm}^3 \cdot \text{min}$

$C^1 \times t = k$

$13.57 \text{ ppm} \times 60 \text{ min} = 814.2 \text{ ppm min}$

10-minute AEGL-3 $C^3 \times 10 \text{ min} = 149930 \text{ ppm}^3 \cdot \text{min}$
$C = 25 \text{ ppm}$

30-minute AEGL-3 $C^3 \times 30 \text{ min} = 149930 \text{ ppm}^3 \cdot \text{min}$
$C = 17 \text{ ppm}$

1-hour AEGL-3 $C^3 \times 60 \text{ min} = 149930 \text{ ppm}^3 \cdot \text{min}$
$C = 14 \text{ ppm}$

4-hour AEGL-3 $C^1 \times 240 \text{ min} = 814.2 \text{ppm} \cdot \text{min}$
$C = 3.4 \text{ ppm}$

8-hour AEGL-3 $C^1 \times 480 \text{ min} = 814.2 \text{ppm} \cdot \text{min}$
$C = 1.7 \text{ ppm}$

APPENDIX B: Time-Scaling Calculations

Data were unavailable to empirically derive a scaling factor (n) for thionyl chloride. The concentration exposure time relationship for many irritant and systemically acting vapors and gases may be described by $C^n \times t = k$, where the exponent ranges from 0.8 to 3.5 (ten Berge et al. 1986). In the absence of an empirically derived exponent (n), and to obtain AEGL values, temporal scaling was performed, using n = 3 when extrapolating to shorter time points and n = 1 when extrapolating to longer time points using the $C^n \times t = k$ equation (NRC 2001).

APPENDIX C: Derivation Summary for Thionyl Chloride

ACUTE EXPOSURE GUIDELINE LEVELS FOR
THIONYL CHLORDE (CAS Reg. No. 7719-09-7)
DERIVATION SUMMARY

AEGL-1 VALUES

10-minute	30-minute	1-hour	4-hour	8-hour
NR	**NR**	**NR**	**NR**	**NR**

Key Reference: There were insufficient data to derive AEGL-1 values for thionyl chloride.

Test Species/Strain/Number: Not Applicable

Exposure Route/Concentrations/Durations: Not Applicable

Effects: Not Applicable

Endpoint/Concentration/Rationale: Not Applicable

Uncertainty Factors/Rationale: Not Applicable

Modifying Factor: Not Applicable

Animal to Human Dosimetric Adjustment: Not Applicable

Time Scaling: Not Applicable

Data Adequacy: NR-Not recommended. Numeric values for AEGL-1 are not recommended because of insufficient data. Absence of an AEGL-1 value does not imply that exposure below the AEGL-2 concentration is without adverse effects.

AEGL-2 VALUES

10-minute	30-minute	1-hour	4-hour	8-hour
4.3 ppm	**3.0 ppm**	**2.4 ppm**	**0.59 ppm**	**0.30 ppm**

Key Reference: Pauluhn, J. 1987. Study for acute inhalation toxicity in rats in accordance with OECG Guideline No. 403 (Exposure: 1 x 1 Hour). Report No. 15403. Leverkusen, Germany: Bayer AG.

Test Species/Strain/Number: Male and female Wistar rats, 5/gender/group

Exposure Route/Concentrations/Durations: Inhalation (Head/Nose Only): 0, 71, 407, 769, 2121, and 3441 ppm for 1 hour

Effects: dyspnea, reddened and swollen noses

71 ppm 0% mortality , reddened and swollen noses, slight dyspnea (determinant for AEGL-2)

407 ppm 0% mortality , reddened and swollen noses, moderate dyspnea

769 ppm 0% mortality , reddened and swollen noses, moderate dyspnea , wheezing, necrotic nasal changes, lung distention

2121 ppm 80% mortality (80% male: 4 post exposure, 80% female: 4 post exposure)

3441 ppm 90% mortality (100% male: 5 post exposure, 80% female: 4 post exposure)

Endpoint/Concentration/Rationale: 71 ppm for 1 hour considered for basis for AEGL-2 values

Uncertainty Factors/Rationale: Total uncertainty factor: 30

Interspecies: 3- An appropriate animal model was used and, the mechanism of action (bronchoconstriction, irritation of the epithelial lining, and increased mucus production via goblet cell proliferation) would not differ across species. Although human data did not provide quantitative exposure data, they did provide show similar effects; irritation and hyperinflation of the lungs and pulmonary edema.

Intraspecies: 10- Although data on a sensitive subpopulation are lacking for thionyl chloride, it is known that asthmatics are sensitive to sulfur dioxide, one of thionyl chloride's hydrolysis products. It is believed that the intraspecies uncertainty factor of 10 is protective of asthmatics and other sensitive populations.

Modifying Factor: Not Applicable

Animal to Human Dosimetric Adjustment: None applied, insufficient data.

Time Scaling: In the absence of an empirically derived exponent (n), and to obtain AEGL values, $C^n \times t = k$, temporal scaling, using n = 3 when extrapolating to shorter time points and n = 1 when extrapolating to longer time points. The concentration exposure time relationship for many irritant and systemically acting vapors and gases may be described by $C^n \times t = k$, where the exponent ranges from 0.8 to 3.5 (ten Berge et al. 1986).

Data Adequacy: The study was considered adequate for AEGL-2 derivation. It was a well-designed and performed OECD Guideline study, adequate numbers of animals were used, and an endpoint consistent with AEGL-2 definition and toxicity of thionyl chloride was observed.

AEGL-3 VALUES

10-minute	30-minute	1-hour	4-hour	8-hour
25 ppm	**17 ppm**	**14 ppm**	**3.4 ppm**	**1.7 ppm**

Key Reference: Pauluhn, J. 1987. Study for acute inhalation toxicity in rats in accordance with OECG Guideline No. 403 (Exposure: 1 x 1 Hour). Report No. 15403. Leverkusen, Germany: Bayer AG. Nachreiner, D.J. 1993. Thionyl chloride: Acute vapor inhalation toxicity study in rats. Union Carbide Chemicals and Plastics Company, Inc. Export, PA

Test Species/Strain/Number: Male and female Wistar rats, 5/gender/group; Male and female Wistar rats, 6/gender/group

Exposure Route/Concentrations/Durations: Inhalation (Head/Nose Only): 0, 71, 407, 769, 2121, and 3441 ppm for 1 hour; (Nose Only): 0, 196, 371, 593, 954, and 1241 ppm for 1 hour. (The concentration where no deaths were observed, 407 ppm in Pauluhn (1987), was determinant for AEGL-3.)

Effects: Lethality

Pauluhn (1987)

71 ppm 0% mortality , reddened and swollen noses, slight dyspnea (determinant for AEGL-2)
407 ppm 0% mortality , reddened and swollen noses, moderate dyspnea
769 ppm 0% mortality , reddened and swollen noses, moderate dyspnea , wheezing, necrotic nasal changes, lung distention
2121 ppm 80% mortality (80% male: 4 post exposure, 80% female: 4 post exposure)
3441 ppm 90% mortality (100% male: 5 post exposure, 80% female: 4 post exposure)

Nachreiner (1993)

196 ppm 0% mortality, lung discoloration
371 ppm 0% mortality , lung discoloration
593 ppm 58% mortality (83% male: 5 during exposure, 33% female: 2 during exposure)
954 ppm 58% mortality (83% male: 5 during exposure, 33% female: 1 during exposure and 1 post exposure)
1241 ppm 83% mortality (100% male: 3 during exposure and 3 post exposure, 67% female: 2 during exposure and 2 post exposure)

Endpoint/Concentration/Rationale: 407 ppm for 1 hour considered for basis for AEGL-3 values

Uncertainty Factors/Rationale: Total uncertainty factor: 30

Interspecies: 3- An appropriate animal model was used and, the mechanism of action (bronchoconstriction, irritation of the epithelial lining, and increased mucus production via goblet cell proliferation) would not differ across species. Although human data did not provide quantitative exposure data, they did show similar effects; irritation and hyperinflation of the lungs and pulmonary edema.

Intraspecies: 10- Although data on a sensitive subpopulation are lacking for thionyl chloride, it is known that asthmatics are sensitive to sulfur dioxide, one of thionyl chloride's hydrolysis products. It is believed that the intraspecies uncertainty factor of 10 is protective of asthmatics and other sensitive populations.

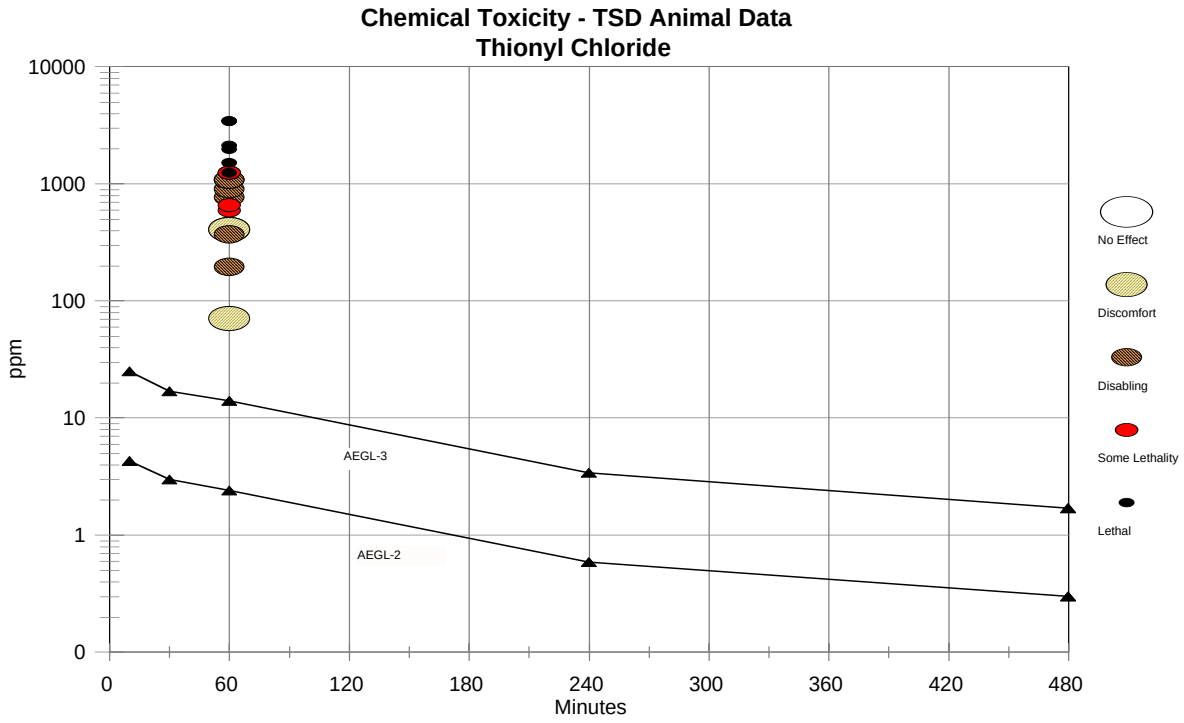
Modifying Factor: None

Animal to Human Dosimetric Adjustment: None applied, insufficient data

Time Scaling: In the absence of an empirically derived exponent (n), and to obtain AEGL values, $C^n \times t = k$, temporal scaling, using n = 3 when extrapolating to shorter time points and n = 1 when extrapolating to longer time points. The concentration exposure time relationship for many irritant and systemically acting vapors and gases may be described by $C^n \times t = k$, where the exponent ranges from 0.8 to 3.5 (ten Berge et al. 1986).

Data Adequacy: The study was considered adequate for AEGL-3 derivation. It was a well-designed and performed study, adequate numbers of animals were used, and an endpoint consistent with theAEGL-3 definition and toxicity of thionyl chloride was observed.

APPENDIX D: Category Plot for Thionyl Chloride


Chemical Toxicity - TSD Animal Data
Thionyl Chloride
10000
1000
100
10
1
0
ppm
0
60
120
180
240
300
360
420
480
Minutes
AEGL-3
AEGL-2
No Effect
Discomfort
Disabling
Some Lethality
Lethal

1