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ACUTE EXPOSURE GUIDELINE LEVELS (AEGLs)

FOR

SULFUR CHLORIDE (CAS No. 10025-67-9)

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/m^3]) 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/m^3) 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/m^3) 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.

TABLE OF CONTENTS

LIST OF TABLES

SUMMARY

Sulfur chloride is a fuming yellowish red oily liquid. It is used in the production of vulcanized rubber, as an intermediate in synthesis of organic chemicals, as a hardening agent for soft woods, for purifying sugar juices, and as a military poison. A survey conducted from 1981-1983 found that about 28,180 workers were potentially exposed to sulfur chloride. Sulfur chloride has an irritating, penetrating, nauseating, or suffocating odor, but the odor detection threshold is not known. It decomposes primarily to sulfur, sulfur dioxide, and hydrochloric acid in water or a moist environment.

The data on sulfur chloride was very limited. No data were found on lethal concentrations. Sulfur chloride vapor causes irritation to the eyes, nose, and throat of humans. The threshold for irritation to humans is 2 ppm and mild irritation was reported to occur at 2-9 ppm. The LC_{50} for rats exposed to sulfur chloride for 4 hours was 483 ppm (2670 mg/m^3). An acute inhalation study in rats was used for deriving AEGL values for all three levels. The degradation products of sulfur chloride (hydrogen chloride and sulfur dioxide) should not be considered surrogates for deriving AEGL values for sulfur chloride because (1) the degradation level is dependent on the moisture content of the environment and under dry conditions very little degradation would be expected to occur and (2) unlike hydrogen chloride and sulfur dioxide, sulfur chloride is not water soluble and would not be efficiently scrubbed in the upper respiratory tract, thus allowing the parent compound to reach the pulmonary region of the respiratory tract. No odor data were available; therefore, a level of distinct odor awareness (LOA) could not be calculated.

AEGL-1 values were based on the no-observed-effect level (NOEL) of 33.3 ppm (point-of-departure, POD) for upper respiratory tract irritation, breathing abnormalities, and other clinical signs (reduced activity, piloerection, and ungroomed fur) that suggest discomfort in rats exposed to sulfur chloride for 4 hours. Very little is known about the toxicity of inhaled sulfur chloride and no data were available to compare the toxicity of sulfur chloride in different species or to evaluate the toxicity in sensitive individuals in the human population. Therefore, the default uncertainty factors, 10 for interspecies sensitivity and 10 for intraspecies variability (total uncertainty factor was 100) were applied to the exposure concentration of 33.3 ppm. The 4-hour exposure duration was extrapolated to the relevant AEGL time frames using the equation: $C^n \times t = k$. Data were not available to derive n empirically; therefore, the defaults values $n = 3$ and $n = 1$ were used to extrapolate from the 4-hour exposure duration to the shorter and longer time frames, respectively. Time scaling was applied for all exposure durations except the 10-minute exposure because sulfur chloride is not water soluble and would not be scrubbed in the upper respiratory tract; therefore, the potential for pulmonary effects exist for all exposure concentrations. In addition, AEGL-1 value for 10 minutes is assigned the same value as the 30-minute AEGL, because the data did not support extrapolating from a 4-hour exposure duration to a 10-minute time frame.

AEGL-2 values were based on a 4-hour exposure to 242 ppm (POD) that caused upper respiratory irritation (bloody and serous nasal discharge), abnormal breathing (dyspnea and decelerated breathing), and reduced activity. Although piloerection and ungroomed fur were

observed, these findings are too mild to be considered endpoints for AEGL-2 derivation. A total uncertainty factor of 30 was applied to the POD: 10 for interspecies sensitivity because only one animal study was available for deriving AEGL values and interspecies sensitivity could not be evaluated and 3 for intraspecies variability because sulfur chloride is a respiratory irritant and the response in humans is not expected to vary by more than a factor of 3. A modifying factor of 2 was applied because, the respiratory effects at 242 ppm were slightly more severe than described by the definition for AEGL-2 endpoints, and the modifying factor of 2 would provide a reasonable estimate of the threshold for AEGL-2 respiratory effects. In addition, the observed effects are likely to be reversible, and the AEGL-2 values would approach the no-effect level if either a larger uncertainty or modifying factor was applied. The time-scaling approach was the same as described for AEGL-1.

The 4-hour inhalation study in rats also served as the basis for deriving AEGL-3 values. The $BMDL_{05}$ for lethality was derived using the log/probit model from EPA's Benchmark Dose Software, Version 1.3.2. The $BMDL_{05}$ was 288 ppm (POD). The rationale for selecting a total uncertainty factor of 30 (10 for interspecies sensitivity and 3 for intraspecies variability) and the time scaling method were the same as described for AEGL-1.

Proposed AEGL Values For Sulfur Chloride

Classification	10 minute	30 minute	1 hour	4 hour	8 hour	Endpoint (Reference)
AEGL-1 (Nondisabling)	0.67 ppm [3.7 mg/m^3]	0.67 ppm [3.7 mg/m^3]	0.53 ppm [2.9 mg/m^3]	0.33 ppm [1.8 mg/m^3]	0.17 ppm [0.94 mg/m^3]	No effect level (Bomhard et al., 2000)
AEGL-2 (Disabling)	8.1 ppm [45 mg/m^3]	8.1 ppm [45 mg/m^3]	6.4 ppm [35 mg/m^3]	4.0 ppm [22 mg/m^3]	2.0 ppm [11 mg/m^3]	Upper respiratory tract irritation and breathing difficulty (Bomhard et al., 2000)
AEGL-3 (Lethal)	19 ppm [105 mg/m^3]	19 ppm [105 mg/m^3]	15 ppm [82 mg/m^3]	9.6 ppm [53 mg/m^3]	4.8 ppm [27 mg/m^3]	$BMDL_{50}$ for lethality (Bomhard et al., 2000)

Reference:

Bomhard, E.; Loser, E., and Pauluhn, J. 2000. Acute toxicologic evaluation of disulfur dichloride. *International Journal of Toxicology*. 19: 342.

1. INTRODUCTION

Sulfur chloride is a fuming oily liquid that has a vapor pressure of 7 mm Hg (O'Neil et al., 2001 NIOSH, 2003). Sulfur chloride is used in vulcanizing and curing rubber; as an intermediate and chlorinating agent for manufacturing organic chemicals, sulfur dyes, and insecticides; for hardening soft woods; for purifying sugar juices, as a military poison; for for extraction of gold from ores; and as a polymerization catalyst for vegetable oils (Lewis, 1993; Bingham, 2001; O'Neil et al., 2001). The National Occupational Exposure Survey (NOES) from 1981-1983 estimated that 28,180 workers were potentially exposed to sulfur chloride in small, medium, and large facilities (Pedersen et al., 2001; NIOSH/NOES, 2003, http://www.cdc.gov/noes/noes4/siocsyns.html).

Sulfur chloride decomposes to sulfur, sulfur dioxide, and hydrochloric acid as well as hydrogen sulfide, sulfite, and thiosulfate in water or a moist environment (Henderson and Haggard, 1943). Therefore, individuals may be exposed to concentrations of sulfur chloride and its decomposition products that would vary depending on the environmental conditions. Physical/chemical data for sulfur chloride are presented in Table 1.

TABLE 1. Physical/Chemical Data

Parameter	Value	Reference
Chemical Name	Sulfur monochloride	
Synonym	sulfur monochloride, disulfur dichloride, sulfur subchloride, thiosulfurous dichloride	RTECS, 2003
CAS Registry No.	10025-67-9	RTECS, 2003
Chemical Formula	C_2S_2	RTECS, 2003
Molecular Weight	135.04	O'Neil et al., 2001
Physical State	light amber to yellowish red, fuming, oily liquid	O'Neil et al., 2001
Vapor Pressure	6.7 torr @ 20EC	HSDB, 2003
Vapor Density	4.66 (air = 1)	HSDB, 2003
Density	1.6885 @ 15.5EC	O'Neil et al, 2001
Freezing Point	-80EC	Lewis, 1993
Boiling Point	138EC @ 760 mm Hg; 72.0EC @ 100 mm Hg; 19.1EC @ 10 mm Hg	O'Neil et al., 2001
Solubility	soluble in alcohol, ether, benzene, carbon disulfide, amyl acetate, carbon tetrachloride, oils	O'Neil et al., 2001; Lewis, 1993
Flash point	130EC	Lewis, 1993
Conversion factors	1 mg/m^3 = 0.181 ppm; 1 ppm = 5.52 mg/m^3	

2. HUMAN TOXICITY DATA

No toxicity data from primary sources were found in the literature and no secondary data were found that reported deaths caused by exposure to sulfur chloride. Sulfur chloride is considered an upper respiratory tract irritant (Bingham, 2001). The following is a summary of the secondary information found in the literature. Bingham (2001) reported that sulfur chloride poured into an open container and placed on steam coils on the floor of curing ovens with little or no ventilation resulted in brief exposure to relatively high concentrations due to leakage into the room (work area). The resulting exposure to sulfur chloride caused pronounced irritation to the eyes and nose. Bingham (2001) also noted that exposure to sulfur chloride caused irritation to the throat. Respiratory tract irritation was attributed to decomposition products, hydrogen chloride and sulfur dioxide released during hydrolysis of sulfur chloride (Bingham, 2001). Ruth (1986) reported an irritation threshold of 12 mg/m^3 (2.2 ppm) for sulfur chloride. Elkins (1959) reported that sulfur chloride at concentrations of 2-9 ppm (11-49.7 mg/m^3) found in rubber factories were mildly irritating. ACGIH (1991) noted that the analytical methods used by Elkins (1959) involved absorption in alkali and determination of chloride, which may have included a high proportion of hydrogen chloride. The odor threshold for sulfur chloride has not been reported, but the odor has been described as irritating, nauseating, penetrating, or suffocating (Ruth, 1986; O'Neil et al., 2001; Bingham, 2001; NIOSH, 2003).

3. ANIMAL TOXICITY DATA

3.1. Acute Lethality

3.1.1. Rat

In an acute inhalation toxicity study, groups of five male and five female Wistar rats were exposed head-nose only to vapors of sulfur chloride at nominal concentrations of 0, 25, 303, 1853, 1938, 3702, 4143, or 5511 mg/m^3 for 4 hours (Bomhard et al., 2000). The analytical concentrations were 0, 8, 184, 1335, 1723, 2500, 2870, or 3487 mg/m^3 (0, 1.45, 33.3, 242, 312, 453, 519, and 997 ppm, respectively), respectively. The surviving animals were observed 14 days for mortality, body weights, clinical signs, and gross pathologic changes. The rats were exposed in a 7-L stainless-steel chamber. Decomposition and other potential reaction products are unlikely to be a problem in this study because the design of the chamber and exposure method prevented mixing of test atmosphere with exhaled air. The compressed air used to dilute the test material was dried and conditioned to eliminate water and oil from the test atmosphere. The chamber atmosphere was sampled at three positions in the breathing zones of the rats after steady state was attained at the beginning of exposure, about half way through exposure, and near the end of exposure. Sulfur chloride in the test atmosphere was assessed by hydrogen chloride production in sodium hydroxide. The reaction of chloride ions with mercury thiocyanate produces Hg(II)-chloride (low solubility) and thiocyanate. A yellowish-brown complex is produced in presence of iron(III)-ions that is measured in a spectrophometer at 456 nm.

In the male and female groups combined none of the 10 rats/group died at concentrations of #312 ppm; 30% (3/10), 60% (6/10), and 100% (10/10) of the rats died after exposure to 453, 519, and 997 ppm. The LC_{50} calculated by probit analysis was 2670 mg/m^3 (483 ppm) (NCSS,

Version 5.5). Clinical signs at $242 ppm included bloody and serous nasal discharge, dyspnea (difficult or labored breathing), decelerated breathing, reduced activity, piloerection, and ungroomed fur. Additional clinical signs observed at 453 ppm included extreme bradypnea (slowed breathing), cyanosis, corneal opacity, and necrotic lesions in the nose/muzzle area. Gross observation of animals that died showed emphysema, edema in liver-like areas of the lungs, hydrothorax (fluid in the pleural cavity), pale spleen and liver, bloody, yellowish mucous substance in the gastrointestinal tract, reddening of the glandular stomach, and reddening and necrosis of the rhinarium (nose). Gross observation of some survivors (assumed to include animals at $453 ppm) showed emphysema and edema in liver-like or dark-red areas of the lungs. No clinical signs, deaths, or pathologic effects were observed in rats exposed to 1.45 or 33.3 ppm.

3.1.2. Other Species

Mice died after exposure to 150 ppm (829 mg/m^3) for 1 minute and cats died a few days after exposure to 48 ppm (265 mg/m^3) for 15 min (Flury and Zernik, 1931, cited by Henderson and Haggard, 1943), but cats tolerated exposure to 12 ppm (66 mg/m^3) for 15 minutes (Flury and Zernik, 1931, cited by Henderson and Haggard, 1943 and ACGIH, 1991). The degree to which sulfur chloride had decomposed to hydrogen chloride and sulfur dioxide was not known. The Flury and Zernik (1931) data were cited from secondary sources, which provided no additional information on toxicity or analytical methods.

3.2. Nonlethal Toxicity

No studies were found that specifically addressed the nonlethal effects due to inhalation exposure to sulfur chloride. No data was found on other relevant endpoints (developmental, reproductive, or genetic toxicity or carcinogenicity).

4. SPECIAL CONSIDERATIONS

Sulfur chloride decomposes to hydrogen chloride and sulfur dioxide in a moist environment; the stoichiometry of decomposition in environments with varying moisture content is not known. Hydrogen chloride (NRC, 2003) and sulfur dioxide (Bingham, 2001) are upper respiratory irritants. The upper respiratory tract irritation after exposure to sulfur chloride has been attributed to the decomposition products (Bingham, 2001). Sulfur chloride is not water soluble and would be poorly scrubbed in the upper respiratory tract. Therefore, any undecomposed sulfur chloride could reach the lower respiratory tract thereby causing damage to the bronchiolar and alveolar regions of the lungs.

5. DATA ANALYSIS AND PROPOSED AEGL-1

5.1. Human Data Relevant to AEGL-1

Sulfur chloride is irritating to the eyes and upper respiratory tract. Ruth (1986) reported that the irritation threshold for sulfur chloride is 2.2 ppm, and Elkins (1959) reported that concentrations from 2-9 ppm were mildly irritating. No other human data are available for deriving AEGL-1 values.

5.2. Animal Data Relevant to AEGL-1

No animal studies designed specifically to examine the nonlethal effects of exposure to sulfur chloride were found in the literature. However, in a 4-hour acute inhalation study, no clinical signs, gross lesions, or deaths were observed in rats exposed to 1.45 or 33.3 ppm for 4 hours (Bomhard et al. 2000). Lesions in the nasal cavity (bloody and serous discharge) and breathing difficulty were observed at 242 ppm. Piloerection, reduced activity, and ungroomed fur also observed at 242 ppm were probably indicative of discomfort during exposure.

5.3. Derivation of AEGL-1

No details were available for the human data, so these data were not used to derive AEGL-1 values. The only data available for deriving AEGL-1 values was the 4-hour acute inhalation study in rats (Bomhard et al., 2000). In moist environments, sulfur chloride decomposes to hydrogen chloride and sulfur dioxide, which are primarily upper respiratory irritants. The proportion of parent compound that could reach the lower respiratory tract and cause pulmonary damage would vary with the moisture content of the environment. Therefore, because of the uncertainty associated with the environment, AEGL values should not be based on the decomposition products but on the potentially more toxic sulfur chloride.

The starting point for AEGL-1 derivation is 33.3 ppm (point-of-departure, POD), the highest concentration causing no clinical signs, gross lesions, or deaths. A total uncertainty factor of 100 (default) was applied to the 33.3 ppm exposure concentration; 10 each for interspecies sensitivity and intraspecies variability. Very little is known about the toxicity of sulfur chloride, and no data were available to assess the species differences or the response of sensitive groups in the population to sulfur chloride exposure. The decomposition products are primary sensory irritants, and sulfur chloride is an irritant, but it is not water soluble and may or may not be a primary irritant. The exposure concentration for 4 hours was scaled to the pertinent AEGL time frames using the equation: $C^n \times t = k$, where C is the exposure concentration, t is the exposure duration, and k is a constant (ten Berge et al., 1986). Data were not available for an empirical derivation of n, thus the defaults values $n = 3$ and $n = 1$ were applied when extrapolating from the 4-hour exposure duration to the shorter and longer time frames, respectively. Time scaling was applied to all exposure duration except the 10-minute exposure because sulfur chloride in not water soluble and there is a potential for pulmonary toxicity at all exposure concentrations. Because of the uncertainty of extrapolating from a 4-hour study to a 10-minute exposure duration, the 30-minute AEGL is retained for the 10-minute exposure duration. AEGL-1 values are presented in Table 2 and the calculations are presented in Appendix A.

Table 2. AEGL-1 Values for Sulfur Chloride

10 minutes	30 minutes	1 hour	4 hours	8 hours
0.67 ppm [3.7 mg/m^3]	0.67 ppm [3.7 mg/m^3]	0.53 ppm [2.9 mg/m^3]	0.33 ppm [1.8 mg/m^3]	0.17 ppm [0.94 mg/m^3]

6. DATA ANALYSIS AND PROPOSED AEGL-2

6.1. Human Data Relevant to AEGL-2

No relevant human data are available for deriving AEGL-2 values

6.2. Animal Data Relevant to AEGL-2

The clinical signs Bomhard et al. (2000) reported for rats exposed to sulfur chloride at 242 ppm for 4 hours, which included bloody and serous discharge from the nose, some breathing difficulty, and signs of discomfort and no deaths, are consistent with but slightly more severe than the definition of AEGL-2 endpoints.

6.3. Derivation of AEGL-2

The only study available for deriving AEGL-2 values is the 4-hour acute inhalation study in rats (Bomhard et al., 2000). The starting point for AEGL-2 derivation is 242 ppm (POD) that caused signs of upper respiratory tract irritation, dyspnea and decelerated breathing, and signs of discomfort. A total uncertainty factor of 30 was applied to the POD: 10 for interspecies sensitivity because only one animal study was available for deriving AEGL values and species sensitivity could not be evaluated and 3 for intraspecies variability because sulfur chloride is a respiratory irritant and the response in humans is not expected to vary by more than a factor of 3. A modifying factor or 2 also was applied to the POD because the effects appeared slightly more severe than described by the definition of AEGL-2 and the modifying factor would provide a better estimate of the threshold for the respiratory effects. In addition, the wide spacing between the no-effect level of 33.3 ppm and 242 ppm suggests that the threshold is between these two concentrations. If a larger modifying factor (or uncertainty factor) was used, the AEGL-2 would approach the no-effect level. The time-scaling method was the same as described for AEGL-1. AEGL-2 values are presented in Table 3 and the calculations are presented in Appendix A.

Table 3. AEGL-2 Values for Sulfur Chloride

10 minutes	30 minutes	1 hour	4 hours	8 hours
8.1 ppm [45 mg/m^3]	8.1 ppm [45 mg/m^3]	6.4 ppm [35 mg/m^3]	4.0 ppm [22 mg/m^3]	2.0 ppm [11 mg/m^3]

7. DATA ANALYSIS AND PROPOSED AEGL-3

7.1. Human Data Relevant to AEGL-3

No human data relevant to deriving AEGL-3 values were found in the literature.

7.2 Animal Data Relevant to AEGL-3

Secondary sources reported that mice died after exposure to 150 ppm for 1 minute and cats died after exposure to 48 ppm for 15 minutes (Henderson and Haggard, 1943). These data could not be corroborated and no analytical methods were described. A 4-hour acute inhalation study in rats showed an exposure-related increase in mortality at 453 ppm and above, and the LC_{50} was 483 ppm (Bomhard et al., 2000).

7.3. Derivation of AEGL-3

AEGL-3 values can be derived from the 4-hour inhalation study using rats. The lethality threshold (LC_{01}) estimated by probit analysis was 296 ppm (NCSS, Version 5.5) and the 95% lower confidence limit on the LC_{05} (BMDL) was 288 ppm using the log/probit model from EPA's Benchmark Dose Software, Version 1.3.2.(U.S. EPA, 2003). The BMDL of 288 ppm (POD) was used to derive AEGL-3 values. The application of uncertainty factors (10 for interspecies sensitivity and 3 for intraspecies variability) was the same as described for AEGL-2 and the time scaling method was the same as described for AEGL-1. AEGL-3 values are presented in Table 4 and the calculations are presented in Appendix A.

Table 4. AEGL-3 Values for Sulfur Chloride [ppm (mg/m^3)]

10 minutes	30 minutes	1 hour	4 hours	8 hours
19 ppm [105 mg/m^3]	19 ppm [105 mg/m^3]	15 ppm [82 mg/m^3]	9.6 ppm [53mg/m^3]	4.8 ppm [27 mg/m^3]

8. SUMMARY OF PROPOSED AEGLs

8.1. Proposed AEGLs

The proposed AEGL values are presented in Table 5. All AEGL values were based on a single acute inhalation study in rats. AEGL-1 values were based on the highest no effect level, AEGL-2 values were based on an estimate of the threshold for upper respiratory tract irritation and abnormal respiration, and AEGL-3 values were based on an $BMDL_{05}$ for lethality. There were no other reliable data to compare with the proposed AEGL values.

TABLE 5. Proposed AEGL Values For Sulfur Chloride

Classification	10 minute	30 minute	1 hour	4 hour	8 hour	Endpoint (Reference)
AEGL-1 (Nondisabling)	0.67 ppm [3.7 mg/m^3]	0.67 ppm [3.7 mg/m^3]	0.53 ppm [2.9 mg/m^3]	0.33 ppm [1.8 mg/m^3]	0.17 ppm [0.94 mg/m^3]	No effect level, (Bomhard et al., 2000)
AEGL-2 (Disabling)	8.1 ppm [45 mg/m^3]	8.1 ppm [45 mg/m^3]	6.4 ppm [35 mg/m^3]	4.0 ppm [22 mg/m^3]	2.0 ppm [11 mg/m^3]	Upper respiratory tract irritation and dyspnea (Bomhard et al., 2000)
AEGL-3 (Lethal)	19 ppm [105 mg/m^3]	19 ppm [105 mg/m^3]	15 ppm [82 mg/m^3]	9.6 ppm [53 mg/m^3]	4.8 ppm [27 mg/m^3]	$BMDL_{05}$ for lethality (Bomhard et al., 2000)

8.2. Comparison of AEGLs with Other Standards and Criteria

Table 6 summarizes standards and guidelines established by various agencies and organizations. AIHA has not evaluated sulfur chloride; therefore, no ERPG values have been proposed. ACGIH (1991) considered sulfur chloride to be a primary irritant and proposed 1 ppm as a ceiling limit and concluded that this level should be protective of respiratory injury and discomfort. The IDLH value is based on the animal inhalation toxicity data reported by Flury and Zernik (1931) and Henderson and Haggard (1943). The NIOSH REL is a ceiling level not an 8-hour TWA. The AEGL values are higher than the standards and guidelines listed below;

the standards and criteria were based on very early and unreliable data and not the more recent data (Bomhard et al., 2000) that served as the basis for AEGL derivations.

TABLE 6. Extant Standards and Guidelines for Sulfur Chloride

Guideline	Guideline Value				
	10 minutes	30 minutes	1 hour	4 hours	8 hours
AEGL-1	0.67 ppm	0.67 ppm	0.53 ppm	0.33 ppm	0.17 ppm
AEGL-2	8.1 ppm	8.1 ppm	6.4 ppm	4.0 ppm	2.0 ppm
AEGL-3	19 ppm	19 ppm	15 ppm	9.6 ppm	4.8 ppm
[a]OSHA PEL -TWA	1 ppm				
[e]NIOSH REL	1 ppm (6 mg/m^3) (ceiling)				
[c]NIOSH IDLH	15 ppm (30 minutes)				
[d]ACGIH TLV	1 ppm (ceiling)				
[e]MAK (German)	Insufficient data				
[f]MAC (Dutch) (MSAE, 1999)	No recommendation				

[a]**OSHA PEL-TWA (Occupational Safety and Health Administration, Permissible Exposure Limits - Time Weighted Average)** (OSHA 1999) is defined analogous to the ACGIH-TLV-TWA, but is for exposures of no more than 10 hours/day, 40 hours/week.

[b]**NIOSH REL-Ceiling (National Institute of Occupational Safety and Health, Recommended Exposure Limits - Time Weighted Average)** (NIOSH, 2003) is defined analogous to the ACGIH-TLV-TWA.

[c]**IDLH (Immediately Dangerous to Life and Health, National Institute of Occupational Safety and Health)** (NIOSH, 1994, 2003) represents the maximum concentration from which one could escape within 30 minutes without any escape-impairing symptoms, or any irreversible health effects.

[d]**ACGIH TLV-TWA (American Conference of Governmental Industrial Hygienists, Threshold Limit Value - Time Weighted Average)** (ACGIH, 2003) is the time-weighted average concentration for a normal 8-hour workday and a 40-hour work week, to which nearly all workers may be repeatedly exposed, day after day, without adverse effect.

[e]**MAK Spitzenbegrenzung (Peak Limit [give category])** (German Research Association 2002)constitutes the maximum average concentration to which workers can be exposed for a period up to 30 minutes with no more than 2 exposure periods per work shift; total exposure may not exceed 8-hour MAK.

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

8.3. Data Adequacy and Research Needs

AEGL-1, -2, and -3 values for sulfur chloride were derived from a single acute inhalation study in one species with concentrations encompassing two no-effect levels and 100% mortality. Data quality would be improved greatly by another acute inhalation study with a shorter exposure duration in rats and an acute inhalation study in another species. Studies designed specifically to examine non-lethal toxicity of sulfur chloride also would improve the confidence in AEGL-1 and AEGL-2 values.

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APPENDIX A: DERIVATION OF AEGLs

1

Derivation of AEGL-1

Key Study:	Bomhard et al., 2000
Toxicity Endpoint:	NOEL for upper respiratory irritation, breathing difficulty, signs of discomfort.
Time Scaling:	$C^n \times t = k$; n = 3 and n = 1 for scaling to shorter and longer durations, respectively.
Uncertainty Factors:	100: 10 for interspecies differences; 10 for intraspecies variability (defaults).
Calculations:	
4-hour AEGL-1	C = 33.3 ppm/100 (uncertainty factor) = 0.33 ppm
	$C^n \times t = k$; C = 0.33 ppm, t = 240 minutes, n = 1
	k = 79.9 ppm•minutes
	$C = (k/t)^n = (79.9 \text{ ppm•minutes}/240 \text{ min})^1 = 0.33$ ppm
8-hour AEGL-1	$C = (k/t)^{1/n} = (79.9 \text{ ppm•minutes}/480 \text{ min})^1 = 0.17$ ppm
1-hour AEGL-1	$C^n \times t = k$; C = 0.33 ppm, t = 240 minutes, n = 3
	k = 8.86 ppm•minutes
	$C = (k/t)^{1/n} = (8.86 \text{ ppm•minutes}/60 \text{ min})^{1/3} = 0.53$ ppm
30-minute AEGL-1	$C = (k/t)^{1/n} = (8.86 \text{ ppm•minutes}/30 \text{ min})^{1/3} = 0.67$ ppm
10-minute AEGL-1	same as 30-minute AEGL = 0.67 ppm

Derivation of AEGL-2

Key Study:	Bomhard et al., 2000
Toxicity Endpoint:	Upper respiratory irritation, breathing difficulty, signs of discomfort.
Time Scaling:	$C^n \times t = k$; n = 3 and n = 1 for scaling to shorter and longer durations, respectively.
Uncertainty Factors:	100: 10 for interspecies differences; 3 for intraspecies variability (defaults).
Modifying Factor:	2: effects slightly more severe than AEGL-2 definition
Calculations:	
4-hour AEGL-2	C = 242 ppm/(30 [uncertainty factor]/2 [modifying factor) = 4.0 ppm
	$C^n \times t = k$; C = 4.0 ppm, t = 240 minutes, n = 1
	k = 968 ppm℃minutes
	$C = (k/t)^n = (968 \text{ ppm℃minutes}/240 \text{ min})^1 = 4.0$ ppm
8-hour AEGL-2	$C = (k/t)^{1/n} = (968 \text{ ppm℃minutes}/480 \text{ min})^1 = 2.0$ ppm
1-hour AEGL-2	$C^n \times t = k$; C = 4.0 ppm, t = 240 minutes, n = 3
	k = 15747 ppm℃minutes
	$C = (k/t)^{1/n} = (15747 \text{ ppm℃minutes}/60 \text{ min})^{1/3} = 6.4$ ppm
30-minute AEGL-2	$C = (k/t)^{1/n} = (15747 \text{ ppm℃minutes}/30 \text{ min})^{1/3} = 8.1$ ppm
10-minute AEGL-2	same as 30-minute AEGL = 8.1 ppm

Derivation of AEGL-3

Key Study:	Bomhard et al., 2000
Toxicity Endpoint:	$BMDL_{05}$ for lethality
Time Scaling:	$C^n \times t = k$; n = 3 and n = 1 for scaling to shorter and longer durations, respectively.
Uncertainty Factors:	100: 10 for interspecies differences; 10 for intraspecies variability (defaults).
Calculations:	
4-hour AEGL-3	C = 288 ppm/30 (uncertainty factor) = 9.6 ppm
	$C^n \times t = k$; C = 9.6 ppm, t = 240 minutes, n = 1
	k = 2304 ppm•minutes
	$C = (k/t)^n = (2304 ppm•minutes/240 min)^1 = 9.6$ ppm
8-hour AEGL-3	$C =(k/t)^{1/n} = (2304$ ppm•minutes/480 min$)^1 = 4.8$ ppm
1-hour AEGL-3	$C^n \times t = k$; C = 9.6 ppm, t = 240 minutes, n = 3
	k = 21,234 ppm•minutes
	$C =(k/t)^{1/n} = (21,234$ ppm•minutes/60 min$)^{1/3} = 15$ ppm
30-minute AEGL-3	$C = (k/t)^{1/n} = (21,234$ ppm•minutes/30 min$)^{1/3} = 19$ ppm
10-minute AEGL-3	same as 30-minute AEGL = 19 ppm

APPENDIX B: DERIVATION SUMMARY FOR SULFUR CHLORIDE AEGLs

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ACUTE EXPOSURE GUIDELINES FOR SULFUR CHLORIDE DERIVATION SUMMARY

AEGL -1 VALUES				
10 minutes	**30 minute**	**1 hour**	**4 hour**	**8 hour**
0.67 ppm [3.7 mg/m^3]	0.67 ppm [3.7 mg/m^3]	0.53 ppm [2.9 mg/m^3]	0.33 ppm [1.8 mg/m^3]	0.17 ppm [0.94 mg/m^3]

Key Reference: Bomhard, E.; Loser, E., and Pauluhn, J. 2000. Acute toxicologic evaluation of disulfur dichloride. Int. J. Toxicol. 19: 342.

Test Species/Strain/Number: rat/strain not specified/ 5 of each sex/exposure group

Exposure Route/Concentration/Durations: Inhalation: 0, 1.45, 33.3, 242, 312, 453, 519, or 997 ppm for 4 hours

Effects:	1.45 and 33.3 ppm	no effects
	242 ppm	bloody and serous nasal discharge, breathing difficulty, piloerection, reduced activity, and ungroomed fur (signs of discomfort)
	312 ppm	same as 242 ppm but probably more severe, no deaths
	453 ppm	3/10 died, breathing difficulty, cyanosis, corneal opacity, necrosis in the nose; emphysema, pulmonary edema, effect in liver and spleen, gastrointestinal irritation.
	519 ppm	6/10 died; effect same as described above
	997 ppm	10/10 died: effects same as described above

Endpoint/Concentration/Rationale: NOEL for upper respiratory irritation, breathing difficulty, signs of discomfort at 33.3 ppm

Uncertainty Factors/Rationale: not applicable

Total uncertainty factor:	100 (default)
Interspecies:	10 (default)
Intraspecies:	10 (default)

Modifying Factor: 1

Animal to Human Dosimetric Adjustment: 1

Time Scaling: $C^n \times t = k$, n = 3 and n = 1 when scaling to shorter and longer durations, respectively (default)

Data Adequacy: Only one acute inhalation study was available for deriving AEGLs. This study showed clear concentration-response relationships for lethal and non-lethal effects. This study also appeared to be well-conducted and in concordance with GLP.

AEGL -2 VALUES				
10 minute	**30 minute**	**1 hour**	**4 hour**	**8 hour**
8.1 ppm [45 mg/m^3]	8.1 ppm [45 mg/m^3]	6.4 ppm [35 mg/m^3]	4.0 ppm [22 mg/m^3]	2.0 ppm [11 mg/m^3]

Key Reference: Bomhard, E.; Loser, E., and Pauluhn, J. 2000. Acute toxicologic evaluation of disulfur dichloride. Int. J. Toxicol. 19: 342.

Test Species/Strain/Number: rat/strain not specified/ 5 of each sex/exposure group

Exposure Route/Concentration/Durations: 0, 1.45, 33.3, 242, 312, 453, 519, or 997 ppm for 4 hours

Effects:

1.45 and 33.3 ppm	no effects
242 ppm	bloody and serous nasal discharge, breathing difficulty, piloerection, reduced activity, and ungroomed fur (signs of discomfort)
312 ppm	same as 242 ppm but probably more severe, no deaths
453 ppm	3/10 died, breathing difficulty, cyanosis, corneal opacity, necrosis in the nose; emphysema, pulmonary edema, effect in liver and spleen, gastrointestinal irritation.
519 ppm	6/10 died; effect same as described above
997 ppm	10/10 died, other effects were the same as described above

Endpoint/Concentration/Rationale: upper respiratory irritation, breathing difficulty, signs of discomfort at 242 ppm

Uncertainty Factors/Rationale:

Total uncertainty factor:	30
Interspecies:	10 (default): no data was available to assess interspecies sensitivity
Intraspecies:	3: sulfur chloride is a respiratory irritant and the human response is not expected to vary by more than a factor of 3.

Modifying Factor: 2: the endpoints are slightly greater than the definition of AEGL-2, the effects are likely to be reversible, and a larger modifying factor would place the AEGL-2 close to the no-effect level.

Animal to Human Dosimetric Adjustment: 1

Time Scaling: $C^n \times t = k$, n = 3 and n = 1 when scaling to shorter and longer durations, respectively (default)

Data Adequacy: Only one acute inhalation study was available for deriving AEGLs. This study showed clear concentration-response relationships for lethal and non-lethal effects. This study also appeared to be well-conducted and in concordance with GLP.

AEGL -3 VALUES				
10 minute	**30 minute**	**1 hour**	**4 hour**	**8 hour**
19 ppm [105 mg/m^3]	19 ppm [105 mg/m^3]	15 ppm [82 mg/m^3]	9.6 ppm [53 mg/m^3]	4.8 ppm [27 mg/m^3]

Key Reference: Bomhard, E.; Loser, E., and Pauluhn, J. 2000. Acute toxicologic evaluation of disulfur dichloride. Int. J. Toxicol. 19: 342.

Test Species/Strain/Number: rat/strain not specified/ 5 of each sex/exposure group

Exposure Route/Concentration/Durations: 0, 1.45, 33.3, 242, 312, 453, 519, or 997 ppm for 4 hours

Effects:

1.45 and 33.3 ppm	no effects
242 ppm	bloody and serous nasal discharge, breathing difficulty, piloerection, reduced activity, and ungroomed fur (signs of discomfort)
312 ppm	same as 242 ppm but probably more severe, no deaths
453 ppm	3/10 died, breathing difficulty, cyanosis, corneal opacity, necrosis in the nose; emphysema, pulmonary edema, effect in liver and spleen, gastrointestinal irritation.
519 ppm	6/10 died; effect same as described above
997 ppm	10/10 died, other effects were the same as described above

Endpoint/Concentration/Rationale: $BMDL_{05}$ for lethality ($BMDL_{05}$ = 288 ppm) for a 4-hour exposure

Uncertainty Factors/Rationale:

Total uncertainty factor:	30
Interspecies:	10 (default): no data were available to assess interspecies sensitivity
Intraspecies:	3: sulfur chloride is a respiratory tract irritant and the human response is not expected to vary by more than a factor of 3.

Modifying Factor: 1

Animal to Human Dosimetric Adjustment: 1

Time Scaling: $C^n \times t = k$, n = 3 and n = 1 when scaling to shorter and longer durations, respectively (default)

Data Adequacy: Only one acute inhalation study was available for deriving AEGLs. This study showed clear concentration-response relationships for lethal and non-lethal effects. This study also appeared to be well-conducted and was conducted in concordance with GLP.

APPENDIX C: CATEGORY PLOT FOR SULFUR CHLORIDE

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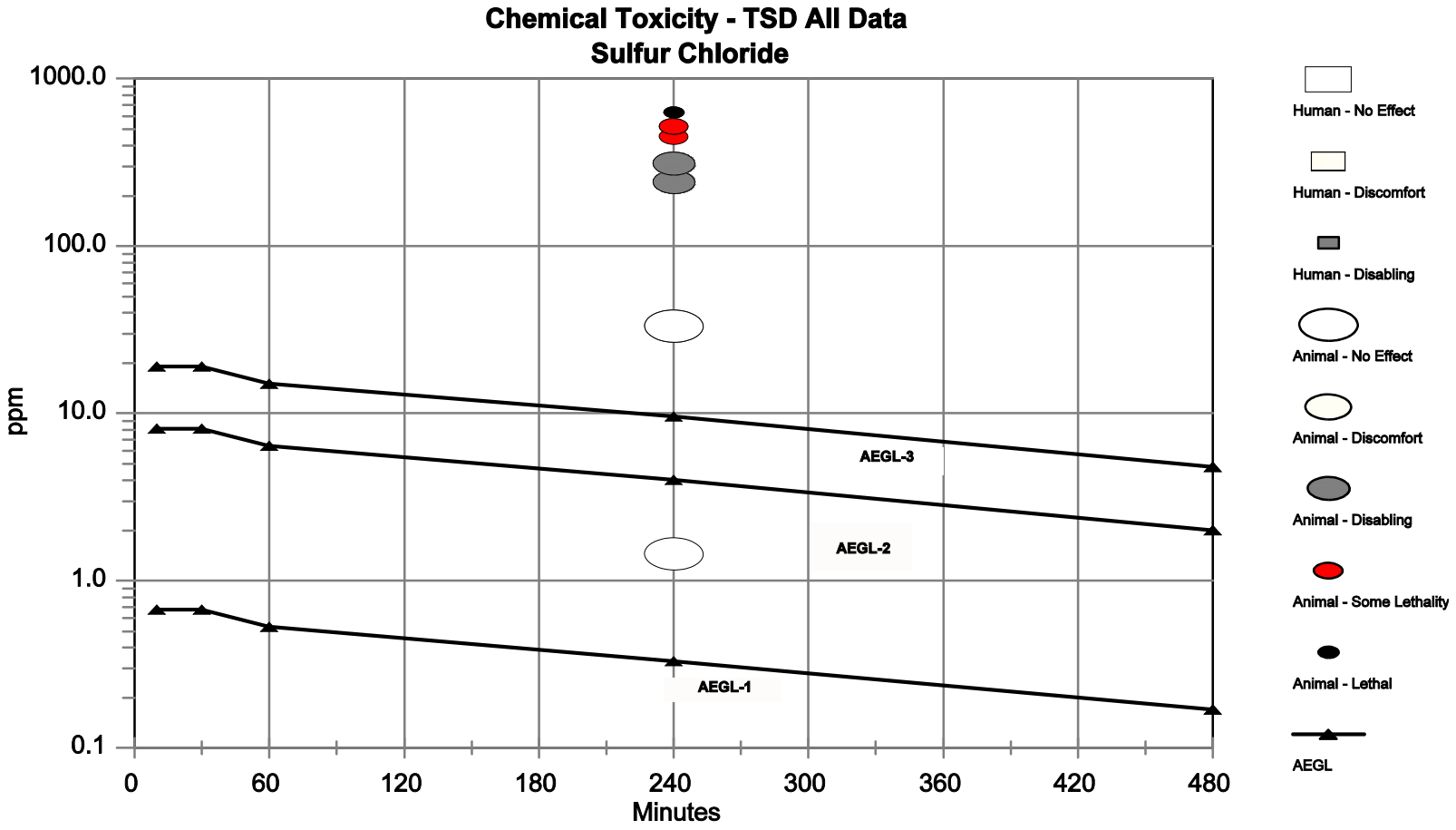
Chemical Toxicity - TSD All Data
Sulfur Chloride
1000.0
100.0
10.0
1.0
0.1
ppm
0
60
120
180
240
300
360
420
480
Minutes
AEGL-3
AEGL-2
AEGL-1
Human - No Effect
Human - Discomfort
Human - Disabling
Animal - No Effect
Animal - Discomfort
Animal - Disabling
Animal - Some Lethality
Animal - Lethal
AEGL