INTERIM ACUTE EXPOSURE GUIDELINE LEVELS (AEGLs) FOR Selenium Hexafluoride (CAS Reg. No. 7783-79-1)

$Se-F_6$

INTERIM ACUTE EXPOSURE GUIDELINE LEVELS (AEGLs) FOR SELENIUM HEXAFLUORIDE (CAS Reg. No. 7783-79-1)

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

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EXECUTIVE SUMMARY

Selenium hexafluoride is a colorless, irritating gas. It is insoluble in water, but decomposes slowly in moisture to form hydrogen fluoride and selenium oxide. It is corrosive and severely irritating to skin, eyes, and causes respiratory distress and pulmonary edema; the irritation is immediate, but pulmonary edema may be delayed several hours. Selenium hexafluoride is used as a gaseous electric insulator.

A NOEL for irritation in the guinea pig, rabbit, rats, and mice (1 ppm for 4-hours) (Kimmerle, 1960) was used to derive AEGL-1 values. An intraspecies uncertainty factor of 3 was applied because selenium hexafluoride is highly irritating and corrosive, and much of the toxicity is likely caused by a direct chemical effect on the tissues; this type of port-of-entry effect is not expected to vary greatly among individuals. An interspecies uncertainty factor of 1 was applied because the limited data suggest that the guinea pig, rabbit, rat, and mouse are similarly sensitive to the acute effects of selenium hexafluoride. A modifying factor of 10 was also applied to account for potential effects of the selenium moiety and the sparse database. Thus, the total adjustment is 30. 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). To obtain conservative and protective AEGL values in the absence of an empirically derived chemical-specific scaling exponent, temporal scaling was performed using n=3 when extrapolating to shorter time points (30-minutes and 1-hour) and n = 1 (8-hours) when extrapolating to longer time points using the $C^n \times t = k$ equation. The 30-minute AEGL-1 value was also adopted as the 10-minute AEGL-1 value due to the added uncertainty of extrapolating from a 4-hour time point to 10-minutes. Although AEGL-1 values might normally be held constant across all time points because minor irritation does not vary over time, time scaling was used for selenium hexafluoride AEGL-1 values to account for any potential enzymatic effects resulting from the selenium moiety.

In the absence of empirical data, the AEGL-3 values were divided by 3 to obtain AEGL-2 values for selenium hexafluoride. This approach is justified based on a steep concentration response curve (no effects in rabbit, guinea pig, rat, or mouse for 4-hour exposures at 1 ppm, difficulty breathing and pulmonary edema, but no mortality at 5 ppm, and 100% mortality at 10 ppm) (Kimmerle, 1960).

The highest concentration causing no mortality in the guinea pig, rabbit, rats, and mice (5 ppm for 4-hours) (Kimmerle, 1960) was used to derive AEGL-3 values. An intraspecies uncertainty factor of 3 was applied because selenium hexafluoride is highly irritating and corrosive, and much of the toxicity is likely caused by a direct chemical effect on the tissues; this type of port-of-entry effect is not expected to vary greatly among individuals. An interspecies uncertainty factor of 1 was applied because the limited data suggest that the guinea pig, rabbit, rat, and mouse are similarly sensitive to the acute effects of selenium hexafluoride. A modifying factor of 10 was also applied to account for potential effects of the selenium moiety and the sparse database. Thus, the total adjustment is 30. 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). To obtain conservative and protective AEGL values in the absence of an empirically derived chemical-specific scaling

exponent, temporal scaling was performed using n=3 when extrapolating to shorter time points (30-minutes and 1-hour) and n = 1 when extrapolating to longer time points (8-hours) using the $C^n \times t = k$ equation. The 30-minute AEGL-3 value was also adopted as the 10-minute AEGL-3 value due to the added uncertainty of extrapolating from a 4-hour time point to 10-minutes.

The calculated values are listed in the table below.

TABLE 1. Summary of AEGL Values for Name of Selenium Hexafluoride

Classification	10-minute	30-minute	1-hour	4-hour	8-hour	Endpoint (Reference)
AEGL−1 (Nondisabling)	0.067 ppm (0.53 mg/m^3)	0.067 ppm (0.53 mg/m^3)	0.053 ppm (0.42 mg/m^3)	0.033 ppm (0.26 mg/m^3)	0.017 ppm (0.13 mg/m^3)	NOEL for irritation in rabbit, guinea pig, rats, and mice (1 ppm, 4-hrs) (Kimmerle, 1960)
AEGL−2 (Disabling)	0.11 ppm (0.87 mg/m^3)	0.11 ppm (0.87 mg/m^3)	0.087 ppm (0.69 mg/m^3)	0.057 pm (0.45 mg/m^3)	0.028 ppm (0.22 mg/m^3)	One-third of the AEGL-3 values
AEGL−3 (Lethal)	0.33 ppm (2.6 mg/m^3)	0.33 ppm (2.6 mg/m^3)	0.26 ppm (2.1 mg/m^3)	0.17 ppm (1.3 mg/m^3)	0.083 ppm (0.66 mg/m^3)	Highest concentration causing no mortality in rabbit, guinea pig, rats, and mice (1 ppm, 4-hrs) (Kimmerle, 1960)

1. INTRODUCTION

Selenium hexafluoride is a colorless, irritating gas. It is insoluble in water, but decomposes slowly in moisture to form hydrogen fluoride and selenium oxide. It reacts with ammonia to produce selenium, nitrogen, and hydrogen fluoride, and is covalently saturated and does not attack glass. Selenium hexafluoride is corrosive and severely irritating to skin, eyes, and causes respiratory distress and pulmonary edema; the irritation is immediate, but pulmonary edema may be delayed several hours (ATSDR, 2006).

Selenium hexafluoride is used as a gaseous electric insulator and is prepared by passing gaseous fluorine over finely divided selenium in a copper vessel (O'Neil et al., 2001). Recent production and transport data were not located. Chemical and physical properties are listed in Table 2.

TABLE 2. Chemical and Physical Properties

Parameter	Value	References
Synonyms	Selenium fluoride; selenium (VI) fluoride	ATSDR, 2006
Chemical formula	SeF_6	O'Neil et al. 2001
Molecular weight	192.96	O'Neil et al. 2001
CAS Reg. No.	7783-79-1	O'Neil et al. 2001
Physical state	Colorless gas	O'Neil et al. 2001
Solubility in water	Insoluble. Slowly decomposes to form hydrogen fluoride and selenium oxide	ATSDR, 2006
Vapor pressure	651.2 mm Hg at -48.7 °C	HSDB, 2006
Vapor density (air =1)	6.7	HSDB, 2006
Liquid density (water =1)	Not applicable	
Melting point	-39 °C	ACGIH, 1991
Boiling point	-34.5 °C	ACGIH, 1991
Flammability limits	Nonflammable	IPCS, CEC, 2006
Conversion factors	1 ppm = 7.9 mg/m^3 1 mg/m^3 = 0.13 ppm	

2. HUMAN TOXICITY DATA

No information on human exposure was available. Selenium hexafluoride is a strong irritant to the skin, eyes, mucous membranes, and respiratory tract; direct contact with the skin may cause frostbite (IPCS, CEC, 2006). No information on the odor threshold or odor characterization was found.

3. ANIMAL TOXICITY DATA

3.1. Acute Toxicity

Kimmerle (1960) exposed groups of one guinea pig, one rabbit, two male white rats, and four male white mice to 1, 5, 10, 25, 50, or 100 ppm (nominal concentrations) selenium hexafluoride for up to 4-hours, followed by a 3-week observation period. Exposures were carried out in a 2

cubic meter chamber and the selenium hexafluoride was 99% pure. The test compound was introduced into the chamber through a glass burette and mixed with air by a propeller. All animals in the 10, 25, 50, and 100 ppm groups died in the exposure chamber. There was no mortality in animals exposed to 5 ppm selenium hexafluoride; however, all animals exhibited difficulty breathing and pulmonary edema, both of which resolved during the follow-up period. No effects were noted in animals exposed to 1 ppm. Time to death for the 4-hour exposure is summarized in Table 3.

Table 3. Time to Death (min.) for Animals Exposed to Selenium Hexafluoride for 4-hours

	1 ppm	5 ppm	10 ppm	25 ppm	50 ppm	100 ppm
Rabbit	-	-	240	190	65	31
Guinea Pig	-	-	240	170	80	42
Rat-1	-	-	240	165	80	15
Rat-2	-	-	240	240	80	28
Mouse-1	-	-	240	210	85	40
Mouse-2	-	-	180	165	80	32
Mouse-3	-	-	200	145	90	30
Mouse-4	-	-	605	205	100	25

Kimmerle (1960) also exposed groups of one guinea pig, one rabbit, two male white rats, and four male white mice to 10 ppm (nominal concentration) selenium hexafluoride for 1-hour, followed by a 3-week observation period. The guinea pig, both rats, and 2 of the mice died in the exposure chamber; whereas, the rabbit and the other mice survived the 3-week follow-up period. The presence or absence of clinical signs was not reported.

In a repeated-exposure phase of the study, Kimmerle exposed groups of one guinea pig, one rabbit, two male white rats, and four male white mice to 1 or 5 ppm (nominal concentrations) selenium hexafluoride 1-hour/day for 5 consecutive days, followed by a 3-week observation period. No mortality was observed. All animals in the 5 ppm group had difficulty breathing and were “in bad shape overall.” No treatment-related clinical signs or gross effects were noted at 1 ppm.

3.2. Developmental/Reproductive Toxicity

No data on developmental/reproductive toxicity were located.

3.3. Genotoxicity

No data on genotoxicity were located.

3.4. Chronic Toxicity/Carcinogenicity

No data on chronic toxicity/carcinogenicity were located.

3.5. Summary

Only one study that addressed selenium hexafluoride toxicity in animal models was located. Kimmerle (1960). Rabbits, guinea pigs, rats, and mice exposed to 10, 25, 50, and 100 ppm selenium hexafluoride for 4-hours all died; whereas, animals exposed to 1 or 5 ppm for 4-hours survived. Exposure to 10 ppm for 1-hour was lethal to 0/1 rabbit, 1/1 guinea pig, 2/2 rats, and 2/4 mice. Repeated exposure to 1 or 5 ppm 1 hour/day for 5 days resulted in no mortality in any species tested. Animals in the 5 ppm group exhibited signs of respiratory distress; no effects were noted in the 1 ppm group. Clinical signs (respiratory distress) and post-mortem findings (pulmonary edema) were consistent with severe irritation. No data on developmental/reproductive toxicity, genotoxicity, or chronic toxicity/carcinogenicity were located.

4. SPECIAL CONSIDERATIONS

4.1. Metabolism and Disposition

No information was located concerning the metabolism and disposition of selenium hexafluoride. However, selenium hexafluoride may be hydrolyzed in the moist respiratory tract to hydrogen fluoride and selenium oxide (ATSDR, 2006).

4.2. Mechanism of Toxicity

In the moist respiratory tract, it is believed that selenium hexafluoride hydrolyzes into hydrogen fluoride and selenium oxide. Kimmerle (1960) has shown that the toxic effects of inhaled selenium hexafluoride are consistent with severe irritation/corrosivity.

Hydrogen fluoride is a severe irritant to the skin, eyes, and respiratory tract. Penetration to the lungs produces pulmonary hemorrhage and edema and may result in death (NAS 2004).

The mechanism of toxicity of the selenium oxide hydrolysis product is unknown. One possible mechanism for selenium toxicity is an effect on enzyme activity either by inactivation of sulfhydryl enzymes, succinic dehydrogenase system, interference of glutathione metabolism, or substitution for sulfur in biomolecules (ATSDR 2001; IPCS 1986).

4.3. Structure Activity Relationships

Because one mole of selenium hexafluoride may decompose in moist atmospheres to form up to 6 moles of hydrogen fluoride, it might be assumed that selenium hexafluoride may be approximately 6-times more toxic than hydrogen fluoride on a molar basis. However, the limited data set suggests that selenium hexafluoride is much more than 6-times as toxic as hydrogen fluoride.

Ranges of one-hour LC_{50} values for hydrogen fluoride for the mouse and rat are 342 to 501 ppm, 966 to1395 ppm, respectively (NAS 2004). If the acute inhalation toxicity of selenium hexafluoride was due only to the hydrogen fluoride hydrolysis product, then approximate 1-hour LC_{50} values for selenium hexafluoride would range from 57-84 ppm for mice and 161-233 ppm for rats. However, 2/4 mice and 2/2 rats died when exposed to only 10 ppm selenium

hexafluoride for 1 hour (Kimmerle, 1960). The increased relative toxicity of selenium hexafluoride may be due to the selenium moiety and the slow hydrolysis rate of selenium hexafluoride.

4.4. Other Relevant Information

No additional relevant information was located.

4.4.1. Species Variability

The limited data of Kimmerle (1960) suggest that the acute toxicity of selenium hexafluoride is similar among rabbits, guinea pigs, rats, and mice. This would be expected for a corrosive/severely irritating chemical.

4.4.2. Susceptible Populations

Individuals with asthma might respond to exposure to selenium hexafluoride with increased bronchial responsiveness. No information on the relative susceptibility of asthmatic and normal individuals to selenium hexafluoride was located.

Individuals under stress, such as those involved in emergency situations and those engaged in physical activity, will experience greater selenium hexafluoride deposition and pulmonary irritation than individuals at rest.

4.4.3. Concentration-Exposure Duration Relationship

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). To obtain conservative and protective AEGL values in the absence of an empirically derived chemical-specific scaling exponent, temporal scaling may be 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 (NAS, 2001).

4.4.4. Concurrent Exposure Issues

No concurrent exposure issues were identified.

5. DATA ANALYSIS FOR AEGL-1

5.1. Summary of Human Data Relevant to AEGL-1

No human data relevant to development of AEGL-1 values were identified.

5.2. Summary of Animal Data Relevant to AEGL-1

One guinea pig, one rabbit, two male white rats, and four male white mice exposed to 1 ppm selenium hexafluoride for 4 hours exhibited no treatment-related effects (Kimmerle, 1960). Severe irritation was noted at the next concentration tested (5 ppm for 4 hours).

5.3. Derivation of AEGL-1

The NOEL for irritation in the guinea pig, rabbit, rats, and mice (1 ppm for 4-hours) (Kimmerle, 1960) will be used to derive AEGL-1 values. An intraspecies uncertainty factor of 3 will be applied because selenium hexafluoride is highly irritating and corrosive, and much of the toxicity is likely caused by a direct chemical effect on the tissues; this type of port-of-entry effect is not expected to vary greatly among individuals. An interspecies uncertainty factor of 1 will also be applied because the limited data suggest that the guinea pig, rabbit, rat, and mouse are similarly sensitive to the acute effects of selenium hexafluoride. A modifying factor of 10 will also be applied to account for potential effects of the selenium moiety and the sparse database. Thus, the total adjustment is 30. 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). To obtain conservative and protective AEGL values in the absence of an empirically derived chemical-specific scaling exponent, temporal scaling was performed using n=3 when extrapolating to shorter time points (30-minutes and 1-hour) and n = 1 (8-hours) when extrapolating to longer time points using the $C^n \times t = k$ equation. The 30-minute AEGL-1 value was also adopted as the 10-minute AEGL-1 value due to the added uncertainty of extrapolating from a 4-hour time point to 10-minutes. Although AEGL-1 values might normally be held constant across all time points because minor irritation does not vary over time, time scaling was used for selenium hexafluoride AEGL-1 values to account for any potential enzymatic effects resulting from the selenium moiety. AEGL-1 values are presented in Table 4, and calculations are presented in Appendix A.

TABLE 4. AEGL-1 Values for Selenium Hexafluoride

10-minute	30-minute	1-hour	4-hour	8-hour
0.067 ppm (0.53 mg/m^3)	0.067 ppm (0.53 mg/m^3)	0.053 ppm (0.42 mg/m^3)	0.033 ppm (0.26 mg/m^3)	0.017 ppm (0.13 mg/m^3)

6. DATA ANALYSIS FOR AEGL-2

6.1. Summary of Human Data Relevant to AEGL-2

No human data relevant to development of AEGL-2 values were identified.

6.2. Summary of Animal Data Relevant to AEGL-2

No animal data relevant to development of AEGL-2 values were identified.

6.3. Derivation of AEGL-2

In the absence of empirical data, the AEGL-3 values will be divided by 3 to obtain AEGL-2 values for selenium hexafluoride. This approach is justified based on a steep concentration response curve (no effects in rabbit, guinea pig, rat, or mouse for 4-hour exposures at 1 ppm, difficulty breathing and pulmonary edema, but no mortality at 5 ppm, and 100% mortality at 10 ppm) (Kimmerle, 1960). AEGL-2 values are presented in Table 5, and calculations are presented in Appendix A.

TABLE 5. AEGL-2 Values for Selenium Hexafluoride

10-minute	30-minute	1-hour	4-hour	8-hour
0.11 ppm (0.87 mg/m^3)	0.11 ppm (0.87 mg/m^3)	0.087 ppm (0.69 mg/m^3)	0.057 pm (0.45 mg/m^3)	0.028 ppm (0.22 mg/m^3)

7. DATA ANALYSIS FOR AEGL-3

7.1. Summary of Human Data Relevant to AEGL-3

No human data relevant to development of AEGL-3 values were identified.

7.2. Summary of Animal Data Relevant to AEGL-3

One guinea pig, one rabbit, two male white rats, and four male white mice exposed to 5 ppm selenium hexafluoride for 4 hours exhibited difficulty breathing and pulmonary edema; however, no deaths were observed (Kimmerle, 1960). Mortality (100%) was noted at the next concentration tested (10 ppm for 4 hours).

7.3. Derivation of AEGL-3

The highest concentration causing no mortality in the guinea pig, rabbit, rats, and mice (5 ppm for 4-hours) (Kimmerle, 1960) will be used to derive AEGL-3 values. An intraspecies uncertainty factor of 3 will be applied because selenium hexafluoride is highly irritating and corrosive, and much of the toxicity is likely caused by a direct chemical effect on the tissues; this type of port-of-entry effect is not expected to vary greatly among individuals. An interspecies uncertainty factor of 1 will be applied because the limited data suggest that the guinea pig, rabbit, rat, and mouse are similarly sensitive to the acute effects of selenium hexafluoride. A modifying factor of 10 will also be applied to account for potential effects of the selenium moiety and the sparse database. Thus, the total adjustment is 30. 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). To obtain conservative and protective AEGL values in the absence of an empirically derived chemical-specific scaling exponent, temporal scaling was performed using n=3 when extrapolating to shorter time points (30-minutes and 1-hour) and n = 1 (8-hours) when extrapolating to longer time points using the $C^n \times t = k$ equation. The 30-minute AEGL-3 value was also adopted as the 10-minute AEGL-3 value due to the added uncertainty of extrapolating from a 4-hour time point to 10-minutes. AEGL-3 values are presented in Table 6, and calculations are presented in Appendix A.

TABLE 6. AEGL-3 Values for Selenium Hexafluoride

10-minute	30-minute	1-hour	4-hour	8-hour
0.33 ppm (2.6 mg/m^3)	0.33 ppm (2.6 mg/m^3)	0.26 ppm (2.1 mg/m^3)	0.17 ppm (1.3 mg/m^3)	0.083 ppm (0.66 mg/m^3)

8. SUMMARY OF AEGLS

8.1. AEGL Values and Toxicity Endpoints

AEGL values are summarized in Table 7. AEGL-1 values were based on a NOEL in a rabbit, guinea pig, rats, and mice exposed to 1 ppm selenium hexafluoride for 4-hours, AEGL-2 values were derived as one-third the AEGL-3 values, and AEGL-3 values were based on the highest concentration causing no death in a rabbit, guinea pig, rats, and mice (5 ppm for 4 hours).

TABLE 7. Summary of AEGL Values

Classification	Exposure Duration				
	10-minute	30-minute	1-hour	4-hour	8-hour
AEGL-1 (Nondisabling)	0.067 ppm (0.53 mg/m^3)	0.067 ppm (0.53 mg/m^3)	0.053 ppm (0.42 mg/m^3)	0.033 ppm (0.26 mg/m^3)	0.017 ppm (0.13 mg/m^3)
AEGL-2 (Disabling)	0.11 ppm (0.87 mg/m^3)	0.11 ppm (0.87 mg/m^3)	0.087 ppm (0.69 mg/m^3)	0.057 pm (0.45 mg/m^3)	0.028 ppm (0.22 mg/m^3)
AEGL-3 (Lethal)	0.33 ppm (2.6 mg/m^3)	0.33 ppm (2.6 mg/m^3)	0.26 ppm (2.1 mg/m^3)	0.17 ppm (1.3 mg/m^3)	0.083 ppm (0.66 mg/m^3)

8.2. Comparison with Other Standards and Guidelines

Extant standards and guidelines for selenium hexafluoride are listed in Table 8.

TABLE 8. Extant Standards and Guidelines for Selenium Hexafluoride

Guideline	**Exposure Duration**				
	10 minute	**30 minute**	**1 hour**	**4 hour**	**8 hour**
AEGL-1	0.067 ppm	0.067 ppm	0.053 ppm	0.033 ppm	0.017 ppm
AEGL-2	0.11 ppm	0.11 ppm	0.087 ppm	0.057 pm	0.028 ppm
AEGL-3	0.33 ppm	0.33 ppm	0.26 ppm	0.17 ppm	0.083 ppm
IDLH (NIOSH)[a]	2 ppm				
REL-TWA (NIOSH)[b]					0.05 ppm
PEL-TWA (OSHA)[c]					0.05 ppm
TLV-TWA (ACGIH)[d]					0.05 ppm
MAC Peak Limit (The Netherlands)[e]					0.025 ppm

[a]Immediately Dangerous to Life and Health (IDLH) is defined by the NIOSH/OSHA Standard Completions Program only for the purpose of respirator selection and represents a maximum concentration from which, in the event of respiratory failure, one could escape within 30 minutes without experiencing any escape-impairing or irreversible health effects (NIOSH, 1996). (Basis: Acute inhalation toxicity in animals, Kimmerle, 1960).

[b]NIOSH REL-TWA (National Institute of Occupational Safety and Health, Recommended Exposure Limits - Time Weighted Average) (NIOSH 2006) is defined analogous to the ACGIH-TLV-TWA.

[c]OSHA PEL-TWA (Occupational Health and Safety Administration, Permissible Exposure Limits - Time Weighted Average) (OSHA 2005) is defined analogous to the ACGIH-TLV-TWA, but is for exposures of no more than 10 hours/day, 40 hours/week.

[d]ACGIH TLV-TWA (American Conference of Governmental Industrial Hygienists, Threshold Limit Value - Time

Weighted Average) (ACGIH 2005) is the time-weighted average concentration for a normal 8-hour workday and a 40-hour workweek, to which nearly all workers may be repeatedly exposed, day after day, without adverse effect.

[e]MAC (Maximal Accepted Concentration – Peak Limit]) (Dutch Expert Committee for Occupational Standards, The Netherlands) (MSZW, 2000) is defined analogous to the ACGIH-TLV-STEL.

8.3. Data Adequacy and Research Needs

There are no human data, and animal data are limited. A single, study that addressed acute toxicity of selenium hexafluoride in a limited number of rabbits, guinea pigs, rats, and mice was available (Kimmerle, 1960). In the moist respiratory tract, selenium hexafluoride is believed to breakdown into hydrogen fluoride and selenium oxide. Additional acute inhalation toxicity studies would be helpful.

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APPENDIX A: Derivation of AEGL Values

Derivation of AEGL-1

Key Study: Kimmerle (1960)

Toxicity endpoint: NOEL for irritation in the guinea pig, rabbit, rats, and mice (1 ppm for 4-hours)

Uncertainty factors: Total of 3

Interspecies: 1, limited data suggest that the guinea pig, rabbit, rat, and mouse are similarly sensitive to the acute effects of selenium hexafluoride.

Intraspecies: 3, selenium hexafluoride is highly irritating and corrosive, and much of the toxicity is likely caused by a direct chemical effect on the tissues; this type of port-of-entry effect is not expected to vary greatly among individuals.

Modifying factor: 10: potential effects of the selenium moiety and sparse database

Total adjustment: 30

Time scaling: $C^3 \times t = k$ (30-min, 1-hr)

$1\ ppm^3 \times 4\text{-hr} = 4\ ppm\text{-hr}$

$C^1 \times t = k$ (8-hr)

$1\ ppm^1 \times 4\text{-hr} = 4\ ppm\text{-hr}$

10-minute AEGL-1: 30-min AEGL-1 value adopted as 10-min value = 0.067 ppm

30-minute AEGL-1: $C^3 \times 0.5\ hr = 4\ ppm\text{-hr}$

$C^3 = 8\ ppm$

$C = 2\ ppm / 30 = 0.067\ ppm$

1-hour AEGL-1: $C^3 \times 1\ hr = 4\ ppm\text{-hr}$

$C^3 = 4\ ppm$

$C = 1.6\ ppm / 30 = 0.053\ ppm$

4-hour AEGL-1: $1\ ppm / 30 = 0.033\ ppm$

8-hour AEGL-1: $C^1 \times 8\ hr = 4\ ppm\text{-hr}$

$C^1 = 0.5\ ppm$

$C = 0.5\ ppm / 30 = 0.017\ ppm$

Derivation of AEGL-2

In the absence of empirical data, and in accord with AEGL derivation guidelines for chemicals with steep dose-response curves (NAS 2001), the AEGL-2 values for selenium hexafluoride were set at one-third of the AEGL-3 values.

10-minute AEGL-2: 0.33 ppm / 3 = 0.11 ppm

30-minute AEGL-2: 0.33 ppm / 3 = 0.11 ppm

1-hour AEGL-2: 0.26 ppm / 3 = 0.087ppm

4-hour AEGL-2: 0.17 ppm /3 = 0.057 ppm

8-hour AEGL-2: 0.083 ppm / 3 = 0.028 ppm

Derivation of AEGL-3

Key Study: Kimmerle (1960)

Toxicity endpoint: Highest concentration causing no mortality in the guinea pig, rabbit, rats, and mice (5 ppm for 4-hours)

Uncertainty factors: Total of 3

Interspecies: 1, limited data suggest that the guinea pig, rabbit, rat, and mouse are similarly sensitive to the acute effects of selenium hexafluoride

Intraspecies: 3, selenium hexafluoride is highly irritating and corrosive, and much of the toxicity is likely caused by a direct chemical effect on the tissues; this type of port-of-entry effect is not expected to vary greatly among individuals.

Modifying factor: 10: potential effects of the selenium moiety and sparse database

Total adjustment: 30

Time scaling: $C^3 \times t = k$ (30-min, 1-hr)
$5\ ppm^3 \times 4\text{-hr} = 500\ ppm\text{-hr}$

$C^1 \times t = k$ (8-hr)
$5\ ppm^1 \times 4\text{-hr} = 20\ ppm\text{-hr}$

10-minute AEGL-3: 30-min AEGL-3 value adopted as 10-min value = 0.33 ppm

30-minute AEGL-3: $C^3 \times 0.5\ hr = 500\ ppm\text{-hr}$
$C^3 = 1000\ ppm$
$C = 10\ ppm / 30 = 0.33\ ppm$

1-hour AEGL-3: $C^3 \times 1\ hr = 500\ ppm\text{-hr}$
$C^3 = 500\ ppm$
$C = 7.9\ ppm / 30 = 0.26\ ppm$

4-hour AEGL-3: $5\ ppm / 30 = 0.17\ ppm$

8-hour AEGL-3: $C^1 \times 8\ hr = 20\ ppm\text{-hr}$
$C^1 = 2.5\ ppm$
$C = 2.5\ ppm / 30 = 0.083\ ppm$

APPENDIX B: Derivation Summary for Selenium Hexafluoride AEGLs

Acute Exposure Guideline Levels for Selenium Hexafluoride (CAS Reg. No. 7783-79-1)
Derivation Summary

AEGL-1 VALUES

10-minute	30-minute	1-hour	4-hour	8-hour
0.067 ppm	**0.067 ppm**	**0.053 ppm**	**0.033 ppm**	**0.017 ppm**

Key Reference: Kimmerle, G. 1960. [Comparative study of the inhalation toxicity of sulfur, selenium, and tellurium hexafluorides. Arch Toxikkol.] 18: 140-144 (in German)

Test Species/Strain/Number: Rabbit (1); Guinea pig (1); Rat (2); Mouse (4)/strain not reported

Exposure Route/Concentrations/Durations: Inhalation/1, 5, 10, 25, 50, 100 ppm/ 4-hours

Effects:
1 ppm : no effects
5 ppm difficulty breathing, reversible pulmonary edema (indicative of severe irritation)
10 ppm: 100% mortality

Endpoint/Concentration/Rationale: NOEL for irritation/ 1 ppm

Uncertainty Factors/Rationale:
Total uncertainty factor: 3

Interspecies: 1: Limited data suggest that the guinea pig, rabbit, rat, and mouse are similarly sensitive to the acute effects of selenium hexafluoride

Intraspecies: 3: selenium hexafluoride is highly irritating and corrosive, and much of the toxicity is likely caused by a direct chemical effect on the tissues; this type of port-of-entry effect is not expected to vary greatly among individuals.

Modifying Factor: 10 , to account for potential effects of the selenium moiety and the sparse data base

Animal to Human Dosimetric Adjustment:

Time Scaling: $c^n \times t = k$, where the exponent, n=3 when extrapolating to shorter time points (30-minutes and 1-hour) and n = 1 (8-hours) when extrapolating to longer time The 30-minute AEGL-1 value was also adopted as the 10-minute AEGL-1 value due to the added uncertainty of extrapolating from a 4-hour time point to 10-minutes. Although AEGL-1 values might normally be held constant across all time points because minor irritation does not vary over time, time scaling was used for selenium hexafluoride AEGL-1 values to account for any potential enzymatic effects resulting from the selenium moiety

Data Adequacy: Very sparse data base.

AEGL-2 VALUES

10-minute	30-minute	1-hour	4-hour	8-hour
0.11 ppm	**0.11 ppm**	**0.087 ppm**	**0.057 ppm**	**0.028 ppm**

Key Reference: Kimmerle, G. 1960. [Comparative study of the inhalation toxicity of sulfur, selenium, and tellurium hexafluorides. Arch Toxikkol.] 18: 140-144 (in German)

Test Species/Strain/Number:

Exposure Route/Concentrations/Durations:

Effects:

Endpoint/Concentration/Rationale: In the absence of empirical data, the AEGL-3 values were divided by 3 to obtain AEGL-2 values for selenium hexafluoride. This approach is justified based on a steep concentration response curve (no effects in rabbit, guinea pig, rat, or mouse for 4-hour exposures at 1 ppm, difficulty breathing and pulmonary edema, but no mortality at 5 ppm, and 100% mortality at 10 ppm) (Kimmerle, 1960).

Uncertainty Factors/Rationale:
Total uncertainty factor:
Interspecies:
Intraspecies:

Modifying Factor:

Animal to Human Dosimetric Adjustment:

Time Scaling:

Data Adequacy:

AEGL-3 VALUES

10-minute	30-minute	1-hour	4-hour	8-hour
0.33 ppm	**0.33 ppm**	**0.26 ppm**	**0.17 ppm**	**0.083 ppm**

Key Reference: Kimmerle, G. 1960. [Comparitive study of the inhalation toxicity of sulfur, selenium, and tellurium hexafluorides. Arch Toxikkol.] 18: 140-144 (in German)

Test Species/Strain/Number: Rabbit (1); Guinea pig (1); Rat (2); Mouse (4)/strain not reported

Exposure Route/Concentrations/Durations: Inhalation/1, 5, 10, 25, 50, 100 ppm/ 4-hours

Effects:
1 ppm : no effects
5 ppm difficulty breathing, reversible pulmonary edema (indicative of severe irritation)
10 ppm: 100% mortality

Endpoint/Concentration/Rationale: Highest concentration causing no mortality/ 5 ppm

Uncertainty Factors/Rationale:
Total uncertainty factor: 10

Interspecies: 1: Limited data suggest that the guinea pig, rabbit, rat, and mouse are similarly sensitive to the acute effects of selenium hexafluoride

Intraspecies: 3: selenium hexafluoride is highly irritating and corrosive, and much of the toxicity is likely caused by a direct chemical effect on the tissues; this type of port-of-entry effect is not expected to vary greatly among individuals.

Modifying Factor: 10, to account for potential effects of the selenium moiety and the sparse database

Animal to Human Dosimetric Adjustment:

Time Scaling: $c^n \times t = k$, where the exponent, n=3 when extrapolating to shorter time points (30-minutes and 1-hour) and n = 1 (8-hours) when extrapolating to longer time The 30-minute AEGL-3 value was also adopted as the 10-minute AEGL-3 value due to the added uncertainty of extrapolating from a 4-hour time point to 10-minutes.

Data Adequacy: Very sparse data base.

APPENDIX C: Category Plot for Selenium Hexafluoride