INTERIM

ACUTE EXPOSURE GUIDELINE LEVELS (AEGLs)

FOR

BROMINE PENTAFLUORIDE

(CAS Reg. No. 7789-30-2)

BrF_5

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

Bromine pentafluoride (BrF_5) is a strong oxidizing chemical that is used as a fluorinating agent and as an oxidizer in rocket propellant fuels. No data on human exposures were available. A single study provided information on lethal and non-lethal values for the rat. No information on time scaling could be ascertained from this study, although the data did indicate that the dose-response curve for lethality is steep.

In the absence of empirical data, no AEGL-1 values were developed.

In the absence of data relevant to derivation of AEGL-2 values for BrF_5, data for the structurally-related chemical, chlorine pentafluoride (ClF_5), were used. The data base for ClF_5 is more robust than the data base for BrF_5. Based on lethality data for the rat including the highest 60-minute non-lethal value for ClF_5 of 80 ppm and the highest 40-minute non-lethal value of 500 ppm for BrF_5, ClF_5 is considered more toxic than BrF_5. Setting the BrF_5 values equal to the more toxic ClF_5 values should be protective.

The AEGL-2 values for ClF_5 are based on a series of exposures with four species (MacEwen and Vernot 1972, 1973). Sensory irritation and reversible mild lung congestion were observed in monkeys, rats, and mice following exposures to 30 ppm for 10 minutes, 20 ppm for 30 minutes, or 10 ppm for 60 minutes and following exposure of dogs to 30 ppm for 10 minutes. For all exposures, effects were similar in the four species, although the 10-minute, 30 ppm exposure was slightly more irritating. Therefore, separate data points, i.e., the 10-, 30-, and 60-minute values were used for the relevant AEGL-2 exposure durations. For contact irritants without additional systemic effects, interspecies and intraspecies uncertainty factors of 3 each for a total of 10 are generally applied (NRC 2001). The interspecies uncertainty factor of 3 is supported by the similar toxic effects seen in four species of animals exposed to the same concentrations of ClF_5 in the key study. In addition, 60-minute LC_{50} values differed by a factor of 3 among the four species. For chemicals with similar actions such as hydrogen fluoride (HF) and chlorine trifluoride (ClF_3), interspecies and intraspecies uncertainty factors of 3 each for a total of 10 were considered protective of sensitive individuals. The same total uncertainty factor was applied to the ClF_5 values. In setting the BrF_5 values, a modifying factor was not applied to the ClF_5 data because uncertainties stemming from the limited database were addressed by setting the BrF_5 values equal to those for ClF_5 despite its lower toxicity compared with ClF_5. For ClF_5, a time scaling exponent of 1.9 ($C^{1.9} \times t = k$) was derived from rat lethality data. The exponent of 1.9 was used to derive the 4- and 8-hour exposure values from the 60-minute value.

The AEGL-3 values for BrF_5 are based on the highest non-lethal value in the rat study of Dost et al. (1970), 500 ppm for 40 minutes. This concentration was divided by inter- and intraspecies uncertainty factors of 3 each for a total of 10 and time scaled ($C^n \times t = k$) using the default values for n of 3 for shorter time intervals and 1 for longer time intervals (NRC 2001). For similar irritants, ClF_3 and HF, interspecies and intraspecies uncertainty factors of 3 each were applied for a total of 10. Based on similar irritant and corrosive properties for these halogen fluoride chemicals, these uncertainty factors are applicable to BrF_5.

The calculated values are listed in the table below.

S 1. Summary of AEGL Values for Bromine Pentafluoride						
Classification	**10-min**	**30-min**	**1-hr**	**4-hr**	**8-hr**	**Endpoint (Reference)**
AEGL-1[a] (Nondisabling)	NR	NR	NR	NR	NR	No data
AEGL-2[b] (Disabling)	3.0 ppm (21 mg/m^3)	2.0 ppm (14 mg/m^3)	1.0 ppm (7.2 mg/m^3)	0.48 ppm (3.4 mg/m^3)	0.33 ppm (2.4 mg/m^3)	Based on analogy with chlorine pentafluoride
AEGL-3 (Lethal)	79 ppm (565 mg/m^3)	55 ppm (393 mg/m^3)	33 ppm (236 mg/m^3)	8.3 ppm (59 mg/m^3)	4.2 ppm (30 mg/m^3)	Highest non-lethal concentration in the rat (Dost et al. 1970)

[a] The odor threshold is unknown; the odor has been described as sharp and penetrating.
[b] The 10- and 30-minute and 1-hour AEGL-2 values are based on separate data points.
NR: Not recommended; AEGL-1 values are not recommended due to a lack of data.

1. INTRODUCTION

Bromine pentafluoride (BrF_5) is a colorless or light yellow liquid below its boiling point of 40.8ºC. Above its boiling point, BrF_5 is a colorless, pungent, and corrosive gas. It is stable to heat, shock, and electric sparks (ACGIH 2003). Although nonflammable, fire may result from contact of BrF_5 with combustibles at room temperature. Reaction with water is violent, with potential release of bromine, fluorine, hydrogen bromide and hydrogen fluoride (Dost et al. 1968; NIOSH 1992; Teitelbaum 2001). Chemical and physical properties are listed in Table 1.

Bromine pentafluoride is manufactured by the fluorination of bromine at 200ºC in a metal apparatus (O'Neil et al. 2001). It can also be prepared by heating a mixture of bromine trifluoride and fluorine to 200ºC. It is shipped in compressed gas containers under its own vapor pressure (Braker and Mossman 1980; NIOSH 1992). Predominant uses include as a fluorinating agent to produce fluorocarbons and as an oxidizer in rocket propellant systems (ACGIH 2003). Metal chlorides, bromides, and iodides are converted to fluorides by treatment with BrF_5 (Braker and Mossman 1980). Uranium is converted to uranium hexafluoride by strong oxidizing agents including BrF_5 (Bailey and Woytek 1994).

TABLE 1. Chemical and Physical Properties		
Parameter	**Value**	**Reference**
Synonyms	Bromine fluoride	NIOSH 1992
Chemical formula	BrF_5	O'Neil et al. 2001
Molecular weight	174.89	O'Neil et al. 2001
CAS Reg. No.	7789-30-2	O'Neil et al. 2001
Physical state	Fuming liquid below 40.3ºC colorless gas above 40.3ºC	O'Neil et al. 2001; NIOSH 1992
Solubility in water	Explodes on contact with water	O'Neil et al. 2001
Vapor pressure	328 mm Hg @ 20ºC	NIOSH 1992
Vapor density (air =1)	6.05 @ Boiling point	NIOSH 1992
Liquid density (water =1)	2.48 @ 20ºC	NIOSH 1992
Melting point	-60.5ºC	O'Neil et al. 2001
Boiling point	40.8ºC	O'Neil et al. 2001
Flammability limits	Not flammable	NIOSH 1992
Conversion factors	1 ppm = 7.15 mg/m^3 1 mg/m^3 = 0.14 ppm	Calculated

2. HUMAN TOXICITY DATA

No information on lethality, sublethal effects, neurotoxicity, developmental/reproductive effects, genotoxicity, or carcinogenicity in humans was located. The odor threshold is unknown. According to Braker and Mossman (1980), BrF_5 provides adequate warning of its presence by its sharp, penetrating odor.

3. ANIMAL TOXICITY DATA

3.1. Acute Lethality

Dost et al. (1968) exposed groups of 10-14 male Sprague-Dawley rats to either 500 or 1000 ppm for various periods of time (Table 2). All rats (10/10) survived a 40-minute exposure to 500 ppm; whereas, 11/14 rats exposed to 500 ppm for 50 minutes died. All rats (10/10) survived a 20-minute exposure to 1000 ppm, whereas, 12/12 exposed for 25 minutes died. Rats were observed for several days following exposures. All rats survived additional exposures to 500 ppm for time periods shorter than 40 minutes, and all rats survived additional exposures to 1000 ppm for time periods shorter than 20 minutes (data not provided). Exposed rats exhibited corrosive damage to the lungs; corneal and conjunctival damage; yellow, sticky fur; and necrotic damage to unprotected areas of the skin (neither concentrations nor exposure durations with which to associate the reported signs were reported).

In citing their earlier, unpublished experiments on BrF_5, Dost et al. (1970), reported a 1-hour 95% lethal concentration of 500 ppm in rats. When groups of 4-6 male Sprague-Dawley rats inhaled 500 ppm BrF_5 for 30 minutes (half of the 95% lethal exposure time) and were sacrificed at intervals of 0, 2, 6, and 20 hours postexposure in order to study systemic fluorine distribution, no deaths were reported.

TABLE 2. Summary of Acute Lethal Inhalation Data in Rats		
Concentration (ppm)	**Exposure Time**	**Effect**
1000	20 minutes 25 minutes	No deaths (0/10) 100% mortality (12/12)
500	30 minutes 40 minutes 50 minutes 60 minutes	No deaths (0/4-6) No deaths (0/10) 79% mortality (11/14) 95% mortality

Source: Dost et al. 1968; 1970.

3.2. Nonlethal Toxicity

No additional data other than that cited in Section 3.1 were located.

3.3. Neurotoxicity

No information on neurotoxicity in animals was located.

3.4. Developmental/Reproductive Toxicity

No information on developmental/reproductive toxicity in animals was located.

3.5. Genotoxicity

No information on genotoxicity was located.

3.6. Chronic Toxicity/Carcinogenicity

No information on chronic toxicity/carcinogenicity was located.

3.7. Summary

Toxicity data are available for one species, the rat. Highest non-lethal concentrations were 500 ppm for 40 minutes and 1000 ppm for 20 minutes (Dost et al. 1968). No information on neurotoxicity, developmental/reproductive toxicity, genotoxicity, or chronic toxicity/ carcinogenicity was located in the available literature.

4. SPECIAL CONSIDERATIONS

4.1. Metabolism and Disposition

Reaction of BrF_5 with water potentially releases bromine, fluorine, hydrogen bromide, and hydrogen fluoride (Dost et al. 1968).

The structurally-related chemical, chlorine pentafluoride (ClF_5), reacts with the moist lining of the respiratory tract according to the following reaction (Darmer 1971):

$$ClF_5 + 2H_2O \rightarrow ClO_2F + 4HF$$

A similar reaction may occur for the brominated fluoride.

Dost et al. (1968) followed the distribution of fluoride in rat tissues following exposure to 500 ppm for 30 minutes. Initially, fluoride deposited at relatively high levels in most tissues (lung, kidney, liver, spleen) and then declined over the 20-hour postexposure period. Conversely, fluoride in bone increased from 300 to 353 µg F^-/gm over the 20-hour postexposure period.

4.2. Mechanism of Toxicity

Like other halogen fluorides, BrF_5 is an irritant at the site of contact, and systemic effects are unlikely to occur. The mechanism of toxicity is the same as that of the other halogen fluorides including ClF_3, ClF_5, and bromine trifluoride (BrF_3). BrF_5 exerts a direct corrosive action on the lungs as well as on any exposed surface. Exposure results in destruction of lung tissue and burns to the eyes and exposed skin (Dost et al. 1968).

4.3. Structure-Activity Relationships

According to Bailey and Woytek (1994), the chemical reactivity of the halogenated fluorine compounds in order of decreasing reactivity are ClF_5, ClF_3, BrF_5, iodine heptafluoride (IF_7), chlorine monofluoride (ClF), bromine trifluoride (BrF_3), and bromine monofluoride (BrF).

Dost et al. (1968) exposed male Sprague-Dawley rats to both ClF_3 and BrF_5. The signs of toxicity for the two chemicals were similar, with more severe damage to the respiratory tract resulting from the exposures to BrF_5. However, it is not clear that the authors were referring to the same concentrations for both chemicals, as the reported exposures for BrF_5 were to 500 and 1000 ppm and the reported exposures to ClF_3 were to 400 and 800 ppm.

It may be anticipated that some relationships exist in the halogen fluorides between structure and their respective toxicities in animals and humans. Symptoms during exposure to BrF_5 are similar to those of other respiratory irritants including ClF_5, ClF_3 and HF. MacEwen and Vernot (1971) and Darmer (1972) compared the toxicities of ClF_5, oxygen difluoride (OF_2), HF, and ClF_3. All of the data for these chemicals were generated at the Wright-Patterson AFB Aerospace Medical Research Laboratory (as was the data on BrF_5 by Dost et al. 1968). Table 3 lists 60-minute LC_{50} values for several species. The chemicals are listed in order of decreasing toxicity.

The available data indicate that chlorine pentafluoride is more toxic than BrF_5. Because BrF_5 was tested at only two exposure concentrations in one species (rat), there are few data with which to make relative toxicity comparisons. In rats exposed to ClF_5 for 30 minutes, the highest nonlethal concentration was 163 ppm (30% mortality occurred at 185 ppm; see Table 5, Chlorine Pentafluoride, this volume), while there were no deaths in rats exposed for 30 or 40 minutes to 500 ppm BrF_5, suggesting that ClF_5 is at least 3-fold more toxic. In rats exposed to ClF_5 for 60 minutes, a concentration of 136 ppm resulted in 80% mortality, while a similar response level (79% mortality) occurred after 50 minutes of exposure to 500 ppm BrF_5 (Table 2). Although the

exposure duration of 50 minutes for BrF_5 is slightly shorter, the concentration of 500 ppm is higher than the concentration of 136 ppm for ClF_5, suggesting lower relative toxicity for BrF_5.

Using the rat data for BrF_5 (Table 2), a 60-minute LC_{50} of 375 ppm can be roughly estimated by assuming that 500 ppm represents the LC_{50} for the time point mid-way between 40 minutes (at which 500 ppm caused no mortality) and 50 minutes (at which 500 ppm caused 80% mortality). Starting with the estimate of 500 ppm as the 45-minute LC_{50}, time scaling ($C^n \times t = k$, where n=1) can be used to estimate a 60-minute LC_{50} of 375 ppm. Using a value of 1.9 for n based on data from ClF_5, a 60-minute LC_{50} of 430 ppm is estimated.

While the estimated 60-minute LC_{50} values in rats are uncertain due to the extrapolations used to calculate the values, these estimates can support the comparative toxicity of $BrF_5$and ClF_5 because the comparison can be made within a single species. Comparing these values with the 60-minute rat LC_{50} of 122 ppm for ClF_5 indicates that ClF_5 may be 3- to 3.5-fold more toxic than BrF_5. Even if the rat LC_{50} for BrF_5 is compared with ClF_5 LC_{50} values for other species (using the monkey, dog, or mouse 60-minute LC_{50} values shown in Table 3 below, and neglecting potential species differences in susceptibility), ClF_5 is shown to be more toxic than BrF_5 by a factor ranging from 2- to 6.5-fold. Thus, the limited data indicate that BrF_5 is less toxic than ClF_5.

TABLE 3. Comparative 60-minute LC_{50} Values for Related Compounds (ppm)

Species	OF_2	ClF_5	ClF_3	HF
Monkey	16.0	173	230	1774
Dog	26.0	122	–	–
Rat	2.6	122	299	1276
Mouse	1.5	57	178	501

Source: Darmer et al. 1972.

4.4. Other Relevant Information

4.4.1. Species Variability

No information on species variability was located. The only experimental animal species was the rat. In lethality studies with the related oxidizing chemical, ClF_5, the rat was similar in sensitivity to the dog and more sensitive than the monkey (Table 3; Darmer et al. 1972). For HF, the rat was intermediate in sensitivity between the monkey and mouse. For ClF_5, 60-minute LC_{50} values differed by a factor of 3 among the four species listed in Table 3. For the endpoint of eye and nose irritation during exposures to ClF_3, the dog responded with more severe symptoms than the rat (Horn and Weir 1956).

4.4.2. Susceptible Populations

There are no human data specific to BrF_5 and sensitive individuals. As with other irritants, individuals with asthma may respond to exposure to irritants with increased bronchial responsiveness. The very old and those who are ill may also have increased susceptibility to the effects of irritants.

4.4.3. Concentration-Exposure Duration Relationship

The limited data on BrF_5 for the endpoint of lethality (Table 2) indicate that the dose-response curve is steep. Using the two nonlethal data points, 500 ppm for 40 minutes and 1000 ppm for 20 minutes, an n value in the relationship $C^n \times t = k$ of 1 might be approximated. For the related chemical ClF_5, time-scaling for lethality at different exposure times yielded an n value of 1.9. The AEGL time-scaling relationship for HF for the endpoint of lethality in the rat is $C^2 \times t = k$ (NRC 2004). However, based on the limited lethality data for BrF_5, the more conservative default time-scaling values for n of 3 and 1, respectively, for the shorter and longer exposure durations were used when time-scaling the AEGL-3 values.

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 located.

5.2. Summary of Animal Data Relevant to AEGL-1

No animal data relevant to development of AEGL-1 values were located.

5.3. Derivation of AEGL-1

In the absence of chemical-specific data, no AEGL-1 values were developed for BrF_5 (Table 4).

TABLE 4. AEGL-1 Values for Bromine Pentafluoride

10-min	30-min	1-hr	4-hr	8-hr
NR	NR	NR	NR	NR

NR = Not recommended.

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 located.

6.2. Summary of Animal Data Relevant to AEGL-2

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

6.3. Derivation of AEGL-2

In the absence of data relevant to derivation of AEGL-2 values for BrF_5, data for the structurally-related chemical, ClF_5, were used. The data base for ClF_5 is more robust than the data base for BrF_5. Based on lethality data for the rat including the highest 60-minute non-lethal value for ClF_5 of 80 ppm and the highest 40-minute non-lethal value of 500 ppm for BrF_5, ClF_5 is considered more toxic than BrF_5. Setting the BrF_5 values equal to the more toxic ClF_5 values should be protective.

The AEGL-2 values for ClF_5 (Table 5) are based on a series of exposures with four species (MacEwen and Vernot 1972, 1973). Sensory irritation and reversible mild lung congestion were observed in monkeys, rats, and mice following exposures to 30 ppm for 10 minutes, 20 ppm for 30 minutes, or 10 ppm for 60 minutes and following exposure of dogs to 30 ppm for 10 minutes. For all exposures, effects were similar in the four species, although the 10-minute, 30 ppm exposure was slightly more irritating. Therefore, separate data points, i.e., the 10-, 30-, and 60-minute values were used for the relevant AEGL-2 exposure durations. For contact irritants without additional systemic effects, interspecies and intraspecies uncertainty factors of 3 each for a total of 10 are generally applied (NRC 2001). The interspecies uncertainty factor of 3 is supported by the similar toxic effects seen in four species of animals exposed to the same concentrations of ClF_5 in the key study. In addition, 60-minute LC_{50} values differed by a factor of 3 among the four species. For chemicals with similar actions such as HF and ClF_3, an intraspecies uncertainty factor of 3 was considered protective of sensitive individuals. The total uncertainty factor of 10 was applied to the ClF_5 values. A modifying factor was not applied to the ClF_5 data because uncertainties stemming from the limited database were addressed by setting the BrF_5 values equal to those for ClF_5 despite its lower toxicity compared with ClF_5. For ClF_5, a time scaling exponent of 1.9 ($C^{1.9} \times t = k$) was derived from rat lethality data. The exponent of 1.9 was used to derive the 4- and 8-hour exposure values from the 60-minute value. The AEGL-2 values for BrF_5, set equal to the AEGL-2 values for ClF_5, are listed in Table 6.

TABLE 5. Summary of AEGL Values for Chlorine Pentafluoride

Classification	10-min	30-min	1-hr	4-hr	8-hr	Endpoint (Reference)
AEGL-1[a] (Nondisabling)	NR	NR	NR	NR	NR	Insufficient data
AEGL-2 (Disabling)	3.0 ppm (16 mg/m^3)	2.0 ppm 11(mg/m^3)	1.0 ppm (5.3 mg/m^3)	0.48 ppm (2.6 mg/m^3)	0.33 ppm (1.8 mg/m^3)	Sensory irritation, mild lung congestion - monkey, dog, rat, and mouse (MacEwen and Vernot 1972; 1973)
AEGL-3 (Lethal)	21 ppm (112 mg/m^3)	12 ppm (64 mg/m^3)	8.0 ppm (43 mg/m^3)	3.9 ppm (21 mg/m^3)	2.7 ppm (1.8 mg/m^3)	Highest non-lethal concentration in rats (Darmer et al. 1972)

NR = Not recommended.
The 10- and 30-minute and 1-hour AEGL-2 values are based on separate data points.

TABLE 6. AEGL-2 Values for Bromine Pentafluoride

10-min	30-min	1-hr	4-hr	8-hr
3.0 ppm (21 mg/m^3)	2.0 ppm (14 mg/m^3)	1.0 ppm (7.2 mg/m^3)	0.48 ppm (3.4 mg/m^3)	0.33 ppm (2.4 mg/m^3)

The 10- and 30-minute and 1-hour AEGL-2 values are based on separate data points

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 located.

7.2. Summary of Animal Data Relevant to AEGL-3

A single study provided lethal and non-lethal concentration-exposure durations for the rat. Dost et al. (1968) reported no deaths in rats following exposures to 500 ppm for 40 minutes and 1000 ppm for 20 minutes (Table 2). Sacrifice times, up to 20 hours postexposure, were short compared with the usual two-week postexposure-observation period, but for most strong oxidizing chemicals, death occurs during or shortly after exposure as concentrations approach lethality (MacEwen and Vernot 1970; Darmer et al. 1972; Dost et al. 1974).

7.3. Derivation of AEGL-3

Data were unavailable for calculation of a benchmark concentration or an LC_{01}. Therefore, the highest exposures that resulted in no mortality in rats were considered. These values were 500 ppm for 40 minutes and 1000 ppm for 20 minutes (Dost et al. 1968). The longer exposure duration was considered more reliable. For similar irritants, ClF_3 and HF, interspecies and intraspecies uncertainty factors of 3 each were applied for a total of 10. Based on similar irritant properties for these halogen fluoride chemicals, these uncertainty factors are applicable for BrF_5. The resulting 40-minute value is 50 ppm. For time scaling ($C^n \times t = k$), the default values of n = 3 and n = 1 for the shorter and longer exposure durations, respectively, were utilized. The time-scaled AEGL-3 concentrations for BrF_5 are summarized in Table 7. Calculations are in Appendix A.

TABLE 7. AEGL-3 Values for Bromine Pentafluoride

10-min	30-min	1-hr	4-hr	8-hr
79 ppm (565 mg/m^3)	55 ppm (393 mg/m^3)	33 ppm (236 mg/m^3)	8.3 ppm (59 mg/m^3)	4.2 ppm (30 mg/m^3)

Because of the sparse data base for BrF_5, application of a modifying factor of 2 was considered when deriving AEGL-3 values. A modifying factor was not applied because the derived AEGL-3 values reflect the toxicity of BrF_5 relative to that of ClF_5 and ClF_3. The AEGL-3 values for the slightly more toxic ClF_3 for the 10-minute through 8-hour exposure durations are 84, 36, 21, 7.3, and 7.3 ppm, respectively (NRC 2007).

8. SUMMARY OF AEGLS

8.1. AEGL Values and Toxicity Endpoints

The AEGL values for BrF_5 are summarized in Table 8. Appendix B is a summary of the derivations.

TABLE 8. Summary of AEGL Values

Classification	Exposure Duration				
	10-min	30-min	1-hr	4-hr	8-hr
AEGL-1 (Nondisabling)	NR	NR	NR	NR	NR
AEGL-2 (Disabling)	3.0 ppm	2.0 ppm	1.0 ppm	0.48 ppm	0.33 ppm
AEGL-3 (Lethal)	79 ppm	55 ppm	33 ppm	8.3 ppm	4.2 ppm

NR = Not recommended.
The 10- and 30-minute and 1-hour AEGL-2 values are based on separate data points.

8.2. Comparison with Other Standards and Guidelines

Bromine pentafluoride has limited uses, and only a few standards and guidelines have been developed. The American Conference of Governmental Industrial Hygienists (ACGIH 2003) has assigned a TLV of 0.1 ppm as an 8-hour TWA exposure that should not be exceeded at any time during a workday. The TLV-TWA was based on the toxicologic analogy with ClF_3 which at the time of the recommendation (1969) had a TLV-Ceiling of 0.1 ppm. The NIOSH REL-TWA for BrF_5 is 0.1 ppm (NIOSH 1977). NIOSH has not established an IDLH. There is no OSHA PEL for BrF_5.

8.3. Data Adequacy and Research Needs

No human data were available. A single study that provided lethal and non-lethal values for the rat was available to derive AEGL-3 values. In the absence of empirical data for the AEGL-1, AEGL-1 values were not recommended. AEGL-2 values were based on the relative reactivity and toxicity of BrF_5 to the similar oxidizing chemical ClF_5.

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APPENDIX A: DERIVATION OF AEGL VALUES

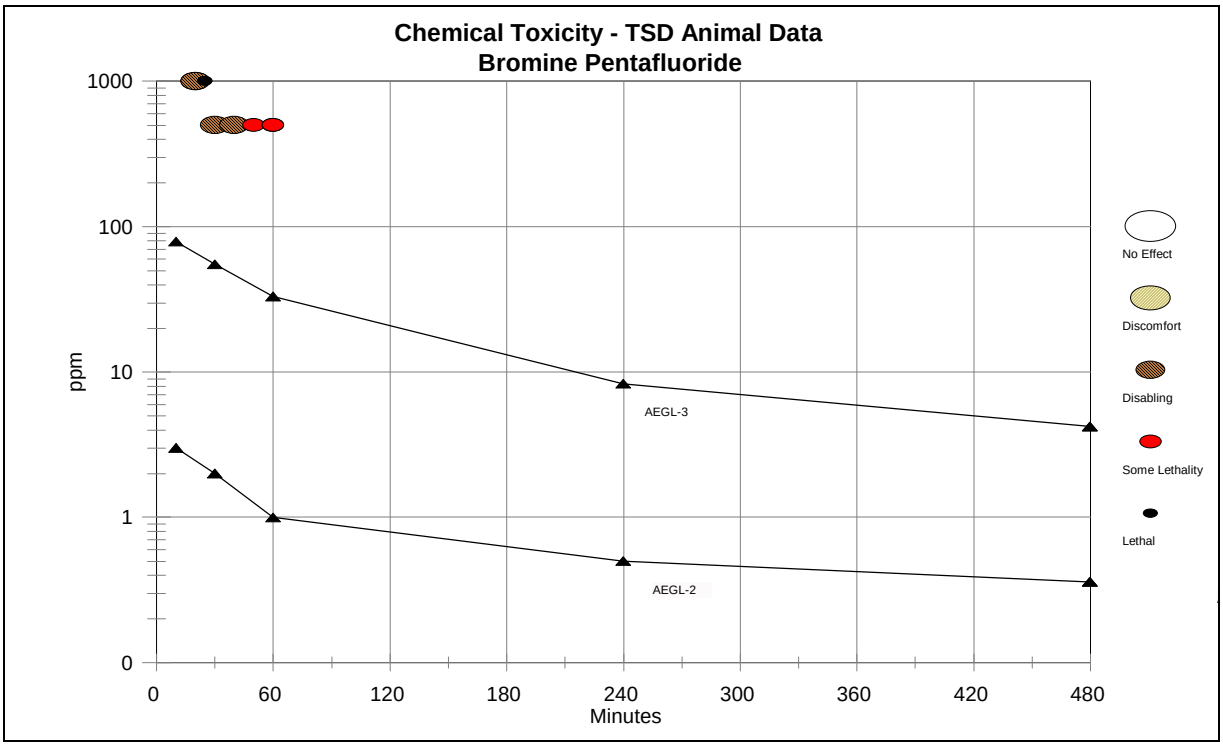
Derivation of AEGL-1:
Not recommended due to lack of empirical data.

Derivation of AEGL-2:
Based on analogy with ClF_5 (see Chlorine Pentafluoride, this volume).

Derivation of AEGL-3:

Key Study:	Dost et al. 1970
Toxicity endpoint:	40-minute highest non-lethal concentration, 500 ppm in the rat.
Uncertainty factors:	Interspecies and intraspecies of 3 each for a total of 10; these factors should be protective of sensitive subjects exposed to irritants (NRC 2001).
Time scaling:	Default values of n = 3 and 1 ($C^n \times t = k$) for shorter and longer exposure durations, respectively (NRC 2001).
Modifying factor:	None applied
Calculations:	$C^3 \times t = k$ $(500 \text{ ppm}/10)^3 \times 40 \text{ minutes} = 5.0 \times 10^6 \text{ ppm}^3\cdot\text{minutes}$ $C^1 \times t = k$ $(500 \text{ ppm}/10) \times 40 \text{ minutes} = 2.0 \times 10^3 \text{ ppm}^3\cdot\text{minutes}$
10-minute AEGL-3:	$C = ([5.0 \times 10^6 \text{ ppm}^3\cdot\text{minutes}/10 \text{ minutes}])^{1/3}$ C = 79 ppm
30-minute AEGL-3:	$C = ([5.0 \times 10^6 \text{ ppm}^3\cdot\text{minutes}/30 \text{ minutes}])^{1/3}$ C = 55 ppm
1-hour AEGL-3:	$C = 2.0 \times 10^3 \text{ ppm}^3\cdot\text{minutes}/60 \text{ minutes})$ C = 33 ppm
4-hour AEGL-3:	$C = 2.0 \times 10^3 \text{ ppm}^3\cdot\text{minutes}/240 \text{ minutes}$ C = 8.3 ppm
8-hour AEGL-3:	$C = 2.0 \times 10^3 \text{ ppm}^3\cdot\text{minutes}$ C = 4.2 ppm

APPENDIX B: CATEGORY GRAPH OF TOXICITY DATA AND AEGL VALUES



Data:

For Category 0 = No effect, 1 = Discomfort, 2 = Disabling, SL = Some Lethality, 3 = Lethal				
Source	**Species**	**ppm**	**Minutes**	**Category**
NAC/AEGL-1		NR	10	AEGL
NAC/AEGL-1		NR	30	AEGL
NAC/AEGL-1		NR	60	AEGL
NAC/AEGL-1		NR	240	AEGL
NAC/AEGL-1		NR	480	AEGL
NAC/AEGL-2		3	10	AEGL
NAC/AEGL-2		2	30	AEGL
NAC/AEGL-2		1	60	AEGL
NAC/AEGL-2		0.48	240	AEGL
NAC/AEGL-2		0.33	480	AEGL
NAC/AEGL-3		79	10	AEGL
NAC/AEGL-3		55	30	AEGL
NAC/AEGL-3		33	60	AEGL
NAC/AEGL-3		8.3	240	AEGL
NAC/AEGL-3		4.2	480	AEGL
Dost et al. 1970	rat	500	30	2, no mortality
		500	40	2, no mortality
		500	50	SL, 79% mortality
		500	60	SL, 95% mortality
		1000	20	2, no mortality
		1000	25	3, 100% mortality

NR = Not recommended.

APPENDIX C: DERIVATION SUMMARY

ACUTE EXPOSURE GUIDELINE LEVELS FOR BROMINE PENTAFLUORIDE (CAS Reg. No. 7789-30-2)

AEGL-1 VALUES				
10 min	**30 min**	**1 hr**	**4 hr**	**8 hr**
NR	**NR**	**NR**	**NR**	**NR**
Key Reference:				
Test Species/Strain/Number:				
Exposure Route/Concentration/Duration:				
Effects:				
Endpoint/Concentration/Rationale: Due to insufficient data, values are not recommended.				
Uncertainty Factors/Rationale:				
Modifying Factor:				
Animal to Human Dosimetric Adjustment:				
Time Scaling:				
Data Adequacy: No data meets the definition of an AEGL-1				

NR = Not recommended.

1

AEGL-2 VALUES				
10 min	**30 min**	**1 hr**	**4 hr**	**8 hr**
3.0 ppm	**2.0 ppm**	**1.0 ppm**	**0.48 ppm**	**0.33 ppm**

Key References: **The following references and derivations are for chlorine pentafluoride (ClF_5)**:

MacEwen, J.D. and E.H. Vernot. 1972. Toxic Hazards Research Unit Annual Technical Report: 1972. AD-755 358; AMRL-TR-72-62; available from National Technical Information Service, Springfield, VA.

MacEwen, J.D. and E.H. Vernot. 1973. Toxic Hazards Research Unit Annual Technical Report: 1973. AD-771 025; AMRL-TR-73-83; available from National Technical Information Service, Springfield, VA.

Test Species/Strain/Sex/Number: Monkey/rhesus/male and female/6; dog/beagle/not specified/8; rat/Sprague-Dawley/male/30; mouse/ICR/male/30

Exposure Route/Concentration/Duration: Inhalation: 30 ppm for 10 minutes, 20 ppm for 30 minutes; 10 ppm for 60 minutes (monkey and rat, and mouse); 30 ppm for 10 minutes (dog)

Effects: Monkeys: lacrimation and nausea; transient weight gain depression; congested lungs following 60-minute exposure; dog, and rat: lacrimation and salivation; no gross lesions; mouse: mild lung congestion.

Endpoint/Concentration/Rationale: 30 ppm for 10 minutes, 20 ppm for 30 minutes, and 10 ppm for 60 minutes resulted in strong signs of irritation (in several species) which is consistent with the definition of the AEGL-2.

Based on similar to less toxicity, the endpoint for ClF_5 was used for BrF_5.

Uncertainty Factors/Rationale:

Total uncertainty factor: 10

Interspecies: 3 - Considered sufficient for similar irritants such as ClF_3 and HF (breakdown product). In addition, LC_{50} values differed by a factor of 3 among four species.

Intraspecies: 3 - Considered sufficient for similar irritants such as ClF_3 and HF. For ClF_5, there was little species variation seen among four animal species. The concentration that induces irritation among the general population should not vary greatly among individuals.

Modifying Factor: Not applicable

Animal to Human Dosimetric Adjustment: Insufficient data.

Time Scaling: $C^n \times t = k$ where n = 1.9; based on the time-concentration relationship for ClF_5 LC_{50} values in rats for exposure durations of 15, 30, and 60 minutes; data from Darmer et al. (1972).

Data Adequacy: Two species were tested. Two additional species (dog and mouse) tested at similar concentrations showed similar effects. Values are in general agreement with those of similar irritants.

1

AEGL-3 VALUES				
10 min	**30 min**	**1 hr**	**4 hr**	**8 hr**
79 ppm	**55 ppm**	**33 ppm**	**8.3 ppm**	**4.2 ppm**

Key Reference:
Dost, F.N., D.J. Reed, A. Finch, and C.H. Wang. 1968. Metabolism and Pharmacology of Inorganic and Fluorine Containing Compounds. AMRL-TR-67-224, AD 681 161, Available from National Technical Information Center, Springfield, VA.

Test Species/Strain/Sex/Number: Rat/Sprague-Dawley/male/10-12 per group

Exposure Route/Concentration/Duration: Inhalation: 500 ppm for 30, 40, 50, or 60 minutes or 1000 ppm for 20 or 25 minutes.

Effects:

Concentration	Time	Effect
500 ppm	30 minutes	no deaths
500 ppm	40 minutes	no deaths
500 ppm	50 minutes	79% mortality
500 ppm	60 minutes	95% mortality
1000 ppm	20 minutes	no deaths
1000 ppm	25 minutes	100% mortality

Endpoint/Concentration/Rationale: The highest non-lethal concentration of 500 ppm for 40 minutes was chosen as the point of departure.

Uncertainty Factors/Rationale:
Total uncertainty factor: 10
Interspecies: 3 - Considered sufficient for similar irritants such as ClF_3 and HF (breakdown product).
Intraspecies: 3 - Considered sufficient for related chemicals, ClF_3 and HF. The concentration at which extreme irritation and pulmonary damage may lead to lethality should not differ by more than a factor of 3 among the general population.

Modifying Factor: Not applicable

Animal to Human Dosimetric Adjustment: Insufficient data.

Time Scaling: $C^n \times t = k$ where n = 3 and 1 for shorter and longer exposure durations, respectively (NRC 2001).

Data Adequacy: The data set is sparse, but data on related chemicals allowed structure-activity relationships to be made. Values are in general agreement with those of similar irritants.

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