Acute Exposure Guideline Levels for Selected Airborne Chemicals: Volume 18

ISBN
978-0-309-31189-2

178 pages
6 x 9
PAPERBACK (2014)

Committee on Acute Exposure Guideline Levels; Committee on Toxicology; Board on Environmental Studies and Toxicology; Division on Earth and Life Studies; National Research Council

Acute Exposure Guideline Levels for Selected Airborne Chemicals

VOLUME 18

Committee on Acute Exposure Guideline Levels

Committee on Toxicology

Board on Environmental Studies and Toxicology

Division on Earth and Life Studies

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THE NATIONAL ACADEMIES PRESS
Washington, D.C.
www.nap.edu

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This project was supported by Contract No. W81K04-11-D-0017 and EP-W-09-007 between the National Academy of Sciences and the U.S. Department of Defense and the U.S. Environmental Protection Agency. Any opinions, findings, conclusions, or recommendations expressed in this publication are those of the author(s) and do not necessarily reflect the view of the organizations or agencies that provided support for this project.

International Standard Book Number-13: 978-0-309-31189-2
International Standard Book Number-10: 0-309-31189-6

Additional copies of this report are available for sale from the National Academies Press, 500 Fifth Street, NW, Keck 360, Washington, DC 20001; (800) 624-6242 or (202) 334-3313; http://www.nap.edu/.

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Preface

Extremely hazardous substances (EHSs)[2] can be released accidentally as a result of chemical spills, industrial explosions, fires, or accidents involving railroad cars and trucks transporting EHSs. Workers and residents in communities surrounding industrial facilities where EHSs are manufactured, used, or stored and in communities along the nation's railways and highways are potentially at risk of being exposed to airborne EHSs during accidental releases or intentional releases by terrorists. Pursuant to the Superfund Amendments and Reauthorization Act of 1986, the U.S. Environmental Protection Agency (EPA) has identified approximately 400 EHSs on the basis of acute lethality data in rodents.

As part of its efforts to develop acute exposure guideline levels for EHSs, EPA and the Agency for Toxic Substances and Disease Registry (ATSDR) in 1991 requested that the National Research Council (NRC) develop guidelines for establishing such levels. In response to that request, the NRC published *Guidelines for Developing Community Emergency Exposure Levels for Hazardous Substances* in 1993. Subsequently, *Standard Operating Procedures for Developing Acute Exposure Guideline Levels for Hazardous Substances* was published in 2001, providing updated procedures, methodologies, and other guidelines used by the National Advisory Committee (NAC) on Acute Exposure Guideline Levels for Hazardous Substances and the Committee on Acute Exposure Guideline Levels (AEGLs) in developing the AEGL values.

Using the 1993 and 2001 NRC guidelines reports, the NAC—consisting of members from EPA, the Department of Defense (DOD), the Department of Energy (DOE), the Department of Transportation (DOT), other federal and state governments, the chemical industry, academia, and other organizations from the private sector—has developed AEGLs for more than 270 EHSs.

In 1998, EPA and DOD requested that the NRC independently review the AEGLs developed by NAC. In response to that request, the NRC organized within its Committee on Toxicology (COT) the Committee on Acute Exposure Guideline Levels, which prepared this report. This report is the eighteenth vol-

[2]As defined pursuant to the Superfund Amendments and Reauthorization Act of 1986.

ume in that series. AEGL documents for bromine chloride, carbonyl fluoride, selected halogen fluorides, and oxygen difluoride are each published as an appendix in this report. The committee concludes that the AEGLs developed in these appendixes are scientifically valid conclusions based on the data reviewed by NAC and are consistent with the NRC guideline reports. AEGL reports for additional chemicals will be presented in subsequent volumes.

The committee's review of the AEGL documents involved both oral and written presentations to the committee by the authors of the documents. The committee examined the draft documents and provided comments and recommendations for how they could be improved in a series of interim reports. The authors revised the draft AEGL documents based on the advice in the interim reports and presented them for reexamination by the committee as many times as necessary until the committee was satisfied that the AEGLs were scientifically justified and consistent with the 1993 and 2001 NRC guideline reports. After these determinations have been made for an AEGL document, it is published as an appendix in a volume such as this one.

The interim reports of the committee that led to this report were reviewed in draft form by individuals selected for their diverse perspectives and technical expertise, in accordance with procedures approved by the NRC's Report Review Committee. The purpose of this independent review is to provide candid and critical comments that will assist the institution in making its published report as sound as possible and to ensure that the report meets institutional standards for objectivity, evidence, and responsiveness to the study charge. The review comments and draft manuscript remain confidential to protect the integrity of the deliberative process. We wish to thank the following individuals for their review of the committee interim reports, which summarize the committee's conclusions and recommendations for improving NAC's AEGL documents for bromine chloride (interim report 22), carbonyl fluoride (interim report 22), selected halogen fluorides (interim reports 16, 18, and 22), and oxygen difluoride (interim report 22): Sam Kacew (University of Ottawa), A. Wallace Hayes (Harvard School of Public Health), Rogene Henderson (Lovelace Respiratory Research Institute [retired]), Charles Reinhardt (DuPont Haskell Laboratory [retired]), Andrew Salmon (California Environmental Protection Agency), Joyce Tsuji (Exponent, Inc.), and Judith Zelikoff (New York University).

Although the reviewers listed above have provided many constructive comments and suggestions, they were not asked to endorse the conclusions or recommendations, nor did they see the final draft of this volume before its release. The review of interim reports was overseen by Robert Goyer (University of Western Ontario [retired]). Appointed by the NRC, he was responsible for making certain that an independent examination of the interim reports was carried out in accordance with institutional procedures and that all review comments were carefully considered. Responsibility for the final content of this report rests entirely with the authoring committee and the institution.

The committee gratefully acknowledges the valuable assistance provided by Ernest Falke and Iris A. Camacho from EPA. The committee also acknowl-

edges Susan Martel, the project director for her work this project. Other staff members who contributed to this effort are James J. Reisa (director of the Board on Environmental Studies and Toxicology), Radiah Rose (manager of editorial projects), Mirsada Karalic-Loncarevic (manager of the Technical Information Center), and Tamara Dawson (program associate). Finally, I would like to thank all members of the committee for their expertise and dedicated effort throughout the development of this report.

Edward C. Bishop, *Chair*
Committee on Acute Exposure
Guideline Levels

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Acute Exposure Guideline Levels for Selected Airborne Chemicals

VOLUME 18

National Research Council Committee Review of Acute Exposure Guideline Levels for Selected Airborne Chemicals

This report is the eighteenth volume in the series *Acute Exposure Guideline Levels for Selected Airborne Chemicals*.

In the Bhopal disaster of 1984, approximately 2,000 residents living near a chemical plant were killed and 20,000 more suffered irreversible damage to their eyes and lungs following accidental release of methyl isocyanate. The toll was particularly high because the community had little idea what chemicals were being used at the plant, how dangerous they might be, or what steps to take in an emergency. This tragedy served to focus international attention on the need for governments to identify hazardous substances and to assist local communities in planning how to deal with emergency exposures.

In the United States, the Superfund Amendments and Reauthorization Act (SARA) of 1986 required that the U.S. Environmental Protection Agency (EPA) identify extremely hazardous substances (EHSs) and, in cooperation with the Federal Emergency Management Agency and the U.S. Department of Transportation, assist local emergency planning committees (LEPCs) by providing guidance for conducting health hazard assessments for the development of emergency response plans for sites where EHSs are produced, stored, transported, or used. SARA also required that the Agency for Toxic Substances and Disease Registry (ATSDR) determine whether chemical substances identified at hazardous waste sites or in the environment present a public health concern.

As a first step in assisting the LEPCs, EPA identified approximately 400 EHSs largely on the basis of their immediately dangerous to life and health values, developed by the National Institute for Occupational Safety and Health. Although several public and private groups, such as the Occupational Safety and Health Administration and the American Conference of Governmental Industrial Hygienists, have established exposure limits for some substances and some exposures (e.g., workplace or ambient air quality), these limits are not easily or directly translated into emergency exposure limits for exposures at high levels

but of short duration, usually less than 1 hour (h), and only once in a lifetime for the general population, which includes infants (from birth to 3 years of age), children, the elderly, and persons with diseases, such as asthma or heart disease.

The National Research Council (NRC) Committee on Toxicology (COT) has published many reports on emergency exposure guidance levels and spacecraft maximum allowable concentrations for chemicals used by the U.S. Department of Defense (DOD) and the National Aeronautics and Space Administration (NASA) (NRC 1968, 1972, 1984a,b,c,d, 1985a,b, 1986a, 1987, 1988, 1994, 1996a,b, 2000a, 2002a, 2007a, 2008a). COT has also published guidelines for developing emergency exposure guidance levels for military personnel and for astronauts (NRC 1986b, 1992, 2000b). Because of COT's experience in recommending emergency exposure levels for short-term exposures, in 1991 EPA and ATSDR requested that COT develop criteria and methods for developing emergency exposure levels for EHSs for the general population. In response to that request, the NRC assigned this project to the COT Subcommittee on Guidelines for Developing Community Emergency Exposure Levels for Hazardous Substances. The report of that subcommittee, *Guidelines for Developing Community Emergency Exposure Levels for Hazardous Substances* (NRC 1993), provides step-by-step guidance for setting emergency exposure levels for EHSs. Guidance is given on what data are needed, what data are available, how to evaluate the data, and how to present the results.

In November 1995, the National Advisory Committee (NAC)[1] for Acute Exposure Guideline Levels for Hazardous Substances was established to identify, review, and interpret relevant toxicologic and other scientific data and to develop acute exposure guideline levels (AEGLs) for high-priority, acutely toxic chemicals. The NRC's previous name for acute exposure levels—community emergency exposure levels (CEELs)—was replaced by the term AEGLs to reflect the broad application of these values to planning, response, and prevention in the community, the workplace, transportation, the military, and the remediation of Superfund sites.

AEGLs represent threshold exposure limits (exposure levels below which adverse health effects are not likely to occur) for the general public and are applicable to emergency exposures ranging from 10 minutes (min) to 8 h. Three levels—AEGL-1, AEGL-2, and AEGL-3—are developed for each of five exposure periods (10 min, 30 min, 1 h, 4 h, and 8 h) and are distinguished by varying degrees of severity of toxic effects. The three AEGLs are defined as follows:

[1]NAC completed its chemical reviews in October 2011. The committee was composed of members from EPA, DOD, many other federal and state agencies, industry, academia, and other organizations. From 1996 to 2011, the NAC discussed over 300 chemicals and developed AEGLs values for at least 272 of the 329 chemicals on the AEGLs priority chemicals lists. Although the work of the NAC has ended, the NAC-reviewed technical support documents are being submitted to the NRC for independent review and finalization.

AEGL-1 is the airborne concentration (expressed as ppm [parts per million] or mg/m^3 [milligrams per cubic meter]) of a substance above which it is predicted that the general population, including susceptible individuals, could experience notable discomfort, irritation, or certain asymptomatic nonsensory 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 adverse health effects or death.

Airborne concentrations below AEGL-1 represent exposure levels that can produce mild and progressively increasing but transient and nondisabling odor, taste, and sensory irritation or certain asymptomatic nonsensory adverse 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 idiosyncratic responses, could experience the effects described at concentrations below the corresponding AEGL.

SUMMARY OF REPORT ON GUIDELINES FOR DEVELOPING AEGLS

As described in *Guidelines for Developing Community Emergency Exposure Levels for Hazardous Substances* (NRC 1993) and the NRC guidelines report *Standing Operating Procedures for Developing Acute Exposure Guideline Levels for Hazardous Chemicals* (NRC 2001a), the first step in establishing AEGLs for a chemical is to collect and review all relevant published and unpublished information. Various types of evidence are assessed in establishing AEGL values for a chemical. These include information from (1) chemical-physical characterizations, (2) structure-activity relationships, (3) in vitro toxicity studies, (4) animal toxicity studies, (5) controlled human studies, (6) observations of humans involved in chemical accidents, and (7) epidemiologic studies. Toxicity data from human studies are most applicable and are used when available in preference to data from animal studies and in vitro studies. Toxicity data from inhalation exposures are most useful for setting AEGLs for airborne chemicals because inhalation is the most likely route of exposure and because extrapolation of data from other routes would lead to additional uncertainty in the AEGL estimate.

For most chemicals, actual human toxicity data are not available or critical information on exposure is lacking, so toxicity data from studies conducted in laboratory animals are extrapolated to estimate the potential toxicity in humans. Such extrapolation requires experienced scientific judgment. The toxicity data for animal species most representative of humans in terms of pharmacodynamic and pharmacokinetic properties are used for determining AEGLs. If data are not available on the species that best represents humans, data from the most sensitive animal species are used. Uncertainty factors are commonly used when animal data are used to estimate risk levels for humans. The magnitude of uncertainty factors depends on the quality of the animal data used to determine the no-observed-adverse-effect level (NOAEL) and the mode of action of the substance in question. When available, pharmacokinetic data on tissue doses are considered for interspecies extrapolation.

For substances that affect several organ systems or have multiple effects, all end points (including reproductive [in both genders], developmental, neurotoxic, respiratory, and other organ-related effects) are evaluated, the most important or most sensitive effect receiving the greatest attention. For carcinogenic chemicals, excess carcinogenic risk is estimated, and the AEGLs corresponding to carcinogenic risks of 1 in 10,000 (1×10^{-4}), 1 in 100,000 (1×10^{-5}), and 1 in 1,000,000 (1×10^{-6}) exposed persons are estimated.

REVIEW OF AEGL REPORTS

As NAC began developing chemical-specific AEGL reports, EPA and DOD asked the NRC to review independently the NAC reports for their scientific validity, completeness, and consistency with the NRC guideline reports (NRC 1993, 2001a). The NRC assigned this project to the COT Committee on Acute Exposure Guideline Levels. The committee has expertise in toxicology, epidemiology, occupational health, pharmacology, medicine, pharmacokinetics, industrial hygiene, and risk assessment.

The AEGL draft reports were initially prepared by ad hoc AEGL development teams consisting of a chemical manager, chemical reviewers, and a staff scientist of the NAC contractors—Oak Ridge National Laboratory and subsequently SRC, Inc. The draft documents were then reviewed by NAC and elevated from "draft" to "proposed" status. After the AEGL documents were approved by NAC, they were published in the *Federal Register* for public comment. The reports were then revised by NAC in response to the public comments, elevated from "proposed" to "interim" status, and sent to the NRC Committee on Acute Exposure Guideline Levels for final evaluation.

The NRC committee's review of the AEGL reports prepared by NAC and its contractors involves oral and written presentations to the committee by the authors of the reports. The NRC committee provides advice and recommendations for revisions to ensure scientific validity and consistency with the NRC guideline reports (NRC 1993, 2001a). The revised reports are presented at subsequent meetings until the committee is satisfied with the reviews.

Because of the enormous amount of data presented in AEGL reports, the NRC committee cannot verify all of the data used by NAC. The NRC committee relies on NAC and the contractors for the accuracy and completeness of the toxicity data cited in the AEGL reports. Thus far, the committee has prepared seventeen reports in the series *Acute Exposure Guideline Levels for Selected Airborne Chemicals* (NRC 2001b, 2002b, 2003, 2004, 2007b, 2008b, 2009, 2010a,b, 2011, 2012a,b,c, 2013a,b, 2014a,b). This report is the eighteenth volume in that series. AEGL documents for bromine chloride, carbonyl fluoride, selected halogen fluorides, and oxygen difluoride are each published as an appendix in this report. The committee concludes that the AEGLs developed in these appendixes are scientifically valid conclusions based on the data reviewed by NAC and are consistent with the NRC guideline reports. AEGL reports for additional chemicals will be presented in subsequent volumes.

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Appendixes

1

Bromine Chloride[1]

Acute Exposure Guideline Levels

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 (min) to 8 hours (h). Three levels—AEGL-1, AEGL-2, and AEGL-3—are developed for each of five exposure periods (10 and 30 min and 1, 4, and 8 h) 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

[1]This document was prepared by the AEGL Development Team composed of Sylvia Talmage (Oak Ridge National Laboratory), Heather Carlson-Lynch (SRC, Inc.), Chemical Manager Marquea King (National Advisory Committee [NAC] on Acute Exposure Guideline Levels for Hazardous Substances), and Ernest V. Falke (U.S. Environmental Protection Agency). The NAC reviewed and revised the document and AEGLs as deemed necessary. Both the document and the AEGL values were then reviewed by the National Research Council (NRC) Committee on Acute Exposure Guideline Levels. The NRC committee has concluded that the AEGLs developed in this document are scientifically valid conclusions based on the data reviewed by the NRC and are consistent with the NRC guidelines reports (NRC 1993, 2001).

experience notable discomfort, irritation, or certain asymptomatic, nonsensory 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 concentrations that could produce mild and progressively increasing but transient and nondisabling odor, taste, and sensory irritation or certain asymptomatic, nonsensory 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 concentrations 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 idiosyncratic responses, could experience the effects described at concentrations below the corresponding AEGL.

SUMMARY

Bromine chloride is a red-brown liquid. It is formed when bromine and chlorine react reversibly in the liquid and vapor phases. When equimolar amounts of the halogens are reacted, about 60% of the mixed halogens are present as bromine chloride (about 40% is dissociated). The interhalogen compounds are very reactive and hydrolyze readily.

Bromine chloride is used as a water-treatment biocide and in organic synthesis involving addition across olefinic double bonds to produce bromochloro compounds and for aromatic brominations, where an aromatic bromide and hydrogen chloride are produced. Bromine chloride also has application as a brominating agent in the preparation of fire-retardant chemicals, pharmaceuticals, high-density brominated liquids, agricultural chemicals, dyes, and bleaching agents.

No data relevant to deriving AEGL-1 values for bromine chloride were found. Thus, AEGL-1 values are not recommended.

Relevant data for deriving AEGL-2 values for bromine chloride were also not found. However, in accordance with the standing operating procedures for developing AEGL values (NRC 2001), AEGL-2 values were determined by dividing the AEGL-3 values by 3, because the dose-response curve for bromine chloride is steep (0% lethality at 40 ppm and almost 100% lethality at 120 ppm).

For AEGL-3 values, the point-of-departure was the threshold for lethality estimated from a study by Dow Chemical (1977). In that study, the mortality rate in rats exposed to bromine chloride at 20, 40, 80, or 120 ppm for 7 h was 0/6, 0/6, 1/6, and 5/6, respectively. Benchmark concentration analysis was used to estimate the no-observed-adverse-effect level (NOAEL) for lethality (NRC 2001). The 7-h $BMCL_{05}$ (benchmark concentration, 95% lower confidence limit with 5% response) was 39.4 ppm. A total uncertainty factor of 10 was applied; a factor of 3 for interspecies differences and a factor of 3 for intraspecies variability. The effects of direct-acting irritants like bromine chloride are not expected to differ significantly between species or among individuals (NRC 2001). In addition, a modifying factor of 3 was applied to account for the sparse data on bromine chloride and the uncertainty in the exposure concentrations in the Dow Chemical study. Time scaling was performed using the equation $C^n \times t = k$. Data on bromine chloride were inadequate to derive an empirical value for n, so default values of n = 3 for extrapolating to shorter durations and n = 1 for extrapolating to longer durations were used (NRC 2001). Because of the uncertainty associated with time scaling a 7-h point-of-departure to a 10-min value, the 10-min AEGL-3 value was set equal to the 30-min value.

The AEGL values for bromine chloride are presented in Table 1-1.

1. INTRODUCTION

Bromine chloride is a red-brown liquid (Lang 2006). It is formed when bromine and chlorine react reversibly in the liquid and vapor phases. When equimolar amounts of the halogens are reacted at room temperature, about 60% of the mixed halogens are present as bromine chloride (about 40% is dissociated) (Dagani et al. 2000).

TABLE 1-1 AEGL Values for Bromine Chloride

Classification	10 min	30 min	1 h	4 h	8 h	End Point (Reference)
AEGL-1 (nondisabling)	NR[a]	NR[a]	NR[a]	NR[a]	NR[a]	Insufficient data.
AEGL-2 (disabling)	1.1 ppm (5.2 mg/m^3)	1.1 ppm (5.2 mg/m^3)	0.83 ppm (3.9 mg/m^3)	0.53 ppm (2.5 mg/m^3)	0.37 ppm (1.7 mg/m^3)	One-third of the AEGL-3 values.
AEGL-3 (lethal)	3.2 ppm (15 mg/m^3)	3.2 ppm (15 mg/m^3)	2.5 ppm (12 mg/m^3)	1.6 ppm (7.6 mg/m^3)	1.1 ppm (5.2 mg/m^3)	Threshold for lethality in the rat (Dow Chemical Co. 1977).

[a]Not recommended. Absence of an AEGL-1 value does not imply that exposures below the AEGL-2 value are without adverse effects.

The physical properties of mixed halogens are generally intermediate between those of the component halogens (Lang 2006; Frim and Ukeles 2011); however, mixed halogens are polar while single halogen molecules are not (Cotton and Wilkinson 1980). Bromine chloride is a strong oxidizing agent (Dagani et al. 2000). In general, interhalogen compounds are more chemically reactive than elemental halogens due to the weakness of the interhalogen bond (Cotton and Wilkinson 1980; Barrie et al. 2012). Among the diatomic interhalogens, bromine chloride is the least stable, dissociating reversibly to its elemental components (Cotton and Wilkinson 1980; Lang 2006).

The mixed halogen compounds readily hydrolyze (Cotton and Wilkinson 1980). Bromine chloride and its dissociation products may react with water to form a variety of weak and strong acids, including hydrochloric, hypochloric, hydrobromic, and hypobromous acids. The relative proportions of the products depend on pH, but have little dependence on temperature (Liu and Margerum 2001). The following equations show some of the primary reactions (Liu and Margerum 2001; Frim and Ukeles 2011):

$$2BrCl \leftrightarrow Br_2 + Cl_2$$

$$BrCl + H_2O \leftrightarrow HCl + HOBr$$

$$Cl_2 + H_2O \leftrightarrow HOCl + HCl$$

$$Br_2 + H_2O \leftrightarrow HOBr + HBr$$

Ions (e.g., Br^-, Cl^-) may also exist in equilibrium with the molecules presented above (Liu and Margerum 2001). As a result of the numerous chemical species that may be formed on contact with water, a release of bromine chloride into the atmosphere may result in human exposure to mixtures of varying composition, depending on the environmental humidity and its pH; physiologic sources of moisture (e.g., sweat, moisture in the upper respiratory tract) may also create localized exposures to mixtures including hydrolysis products.

The vapor density of bromine chloride has not been determined; however, on the basis of molecular weight (115.36 g/mol), bromine chloride vapor is approximately four times heavier than dry air (average molecular weight of 28.96 g/mol at standard temperature and pressure). The chemical and physical properties of bromine chloride are presented in Table 1-2.

Bromine chloride is used as a water-treatment biocide. Its advantages over chlorine include activity over a wider pH range, more rapid disinfection, effectiveness at lower residual concentrations, and lower aquatic toxicity (Frim and Ukeles 2011). Bromine chloride is used in organic synthesis involving addition across olefinic double bonds to produce bromochloro compounds, and for aromatic brominations, where an aromatic bromide and hydrogen chloride are produced. Bromine chloride is also used as a brominating agent in the preparation of fire-retardant chemicals, pharmaceuticals, high density brominated liquids, agricultural chemicals, dyes, and bleaching agents (Frim and Ukeles 2011).

TABLE 1-2 Chemical and Physical Properties of Bromine Chloride

Parameter	Value	References
Synonyms	Bromochloride	HSDB 2011
CAS registry no.	13863-41-7	HSDB 2011
Chemical formula	BrCl	HSDB 2011
Molecular weight	115.36	HSDB 2011
Physical state	Red-brown liquid at ≤5ºC	HSDB 2011
Melting point	-66ºC	HSDB 2011
Boiling point	5ºC (decomposes)	HSDB 2011
Solubility in water	Reacts with water	HSDB 2011
Density (water =1)	2.32 g/L at 25ºC	IPCS 2009
Vapor pressure	2.368 kPa (17.8 mm Hg) at 25ºC	IPCS 2009
Conversion factors	1 ppm = 4.72 mg/m^3 1 mg/m^3 = 0.212 ppm	

2. HUMAN TOXICITY DATA

No human data on the odor threshold, lethal concentrations, developmental toxicity, reproductive toxicity, genotoxicity, or carcinogenicity of bromine chloride were found.

3. ANIMAL TOXICITY DATA

3.1. Acute Lethality

A single, unpublished study of the acute lethality of bromine chloride was found (Dow Chemical Co. 1977). Groups of six male Sprague-Dawley rats were exposed in a 19-L glass cylinder to bromine chloride at nominal concentrations of 550, 960, 2,110, or 2,925 ppm for 7 h. The vapor was metered from a cylinder containing liquid bromine chloride and mixed with clean air before entering the chamber. Flow rates for the vapor and clean air were used to estimate the nominal concentrations. The investigators reported that the vapor had been analyzed and showed 70% chloride and 30% bromine (molar fraction); it is unclear where the sample was taken or how it was analyzed. Relative humidity in the exposure chamber was not reported, but a diagram of the exposure chamber showed that the air supply passed through a desiccant (Drierite scrubber) before entering the chamber, suggesting that the humidity was probably low.

A separate experiment was conducted to measure the actual chamber concentrations, because the rats appeared to have survived exposure at concentrations far above "working tolerance levels." Six rats were exposed to bromine

chloride at a nominal concentration of 1,100 ppm (estimated on the basis of the mass of bromine chloride liquid lost from the cylinder and air flow rate) for 5 h. Air samples were taken from the gas inlet and from the top, middle, and bottom of the chamber, once per hour; the heights of the three chamber sample inlets were not reported. The air samples were scrubbed through a solution of potassium iodide (1 g/50 mL) and a known amount of 0.025 N sodium thiosulfate (quantity not reported) until the scrubbing solution exhibited a yellow color indicating free iodine; subsequently, the samples were titrated iodometrically to a starch-iodide end point. Total halogen concentration in ppm was reported; the investigators indicated that the halogen concentration was calculated using an assumption of 70% Cl and 30% Br. The halogen concentration estimates presented in Table 1-3 show that the concentration in the bottom of the chamber was roughly twice the concentrations of the middle and top of the chamber.

The investigators estimated the actual exposure concentrations of bromine chloride in the acute lethality study as 4% of the nominal values. That estimate appears to be based on the average concentration in the top and middle chambers (approximately 42-45 ppm) divided by the nominal concentration (1,100 ppm). The actual concentrations were estimated to be 20, 40, 80, and 120 ppm (nominal concentrations of 550, 960, 2,110, and 2,925 ppm, respectively).

In the lethality study, the behavior of the rats was consistent with the observed vapor stratification, as rats tried to breathe the air in the top of the chamber. The report did not indicate the frequency or duration of rearing behavior, nor the dimensions of the inhalation chamber; thus, it is unclear whether the rats were exposed primarily to vapor concentrations corresponding to the bottom, middle, or top of the chamber. However, the estimated concentrations may be conservative, as only the concentrations in the top and middle of the chamber, which were lower than those in the bottom of the chamber, were used in the calculations. Furthermore, because chlorine gas is less dense (vapor density of 1.4 [NRC 2004a]) than bromine (vapor density of 3.5 [NRC 2010]) or bromine chloride (estimated vapor density of approximately 4), the upper portions of the chamber may have contained more chlorine gas than other constituents.

All rats exhibited respiratory problems during and after exposure. At all concentrations, rats lost considerable body weight and recovery to normal was slow. The death of a single rat exposed to bromine chloride at 80 ppm occurred 3 days after exposure; deaths at 120 ppm occurred during the exposure. The primary cause of death was severe upper- and lower-respiratory tract irritation. Mortality and observations over a 14-day period after exposure are presented in Table 1-4.

3.2. Developmental and Reproductive Toxicity

No data on the developmental or reproductive toxicity of bromine chloride were found.

TABLE 1-3 Analytic Measurements of Bromine Chloride in the Test Chamber

	Concentration (ppm) in Chamber Where Sample Was Taken[a]			
Time of Sample (h)	Gas inlet	Top	Middle	Bottom
1	529	78[a]	58	96
2	527	53	44	86
3	544	40	32	98
4	507	37	40	86
5	502	32	40	88
6	530	–	–	–
Average	523	48 (41, excluding sample 1)	43	91

[a]Nominal concentration was 1,100 ppm.
[b]Study authors believed that this sample was potentially contaminated by the initial inlet sample.
Source: Adapted from Dow Chemical Co. 1977.

TABLE 1-4 Mortality Data and Observations from a Study of Rats Exposed to Bromine Chloride

Nominal concentration (ppm)	Estimated actual concentration (ppm)	Exposure Duration	Mortality	Observations
550	20	7 h	0/6	Respiratory distress, bloody eyes and noses, yellow fur, and weight loss with slow recovery.
960	40	5 h	0/6	Extreme respiratory irritation, bloody eyes and noses, and yellow fur.
960	40	7 h	0/6	Respiratory distress, bloody eyes and noses, yellow fur, and weight loss with slow recovery.
2,110	80	7 h	1/6	Death on day 3 after exposure; severe respiratory-tract irritation, yellow fur, and considerable weight loss with slow recovery in remaining rats.
2,925	120	7 h	5/6	Deaths during exposure; severe upper- and lower-respiratory tract irritation and subsequent mouth breathing. Yellow fur and extreme weight loss with slow recovery in surviving rat.

Source: Adapted from Dow Chemical Co. 1977.

3.3. Genotoxicity

No data on the genotoxicity of bromine chloride were found.

3.4. Chronic Toxicity and Carcinogenicity

No data on the chronic toxicity or carcinogenicity of bromine chloride were found.

3.5. Summary

A single study on the lethality of bromine chloride was found. Groups of six male Sprague-Dawley rats were exposed at concentrations of 20, 40, 80, or 120 ppm for 7 h (Dow Chemical Co. 1977). Mortality rates at those concentrations were 0/6, 0/6, 1/6, and 5/6, respectively. All rats experienced respiratory problems during and after the exposure. No data on developmental toxicity, reproductive toxicity, genotoxicity, and chronic toxicity or carcinogenicity of bromine chloride were found.

4. SPECIAL CONSIDERATIONS

4.1. Metabolism and Disposition

No information on the metabolism or disposition of bromine chloride in humans or animals is available.

4.2. Mechanism of Toxicity

Halogens are contact irritants. Death in the single study of bromine chloride was due to severe irritation of the upper- and lower-respiratory tract (Dow Chemical Co. 1977), providing evidence for the direct contact mode of action.

4.3. Structure-Activity Relationships

In the atmosphere, bromine chloride is expected to exist in equilibrium with its dissociation and hydrolysis products, including chlorine, bromine, hydrogen chloride, and hydrogen bromide. Although the data on bromine chloride is sparse, information is available on the toxicity of its dissociation and hydrolysis products, all of which exhibit similar direct-contact irritation modes of action. Table 1-5 shows LC_{50} (lethal concentration, 50% lethality) values for the four compounds in the mouse and rat, along with the 7-h rat LC_{50} for bromine chloride. The LC_{50} values suggest that chlorine and bromine are more toxic than the hydrogenated forms, and that chlorine may be somewhat more toxic than

bromine. In addition, time-scaling the 1-h rat LC_{50} values for chlorine using the equation $C^n \times t = k$ (n =2 [NRC 2004a]) results in estimated 7-h LC_{50} values of 110-170 ppm, compared with the LC_{50} of 98 ppm for bromine chloride estimated from the study by Dow Chemical Co. (1977). Thus, on the basis of sparse (and uncertain) data, the lethality of bromine chloride appears to be comparable to that of chlorine.

4.4. Other Relevant Information

4.4.1. Species Variability

No data on species variability in response to bromine chloride were found. For other halogens, the mouse appeared to be slightly more sensitive than the rat (see Table 1-5).

4.4.2. Susceptible Populations

No data on populations susceptible to the effects of bromine chloride were found. Individuals with respiratory diseases or individuals under stress may be more susceptible to the effects of bromine chloride.

TABLE 1-5 Comparison of LC_{50} Values for Bromine Chloride and Its Dissociation and Hydrolysis Products

Chemical	30 min	1 h	2 h	3 h	6 h	7 h
Mouse						
Chlorine[a]	127	137	<170	<10	-	~250
Bromine[b]	174	–	240	>40	<22	>750
Hydrogen chloride[c]	2,600	1,108	–	–	–	–
Hydrogen bromide	–	814[d]	–	–	–	–
Rat						
Bromine chloride	–	–	–	–	–	98[d]
Chlorine[a]	700	293-455	–	–	–	–
Bromine[b]	–	–	–	–	–	–
Hydrogen chloride[c]	4,700	3,124	–	–	–	–
Hydrogen bromide	>1,300[e]	2,858[f]	–	–	–	–

[a]NRC 2004a.
[b]NRC 2010.
[c]NRC 2004b.
[d]Dow Chemical Co. 1977; based on estimated actual exposure concentrations.
[e]Stavert et al. 1991.
[f]MacEwen and Vernot 1972.

4.4.3. Concentration-Exposure Duration Relationship

No data on concentration-exposure duration relationships for bromine chloride were found.

4.4.4. Concurrent Exposure Issues

No data on concurrent exposure issues for bromine chloride were found.

5. DATA ANALYSIS FOR AEGL-1

5.1. Human Data Relevant to AEGL-1

No data on human exposure to bromine chloride were found.

5.2. Animal Data Relevant to AEGL-1

No animal data on bromine chloride relevant to developing AEGL-1 values were found.

5.3. Derivation of AEGL-1 Values

No data relevant to deriving AEGL-1 values for bromine chloride were available. Therefore, AEGL-1 values are not recommended.

6. DATA ANALYSIS FOR AEGL-2

6.1. Human Data Relevant to AEGL-2

No data on human exposure to bromine chloride were found.

6.2. Animal Data Relevant to AEGL-2

Seven-hour exposures of rats to analytically-determined concentrations of bromine chloride at 20, 40, 80, or 120 ppm resulted in mortality rates of 0/6, 0/6, 1/6, and 5/6, respectively (Dow Chemical Co. 1977). Severe clinical signs and respiratory problems were observed at all concentrations. Those effects are more severe than those defined by AEGL-2 values.

6.3. Derivation of AEGL-2 Values

No data relevant to deriving AEGL-2 values for bromine chloride were available. The dose-response curve for bromine chloride is steep, with 0, 17, and

83% mortality at 40, 80, and 120 ppm, respectively (Dow Chemical Company 1977). In accordance with NRC (2001) guidelines for chemicals with steep dose-response curves, the AEGL-2 values were derived by dividing the AEGL-3 values by 3 (see Section 7.3). AEGL-2 values for bromine chloride are presented in Table 1-6; the calculations are presented in Appendix A and a category graph of AEGL values and toxicity data is presented in Appendix B.

7. DATA ANALYSIS FOR AEGL-3

7.1. Human Data Relevant to AEGL-3

No data on human exposure to bromine chloride were found.

7.2. Animal Data Relevant to AEGL-3

Seven-hour exposures of rats to estimated concentrations of bromine chloride at 20, 40, 80, or 120 ppm resulted in mortality rates of 0/6, 0/6, 1/6, and 5/6, respectively (Dow Chemical Co. 1977). Severe clinical signs and respiratory problems were observed at all concentrations. The death at 80 ppm occurred 3 days after exposure.

7.3. Derivation of AEGL-3 Values

Benchmark concentration analysis was applied to the Dow Chemical Co. (1977) data to estimate the NOAEL for lethality (NRC 2001). The data yielded a 7-h $BMCL_{05}$ of 39.4 ppm and BMC_{01} of 60.2 ppm (see Appendix C). The $BMCL_{05}$ of 39.4 ppm was selected as the point-of-departure. A total uncertainty factor of 10 was applied; a factor of 3 for interspecies differences and a factor of 3 for intraspecies variability. The effects of direct-acting irritants like bromine chloride are not expected to differ significantly between species or among individuals (NRC 2001). A modifying factor of 3 was applied to account for the sparse data on bromine chloride and the uncertainty in the exposure concentrations in the Dow Chemical study. Time scaling was performed using the equation $C^n \times t = k$. Data on bromine chloride were inadequate to derive an empirical value for n, so default values of n = 3 for extrapolating to shorter durations and n = 1 for extrapolating to longer durations were used (NRC 2001). Because of the uncertainty associated with time scaling a 7-h point-of-departure to a 10-min value, the 10-min AEGL-3 value was set equal to the 30-min value. AEGL-3 values for bromine chloride are presented in Table 1-7; the calculations are presented in Appendix A and a category graph of AEGL values and toxicity data is presented in Appendix B.

8. SUMMARY OF AEGLS

8.1. AEGL Values and Toxicity End Points

AEGL values for bromine chloride are presented in Table 1-8, and a summary of the derivations is provided in Appendix D.

8.2. Other Standards and Guidelines

There are no other standards or guidelines for bromine chloride. AEGL values for the dissociation and hydrolysis products of bromine chloride (including chlorine, bromine, hydrogen chloride, and hydrogen bromide) are presented in Table 1-9 for comparison with the values derived for bromine chloride. The comparison suggests that the AEGLs for bromine chloride, which are lower than those of chlorine, should be protective. Although bromine appears to be somewhat less toxic than chlorine (see Table 1-5), the AEGL-3 values for bromine are lower than those for chlorine as a consequence of the less robust database on bromine.

8.3. Data Adequacy and Research

The database on bromine chloride is sparse. Only a single, unpublished acute lethality study is available (Dow Chemical Co. 1977). The exposure concentrations in the study are uncertain as a result of vapor stratification in the chamber and lack of concentration measurements during the study. The AEGL values derived for bromine chloride are supported by comparison to AEGL values for its dissociation and hydrolysis products. However, additional studies of the acute toxicity of bromine chloride, with analysis of actual exposure concentrations and speciation of the compounds in the exposure chamber, should be conducted to refine the AEGL-3 values and provide data relevant to AEGL-2 and AEGL-1 end points. Additional studies comparing the acute toxicity of bromine chloride with that of its dissociation and hydrolysis products would also be beneficial.

TABLE 1-6 AEGL-2 Values for Bromine Chloride

10 min	30 min	1 h	4 h	8 h
1.1 ppm (5.2 mg/m^3)	1.1 ppm (5.2 mg/m^3)	0.83 ppm (3.9 mg/m^3)	0.53 ppm (2.5 mg/m^3)	0.37 ppm (1.7 mg/m^3)

TABLE 1-7 AEGL-3 Values for Bromine Chloride

10 min	30 min	1 h	4 h	8 h
3.2 ppm (15 mg/m^3)	3.2 ppm (15 mg/m^3)	2.5 ppm (12 mg/m^3)	1.6 ppm (7.6 mg/m^3)	1.1 ppm (5.2 mg/m^3)

TABLE 1-8 AEGL Values for Bromine Chloride

	Exposure Duration				
Classification	10 min	30 min	1 h	4 h	8 h
AEGL-1 (nondisabling)	NR[a]	NR[a]	NR[a]	NR[a]	NR[a]
AEGL-2 (disabling)	1.1 ppm (5.2 mg/m^3)	1.1 ppm (5.2 mg/m^3)	0.83 ppm (3.9 mg/m^3)	0.53 ppm (2.5 mg/m^3)	0.37 ppm (1.7 mg/m^3)
AEGL-3 (lethal)	3.2 ppm (15 mg/m^3)	3.2 ppm (15 mg/m^3)	2.5 ppm (12 mg/m^3)	1.6 ppm (7.6 mg/m^3)	1.1 ppm (5.2 mg/m^3)

[a]Not recommended. Absence of an AEGL-1 value does not imply that exposures below the AEGL-2 value are without adverse effects.

TABLE 1-9 AEGL Values for Bromine Chloride and Its Dissociation and Hydrolysis Products

	Exposure Duration				
Classification	10 min	30 min	1 h	4 h	8 h
Bromine Chloride					
AEGL-1	NR[a]	NR[a]	NR[a]	NR[a]	NR[a]
AEGL-2	1.1 ppm	1.1 ppm	0.83 ppm	0.53 ppm	0.37 ppm
AEGL-3	3.2 ppm	3.2 ppm	2.5 ppm	1.6 ppm	1.1 ppm
Chlorine (NRC 2004a)					
AEGL-1	0.50 ppm	0.50 ppm	0.50 ppm	0.50 ppm	0.50 ppm
AEGL-2	2.8 ppm	2.8 ppm	2.0 ppm	1.0 ppm	0.70 ppm
AEGL-3	50 ppm	28 ppm	20 ppm	10 ppm	7.1 ppm
Bromine (NRC 2010)					
AEGL-1	0.033 ppm	0.033 ppm	0.033 ppm	0.033 ppm	0.033 ppm
AEGL-2	0.55 ppm	0.33 ppm	0.24 ppm	0.13 ppm	0.095 ppm
AEGL-3	19 ppm	12 ppm	8.5 ppm	4.5 ppm	3.3 ppm
Hydrogen Chloride (NRC 2004b)					
AEGL-1	1.8 ppm	1.8 ppm	1.8 ppm	1.8 ppm	1.8 ppm
AEGL-2	100 ppm	43 ppm	22 ppm	11 ppm	11 ppm
AEGL-3	620 ppm	210 ppm	100 ppm	26 ppm	26 ppm
Hydrogen Bromide (NRC 2014)					
AEGL-1	1.0 ppm	1.0 ppm	1.0 ppm	1.0 ppm	1.0 ppm
AEGL-2	250 ppm	83 ppm	40 ppm	10 ppm	5 ppm
AEGL-3	740 ppm	250 ppm	120 ppm	31 ppm	15 ppm

[a]Not recommended. Absence of an AEGL-1 value does not imply that exposures below the AEGL-2 value are without adverse effects.

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APPENDIX A

DERIVATION OF AEGL VALUES

Derivation of AEGL-1 Values

Data on bromine chloride were insufficient to derive AEGL-1 values; therefore, AEGL-1 values are not recommended.

Derivation of AEGL-2 Values

The AEGL-2 values for bromine chloride were derived by dividing the AEGL-3 values by 3.

10-min AEGL-2: 3.2 ppm ÷ 3 = 1.1 ppm

30-min AEGL-2: 3.2 ppm ÷ 3 = 1.1 ppm

1-h AEGL-2: 2.5 ppm ÷ 3 = 0.83 ppm

4-h AEGL-2: 1.6 ppm ÷ 3 = 0.53 ppm

8-h AEGL-2: 1.1 ppm ÷ 3 = 0.37 ppm

Derivation of AEGL-3 Values

Key study: Dow Chemical Co. 1977. Evaluation of Acute Inhalation Toxicity of Bromine Chloride in Rats. Dow Report No. 77 2993. Submitted to EPA by Dow Chemical Company, Midland, MI, with Cover Letter Dated 05/28/92. EPA Document No. 88-920002267.

Toxicity end point: Lethality threshold, $BMCL_{05}$ of 39.4 ppm for a 7-h exposure (see Appendix C)

Time scaling: $C^n \times t = k$; default values of n = 3 for extrapolating to shorter durations and n = 1 for extrapolating to longer durations (NRC 2001)
$(39.4 \text{ ppm} \div 30)^3 \times 7 \text{ h} = 15.85707 \text{ ppm-h}$
$(39.4 \text{ ppm}/30)^1 \times 7 \text{ h} = 9.19333 \text{ ppm-h}$

Uncertainty factors: Total uncertainty factor: 10
Interspecies: 3, because the mechanism of action of direct-acting irritants is not expected to differ greatly among species.

	Intraspecies: 3, because the mechanism of action of direct-acting irritants is not expected to differ greatly among individuals.
Modifying factor:	3, to account for sparse database and uncertainty associated with the exposure concentrations in the key study.
Calculations:	
10-min AEGL-3:	Set equal to the 30-min AEGL-3 value of 3.2 ppm, because of the uncertainty associate with time-scaling a 7-h point-of-departure to a 10-min value.
30-min AEGL-3:	$(15.85707 \text{ ppm-h} \div 0.5 \text{ h})^{1/3}$ C = 3.2 ppm
1-h AEGL-3:	$(15.85707 \text{ ppm-h} \div 1 \text{ h})^{1/3}$ C = 2.5 ppm
4-h AEGL-3:	$(15.85707 \text{ ppm-h} \div 4 \text{ h})^{1/3}$ C = 1.6 ppm
8-h AEGL-3:	$(9.19333 \text{ ppm-h} \div 8 \text{ h})$ C = 1.1 ppm

APPENDIX B

CATEGORY PLOT FOR BROMINE CHLORIDE

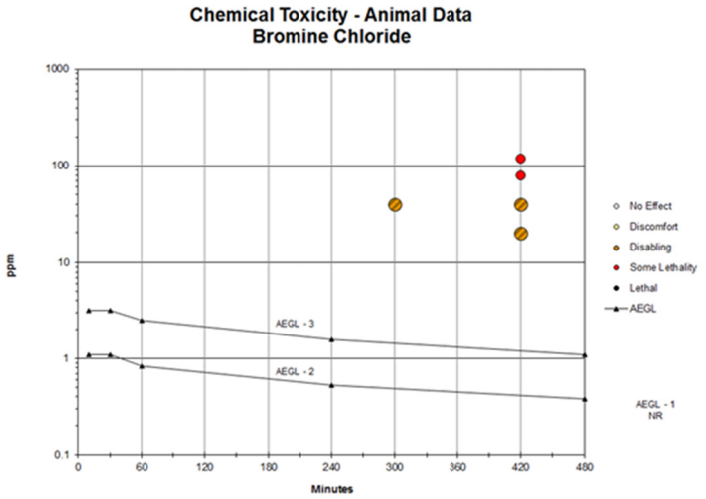

FIGURE B-1 Category plot of toxicity data and AEGL values for bromine chloride.

TABLE B-1 Data Used in Category Plot for Bromine Chloride

Source	Species	ppm	Minutes	Category
AEGL-2		1.1	10	AEGL
AEGL-2		1.1	30	AEGL
AEGL-2		0.83	60	AEGL
AEGL-2		0.53	240	AEGL
AEGL-2		0.37	480	AEGL
AEGL-3		3.2	10	AEGL
AEGL-3		3.2	30	AEGL
AEGL-3		2.5	60	AEGL
AEGL-3		1.6	240	AEGL
AEGL-3		1.1	480	AEGL
Dow Chemical Co. 1977	Rat	20	420	2, respiratory distress
	Rat	40	420	2, respiratory distress
	Rat	40	300	2, extreme respiratory irritation
	Rat	80	420	SL (1/6)
	Rat	120	420	SL (5/6)

For category: 0 = no effect, 1 = discomfort, 2 = disabling, SL = some lethality, 3 = lethality.

APPENDIX C

DERIVATION OF BENCHMARK CONCENTRATION FOR BROMINE CHLORIDE

Probit Model. (Version: 3.2; Date: 10/28/2009)
Input Data File: C:/Users/hclynch.ESC1/Documents/BMDS 220/Data/lnp_Dax_Setting.(d)
Gnuplot Plotting File: C:/Users/hclynch.ESC1/Documents/BMDS 220/Data/lnp_Dax_Setting.plt
Wed Sep 11 12:38:40 2013

BMDS_Model_Run

The form of the probability function is:
P[response] = Background
+ (1-Background) * CumNorm(Intercept+Slope*Log(Dose)),
where CumNorm(.) is the cumulative normal distribution function

Dependent variable = Effect
Independent variable = Dose
Slope parameter is not restricted

Total number of observations = 3
Total number of records with missing values = 0
Maximum number of iterations = 250
Relative Function Convergence has been set to: 1e-008
Parameter Convergence has been set to: 1e-008

User has chosen the log transformed model

Default Initial (and Specified) Parameter Values
Background = 0
Intercept = -9.28868
Slope = 2.05319

Asymptotic Correlation Matrix of Parameter Estimates

(***The model parameter(s) -background have been estimated at a boundary point, or have been specified by the user, and do not appear in the correlation matrix)

	intercept	slope
intercept	1	-1
slope	-1	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Standard Error	Lower Conf. Limit	Upper Conf. Limit
Background	0	NA		
Intercept	-21.8829	9.72809	-40.9496	-2.81617
slope	4.77295	2.11983	0.61815	8.92775

NA - Indicates that this parameter has hit a bound implied by some inequality constraint and thus has no standard error.

Analysis of Deviance Table

Model	Log (likelihood)	No. Parameters	Deviance	Test d.f.	P-value
Full model	-5.40673	3			
Fitted model	-5.40679	2	0.000114402	1	0.9915
Reduced model	-11.4573	1	12.101	2	0.002357

AIC: 14.8136

Goodness of Fit

Dose	Estimated Probability	Expected	Observed	Size	Scaled Residual
40.0000	0.0000	0.000	0.000	6	-0.008
80.0000	0.1666	1.000	1.000	6	0.000
120.0000	0.8334	5.000	5.000	6	-0.000

Chi-square = 0.00 d.f. = 1 P-value = 0.9940

Benchmark Dose Computation
Specified effect = 0.05
Risk Type = Extra risk
Confidence level = 0.95

BMD = 69.4182
BMDL = 39.372

Probit Model. (Version: 3.2; Date: 10/28/2009)
Input Data File: C:/Users/hclynch.ESC1/Documents/BMDS 220/Data/lnp_Dax_Setting.(d)
Gnuplot Plotting File: C:/Users/hclynch.ESC1/Documents/BMDS 220/Data/lnp_Dax_Setting.plt
Wed Sep 11 12:39:15 2013

BMDS_Model_Run

The form of the probability function is:
P[response] = Background + (1-Background) *
CumNorm(Intercept+Slope*Log(Dose)),
where CumNorm(.) is the cumulative normal distribution function

Dependent variable = Effect
Independent variable = Dose
Slope parameter is not restricted

Total number of observations = 3
Total number of records with missing values = 0
Maximum number of iterations = 250
Relative Function Convergence has been set to: 1e-008
Parameter Convergence has been set to: 1e-008

User has chosen the log transformed model

Default Initial (and Specified) Parameter Values
background = 0
intercept = -9.28868
slope = 2.05319

Asymptotic Correlation Matrix of Parameter Estimates

(***The model parameter(s) -background have been estimated at a boundary point, or have been specified by the user, and do not appear in the correlation matrix)

	intercept	slope
intercept	1	-1
slope	-1	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Standard Error	Lower Conf. Limit	Upper Conf. Limit
Background	0	NA		
Intercept	-21.8829	9.72809	-40.9496	-2.81617
slope	4.77295	2.11983	0.61815	8.92775

NA - Indicates that this parameter has hit a bound implied by some inequality constraint and thus has no standard error.

Analysis of Deviance Table

Model	Log (likelihood)	No. Parameters	Deviance	Test d.f.	P-value
Full model	-5.40673	3			
Fitted model	-5.40679	2	0.000114402	1	0.9915
Reduced model	-11.4573	1	12.101	2	0.002357

AIC: 14.8136

Goodness of Fit

Dose	Estimated Probability	Expected	Observed	Size	Scaled Residual
40.0000	0.0000	0.000	0.000	6	-0.008
80.0000	0.1666	1.000	1.000	6	0.000
120.0000	0.8334	5.000	5.000	6	-0.000

Chi-square = 0.00 d.f. = 1 P-value = 0.9940

Benchmark Dose Computation

Specified effect = 0.01
Risk Type = Extra risk
Confidence level = 0.95
BMD = 60.1816
BMDL = 27.4878

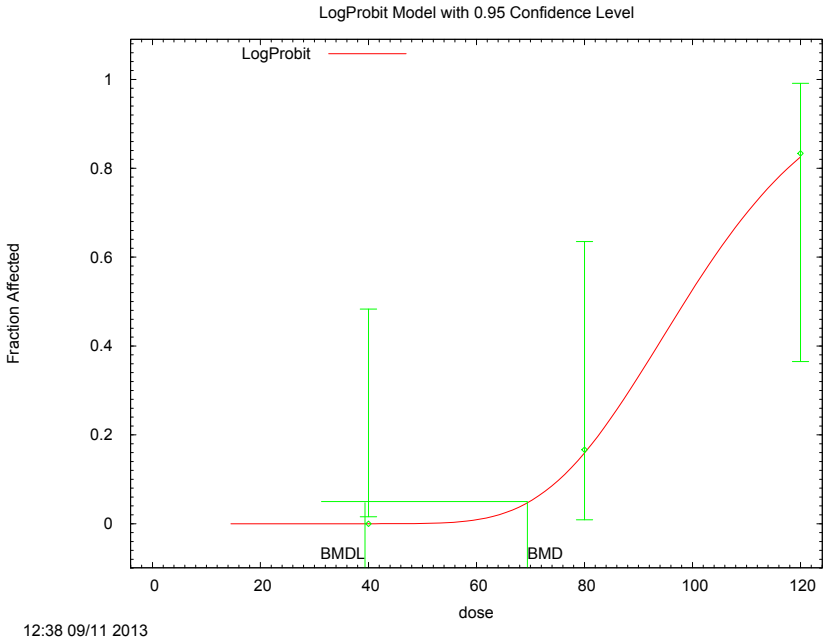

FIGURE C-1 LogProbit model with 0.95 confidence level.

APPENDIX D

ACUTE EXPOSURE GUIDELINE LEVELS FOR BROMINE CHLORIDE

Derivation Summary

AEGL-1 VALUES

Data on bromine chloride were insufficient to derive AEGL-1 values; therefore, AEGL-1 values are not recommended.

AEGL-2 VALUES

10 min	30 min	1 h	4 h	8 h
1.1 ppm	1.1 ppm	0.83 ppm	0.53 ppm	0.37 ppm

Data adequacy: The database on bromine chloride was inadequate for deriving AEGL-2 values. However, because bromine chloride has a steep dose-response curve (0% mortality at 40 ppm and almost 100% mortality at 120 ppm), the AEGL-2 values were derived by dividing the AEGL-3 values by 3 (NRC 2001).

AEGL-3 VALUES

10 min	30 min	1 h	4 h	8 h
3.2 ppm	3.2 ppm	2.5 ppm	1.6 ppm	1.1 ppm

Key reference: Dow Chemical Co. 1977. Evaluation of Acute Inhalation Toxicity of Bromine Chloride in Rats. Dow Report No. 77 2993 EPA Document No.: 88-920002267.

Test species/Strain/Number: Rat; Sprague-Dawley; 6 males/group

Exposure route/Concentrations/Durations: Inhalation; 0, 40, 80, or 120 ppm for 7 h

Effects: Mortality
20 ppm: 0/6
40 ppm: 0/6
80 ppm: 1/6 (death 3 days after exposure)
120 ppm: 5/6 (deaths during exposure)

End point/Concentration/Rationale: Approximate threshold for death, $BMCL_{05}$ of 39.4 ppm for a 7-h exposure

Uncertainty factors/Rationale:
Total uncertainty factor: 10
Interspecies: 3, because the mechanism of action of direct-acting irritants is not expected to differ greatly among species.
Intraspecies: 3, because the mechanism of action of direct-acting irritants in not expected to differ greatly among individuals.

Modifying factor: 3, to account for the sparse database and uncertainty in the exposure concentrations in the key study.

Animal-to-human dosimetric adjustment: Not applied

(Continued)

AEGL-3 VALUES Continued

Time scaling: $C^n \times t = k$; default values of n = 3 for extrapolating to shorter durations and n = 1 for extrapolating to longer durations (NRC 2001). The 30-min value was adopted as the 10-min value.
Data adequacy: The database on lethality from exposure to bromine chloride was considered adequate. The values are supported by the rich database on lethality for the related chemical chlorine.