# Acute Exposure Guideline Levels for Selected Airborne Chemicals: Volume 19

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# Acute Exposure Guideline Levels for Selected Airborne Chemicals

**VOLUME 19**

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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# Preface

Extremely hazardous substances (EHSs)[1] 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 nineteenth volume in that

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

series. AEGL documents for the cyanide salts, diketene, methacrylaldehyde, pentaborane, tellurium hexafluoride, and tetrafluoroethylene 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.

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 report of the committee that led to this report was 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 report, which summarize the committee's conclusions and recommendations for improving NAC's AEGL documents A. Wallace Hayes (Harvard School of Public Health), Sam Kacew (University of Ottawa), 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 the interim report 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 report 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 acknowledges 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

# DEDICATION

The Committee on Acute Exposure Guideline Levels dedicates this volume to our late colleague Dr. Donald E. Gardner. Don was a member of the committee for 12 years, and served as chair for 8 of those years. He was a distinguished toxicologist, respected leader, and valued friend.

# Contents

# Acute Exposure Guideline Levels for Selected Airborne Chemicals

**VOLUME 19**

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

This report is the nineteenth 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 ($1 \times 10^{-4}$), 1 in 100,000 ($1 \times 10^{-5}$), and 1 in 1,000,000 ($1 \times 10^{-6}$) 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 eighteen 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,c). This report is the nineteenth volume in that series. AEGL documents for the cyanide salts, diketene, methacrylaldehyde, pentaborane, tellurium hexafluoride, and tetrafluoroethylene 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.

## REFERENCES

NRC (National Research Council). 1968. Atmospheric Contaminants in Spacecraft. Washington, DC: National Academy of Sciences.

NRC (National Research Council). 1972. Atmospheric Contaminants in Manned Spacecraft. Washington, DC: National Academy of Sciences.

NRC (National Research Council). 1984a. Emergency and Continuous Exposure Limits for Selected Airborne Contaminants, Vol. 1. Washington, DC: National Academy Press.

NRC (National Research Council). 1984b. Emergency and Continuous Exposure Limits for Selected Airborne Contaminants, Vol. 2. Washington, DC: National Academy Press.

NRC (National Research Council). 1984c. Emergency and Continuous Exposure Limits for Selected Airborne Contaminants, Vol. 3. Washington, DC: National Academy Press.

NRC (National Research Council). 1984d. Toxicity Testing: Strategies to Determine Needs and Priorities. Washington, DC: National Academy Press.

NRC (National Research Council). 1985a. Emergency and Continuous Exposure Guidance Levels for Selected Airborne Contaminants, Vol. 4. Washington, DC: National Academy Press.

NRC (National Research Council). 1985b. Emergency and Continuous Exposure Guidance Levels for Selected Airborne Contaminants, Vol. 5. Washington, DC: National Academy Press.

NRC (National Research Council). 1986a. Emergency and Continuous Exposure Guidance Levels for Selected Airborne Contaminants, Vol. 6. Washington, DC: National Academy Press.

NRC (National Research Council). 1986b. Criteria and Methods for Preparing Emergency Exposure Guidance Level (EEGL), Short-Term Public Emergency Guidance Level (SPEGL), and Continuous Exposure Guidance level (CEGL) Documents. Washington, DC: National Academy Press.

NRC (National Research Council). 1987. Emergency and Continuous Exposure Guidance Levels for Selected Airborne Contaminants, Vol. 7. Washington, DC: National Academy Press.

NRC (National Research Council). 1988. Emergency and Continuous Exposure Guidance Levels for Selected Airborne Contaminants, Vol. 8. Washington, DC: National

Academy Press.
NRC (National Research Council). 1992. Guidelines for Developing Spacecraft Maximum Allowable Concentrations for Space Station Contaminants. Washington, DC: National Academy Press.
NRC (National Research Council). 1993. Guidelines for Developing Community Emergency Exposure Levels for Hazardous Substances. Washington, DC: National Academy Press.
NRC (National Research Council). 1994. Spacecraft Maximum Allowable Concentrations for Selected Airborne Contaminants, Vol. 1. Washington, DC: National Academy Press.
NRC (National Research Council). 1996a. Spacecraft Maximum Allowable Concentrations for Selected Airborne Contaminants, Vol. 2. Washington, DC: National Academy Press.
NRC (National Research Council). 1996b. Spacecraft Maximum Allowable Concentrations for Selected Airborne Contaminants, Vol. 3. Washington, DC: National Academy Press.
NRC (National Research Council). 2000a. Spacecraft Maximum Allowable Concentrations for Selected Airborne Contaminants, Vol. 4. Washington, DC: National Academy Press.
NRC (National Research Council). 2000b. Methods for Developing Spacecraft Water Exposure Guidelines. Washington, DC: National Academy Press.
NRC (National Research Council). 2001a. Standing Operating Procedures for Developing Acute Exposure Guideline Levels for Hazardous Chemicals. Washington, DC: National Academy Press.
NRC (National Research Council). 2001b. Acute Exposure Guideline Levels for Selected Airborne Chemicals, Vol. 1. Washington, DC: National Academy Press.
NRC (National Research Council). 2002a. Review of Submarine Escape Action Levels for Selected Chemicals. Washington, DC: The National Academies Press.
NRC (National Research Council). 2002b. Acute Exposure Guideline Levels for Selected Airborne Chemicals, Vol 2. Washington, DC: The National Academies Press.
NRC (National Research Council). 2003. Acute Exposure Guideline Levels for Selected Airborne Chemical, Vol. 3. Washington, DC: The National Academies Press.
NRC (National Research Council). 2004. Acute Exposure Guideline Levels for Selected Airborne Chemicals, Vol. 4. Washington, DC: The National Academies Press.
NRC (National Research Council). 2007a. Emergency and Continuous Exposure Guidance Levels for Selected Submarine Contaminants, Vol. 1. Washington, DC: The National Academies Press.
NRC (National Research Council). 2007b. Acute Exposure Guideline Levels for Selected Airborne Chemicals, Vol. 5. Washington, DC: The National Academies Press.
NRC (National Research Council). 2008a. Emergency and Continuous Exposure Guidance Levels for Selected Submarine Contaminants, Vol. 2. Washington, DC: The National Academies Press.
NRC (National Research Council). 2008b. Acute Exposure Guideline Levels for Selected Airborne Chemicals, Vol. 6. Washington, DC: The National Academies Press.
NRC (National Research Council). 2009. Acute Exposure Guideline Levels for Selected Airborne Chemicals, Vol. 7. Washington, DC: The National Academies Press.
NRC (National Research Council). 2010a. Acute Exposure Guideline Levels for Selected Airborne Chemicals, Vol. 8. Washington, DC: The National Academies Press.
NRC (National Research Council). 2010b. Acute Exposure Guideline Levels for Selected Airborne Chemicals, Vol. 9. Washington, DC: The National Academies Press.

NRC (National Research Council). 2011. Acute Exposure Guideline Levels for Selected Airborne Chemicals, Vol. 10. Washington, DC: The National Academies Press.
NRC (National Research Council). 2012a. Acute Exposure Guideline Levels for Selected Airborne Chemicals, Vol. 11. Washington, DC: The National Academies Press.
NRC (National Research Council). 2012b. Acute Exposure Guideline Levels for Selected Airborne Chemicals, Vol. 12. Washington, DC: The National Academies Press.
NRC (National Research Council). 2012c. Acute Exposure Guideline Levels for Selected Airborne Chemicals, Vol. 13. Washington, DC: The National Academies Press.
NRC (National Research Council). 2013a. Acute Exposure Guideline Levels for Selected Airborne Chemicals, Vol. 14. Washington, DC: The National Academies Press.
NRC (National Research Council). 2013b. Acute Exposure Guideline Levels for Selected Airborne Chemicals, Vol. 15. Washington, DC: The National Academies Press.
NRC (National Research Council). 2014a. Acute Exposure Guideline Levels for Selected Airborne Chemicals, Vol. 16. Washington, DC: The National Academies Press.
NRC (National Research Council). 2014b. Acute Exposure Guideline Levels for Selected Airborne Chemicals, Vol. 17. Washington, DC: The National Academies Press.
NRC (National Research Council). 2014c. Acute Exposure Guideline Levels for Selected Airborne Chemicals, Vol. 18. Washington, DC: The National Academies Press.

# Appendixes

# 5

# Tellurium Hexafluoride[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 experience notable discomfort, irritation, or certain asymptomatic, nonsensory effects. However, the effects are not disabling and are transient and reversible upon cessation of exposure.

[1]This document was prepared by the AEGL Development Team composed of Jennifer Rayner (Oak Ridge National Laboratory), Julie Klotzbach (SRC, Inc.), Chemical Manager George Rusch (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).

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

Tellurium hexafluoride is a byproduct of ore refining. It is a colorless gas with a repulsive odor. It decomposes slowly in water to form hydrogen fluoride and tellurium ion. Tellurium hexafluoride is severely irritating and causes respiratory distress, pulmonary edema, and death in animals. In humans, it is reported to cause "garlic" breath, a metallic taste in the mouth, and fatigue. Inhalation of tellurium hexafluoride is expected to cause breathing difficulties in humans.

AEGL-1 values are not recommended for tellurium hexafluoride because of insufficient data. Absence of AEGL-1 values does not imply that exposures below the AEGL-2 concentrations are without adverse effects.

Data were also inadequate for deriving AEGL-2 values. However, the standing operating procedures for determining AEGL values specifies that AEGL-2 values for chemicals with steep concentrations-response curves may be estimated by dividing the AEGL-3 values by 3 (NRC 2001). Lethality data on tellurium hexafluoride demonstrates a steep-concentration response curve. All rabbits, guinea pigs, rats, and mice exposed for 4 h to tellurium hexafluoride at concentrations of 5 ppm or higher died, and all mice exposed at 5 ppm for 1 h died. All animals exposed at 1 ppm for 1 or 4 h survived (Kimmerle 1960).

The point-of-departure for deriving AEGL-3 values was 1 ppm for 4 h, which was the highest concentration of tellurium hexafluoride at which no mortality occurred in rabbits, guinea pigs, rats, and mice (Kimmerle 1960). An interspecies uncertainty factor of 3 was applied because the four species appear to be

similarly sensitive to the acute effects of tellurium hexafluoride; however, that assessment is based on a small number of test animals (one to four animals per group). An intraspecies uncertainty factor of 3 was applied because tellurium hexafluoride is highly irritating and corrosive, and much of its toxicity is probably caused by a direct chemical effect on tissues; that type of portal-of-entry effect is not expected to vary greatly among individuals. A modifying factor of 10 also was applied to account for the sparse database on tellurium hexafluoride and for the potential effects of tellurium. Time scaling of the values were performed using the equation $C^n \times t = k$, where the exponent n ranges from 0.8 to 3.5 (ten Berge et al. 1986). In the absence of data on tellurium hexafluoride to determine an empirical value for n, default values of n = 3 when extrapolating to shorter durations and n = 1 when extrapolating to longer durations were used.

The AEGL values for tellurium hexafluoride are presented in Table 5-1.

## 1. INTRODUCTION

Tellurium hexafluoride is a colorless gas created by the direct fluorination of tellurium metal (HSDB 2008). It is a byproduct of ore refining, and there are no known uses for it (ACGIH 2001; HSDB 2008). Production data were not found. Tellurium hexafluoride hydrolyzes slowly in water to hydrogen fluoride and telluric acid. Its chemical and physical properties are presented in Table 5-2.

## 2. HUMAN TOXICITY DATA

### 2.1. Acute Lethality

No human data on the acute lethality of tellurium hexafluoride were found.

### 2.2. Nonlethal Toxicity

#### 2.2.1. Odor Threshold and Odor Awareness

Tellurium hexafluoride has a repulsive odor (ACGIH 2001).

#### 2.2.2. Case Reports

Blackadder and Manderson (1975) reported a case of tellurium hexafluoride exposure. Two men, 24 and 26 years old, were exposed when 50 g of tellurium hexafluoride gas leaked from a cylinder while they were doing research. The first man experienced tiredness, a metallic taste in the mouth, and sour garlic odor in his breath, sweat, and urine. He was admitted to the hospital for observation and developed a rash on the hands, arms, and neck after the second

day of observation. He also developed bluish-black patches between the fingers and on the neck and face, which took several weeks to fade. The second man experienced garlic odor of the breath and bluish-black patches on the skin. Liver-function tests, renal-function tests, urinalysis, chest radiographs, blood electrolytes, and blood indices were all normal. The men were not treated and both completely recovered; the garlic odor of the breath and blue-black patches on the skin took several weeks to clear. The skin discoloration was thought to be the result of dermal absorption of tellurium.

**TABLE 5-1** AEGL Values for Tellurium Hexafluoride

| Classification | 10 min | 30 min | 1 h | 4h | 8 h | End Point (Reference) |
|---|---|---|---|---|---|---|
| AEGL-1 (nondisabling) | NR[a] | NR[a] | NR[a] | NR[a] | NR[a] | Insufficient data. |
| AEGL-2 (disabling) | 0.0097 ppm (0.096 mg/m$^3$) | 0.0067 ppm (0.066 mg/m$^3$) | 0.0053 ppm (0.052 mg/m$^3$) | 0.0033 ppm (0.033 mg/m$^3$) | 0.0017 ppm (0.017 mg/m$^3$) | One-third of the AEGL-3 values (NRC 2001). |
| AEGL-3 (lethal) | 0.029 ppm (0.28 mg/m$^3$) | 0.020 ppm (0.20 mg/m$^3$) | 0.016 ppm (0.16 mg/m$^3$) | 0.010 ppm (0.10 mg/m$^3$) | 0.0050 ppm (0.049 mg/m$^3$) | Highest concentration causing no mortality in rabbits, guinea pig, rats, and mice (Kimmerle 1960). |

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

**TABLE 5-2** Chemical and Physical Properties of Tellurium Hexafluoride

| Parameter | Value | References |
|---|---|---|
| Synonyms | Tellurium fluoride (TEF6), (OC-6-11)-; tellurium fluoride (TEF) | HSDB 2008 |
| CAS registry no. | 7783-80-4 | HSDB 2008 |
| Chemical formula | $TeF_6$ | HSDB 2008 |
| Molecular weight | 241.61 | HSDB 2008 |
| Physical state | Colorless gas | HSDB 2008 |
| Melting point | -37.6ºC | ACGIH 2001 |
| Boiling point | -38.9ºC | ACGIH 2001 |
| Vapor density (air = 1) | 8.3 | HSDB 2008 |
| Solubility in water | Decomposes slowly in water to telluric acid | ACGIH 2001 |
| Vapor pressure | >760 torr at 20°C | ACGIH 2001 |
| Flammability limits | Nonflammable gas | NIOSH 2011 |
| Conversion factors | 1 ppm = 9.88 mg/m$^3$<br>1 mg/m$^3$ = 0.10 ppm | NIOSH 2011 |

### 2.2.3. Occupational Exposure

Steinberg et al. (1942) examined 49 workers exposed to fumes of tellurium and its oxides for 15 or 22 months. The most commonly reported subjective symptoms were garlic odor of the breath, mouth dryness, metallic taste, somnolence, and garlic odor of the sweat. A small number of subjects occasionally reported loss of appetite and nausea. Somnolence was observed only in the workers with the highest urinary concentrations of tellurium. No alterations in hematologic or urinalysis parameters were observed.

## 2.3. Neurotoxicity

No human data on the neurotoxicity of tellurium hexafluoride were found.

## 2.4. Developmental and Reproductive Toxicity

No human data on the developmental or reproductive toxicity of tellurium hexafluoride were found.

## 2.5. Genotoxicity

No human data on the genotoxicity of tellurium hexafluoride were found.

## 2.6. Carcinogenicity

No human data on the carcinogenicity of tellurium hexafluoride were found.

## 2.7. Summary

Human exposure to tellurium hexafluoride or fumes of tellurium oxides caused metallic taste in the mouth; tiredness; sour garlic odor of the breath, sweat, and urine; and bluish-black patches on the skin. Tellurium hexafluoride is a respiratory irritant and humans may experience breathing difficulties after inhaling it (NIOSH 1978; OSHA 1996).

# 3. ANIMAL TOXICITY DATA

## 3.1. Acute Lethality

Kimmerle (1960) exposed one rabbit, one guinea pig, two male white rats, and four male white mice per group to tellurium hexafluoride for 1 or 4 h. Exposures were carried out in a 2-$m^3$ chamber. Tellurium hexafluoride was intro-

duced into the chamber through a glass burette and mixed with air by a propeller. The animals were exposed at 1 or 5 ppm (nominal concentrations) for 1 h and 1, 5, 10, 25, 50 or 100 ppm (nominal concentrations) for 4 h. The results are shown in Table 5-3. At 5 ppm for 1 h, severe damage was observed in the respiratory organs of the animals, and all mice died between 24 and 36 h. All animals survived 1-h exposures at 1 ppm. Exposure to tellurium hexafluoride at 1 ppm for 4 h caused respiratory dysfunction in all animals. All animals died from pulmonary edema after exposure at 5 ppm or higher for 4 h.

**TABLE 5-3** Results of Acute Toxicity Studies of Tellurium Hexafluoride by Kimmerle (1960)

| Species | Concentration (ppm) | Duration (h) | Effect |
|---|---|---|---|
| Rabbit | 1 | 4 | Respiratory dysfunction, pulmonary edema. |
| (1/group) | 5 | | Death after 8 h. |
| | 10 | | Death after 140 min. |
| | 25 | | Death after 80 min. |
| | 50 | | Death after 60 min. |
| | 100 | | Death after 15 min |
| Rabbit | 1 | 1 | Significantly increased respiratory frequency. |
| (1/group) | 5 | | Severe damage to respiratory organs. |
| Guinea pig | 1 | 4 | Respiratory dysfunction, pulmonary edema. |
| (1/group) | 5 | | Death after 6 h. |
| | 10 | | Death after 120 min. |
| | 25 | | Death after 100 min. |
| | 50 | | Death after 70 min. |
| | 100 | | Death after 30 min. |
| Guinea pig | 1 | 1 | Significantly increased respiratory frequency. |
| (1/group) | 5 | | Severe damage to respiratory organs. |
| Rat | 1 | 4 | Respiratory dysfunction, pulmonary edema. |
| (2/group) | 5 | | Death after 6 and 24 h. |
| | 10 | | Death after 100 and 115 min. |
| | 25 | | Death after 60 and 85 min. |
| | 50 | | Death after 55 and 70 min. |
| | 100 | | Death after 20 and 25 min. |
| Rat | 1 | 1 | Significantly increased respiratory frequency. |
| (2/group) | 5 | | Severe damage to respiratory organs. |
| Mouse | 1 | 4 | Respiratory dysfunction, pulmonary edema. |
| (4/group) | 5 | | Death within 4-24 h. |
| | 10 | | Death within 110-130 min. |
| | 25 | | Death within 75-110 min. |
| | 50 | | Death within 45-70 min. |
| | 100 | | Death within 10-30 min. |
| Mouse | 1 | 1 | Significantly increased respiratory frequency. |
| (4/group) | 5 | | Death between 24-36 h, severe damage to respiratory organs. |

### 3.2. Nonlethal Toxicity

Kimmerle (1960) exposed one rabbit, one guinea pig, two male white rats, and four male white mice per group to tellurium hexafluoride at 1 or 5 ppm for 1 or 4 h, as described in Section 3.1. Significantly increased respiratory frequency (hyperpnea) was observed in all animals exposed at 1 ppm for 1 h. At 5 ppm for 1 h, severe damage was observed in the respiratory organs of the animals; the rabbit, guinea pigs, and rats survived the exposure but recovered very slowly. Exposure to tellurium hexafluoride at 1 ppm for 4 h caused respiratory dysfunction in all animals. The investigator also exposed the same species to tellurium hexafluoride at 1 ppm for 1 h each day for 5 days and found no visible effects in the animals. In the rabbit, liver-function tests were carried out after the end of the repeat-exposure test and again one week later. No hepatic damage was observed.

There are few data on other tellurium compounds. One study reported that one of four guinea pigs died 24 h after a single injection of tellurium oxide. The remaining guinea pigs survived the 1-week observation period (Amdur 1958). No histologic alterations were observed in the livers or kidneys of the surviving animals.

### 3.3. Developmental and Reproductive Toxicity

No animal data on the developmental or reproductive toxicity of tellurium hexafluoride were found, but a few studies on tellurium and tellurium pulveratum were available.

Oral exposure studies have found that the developing nervous system is sensitive to the toxicity of tellurium. Highly synchronous primary demyelination of peripheral nerves followed by remyelination was observed in developing rats exposed to 1.1% tellurium in the diet (Malczewska-Toth 2012). The demyelination was due to tellurium-induced inhibition of squalene epoxidase activity. Duckett (1970) reported that there were no differences in the size or appearance of the fetuses of dams exposed to tellurium at 3,000 ppm in their diet. Although no anomalies were found by light microscopy of the brains, electron microscopic examination revealed morphologic anomalies in the ependymal layer of tellurium-exposed fetuses; no microvilli were detected in the ventricular plasmalemma and the number of mitochondria was greatly diminished.

In weanling rats (17 days old) fed a diet containing 1% tellurium pulveratum for at least 3 days, partial or complete paralysis of the hind limbs was observed (Lampert et al. 1970). A gradual recovery started on the tenth day of exposure, and weakness of the hind limbs was only occasionally observed after 20-25 days of exposure. The investigators also noted severe wasting in the animals by the tenth exposure day. Consistent with the clinical signs, increased cellularity and demyelination was observed in the lumbar roots and sciatic nerves, with peak damage occurring after 4 days of exposure; remeylination was observed after 10 days of exposure. The investigators suggested that tellurium-induced

neuropathy was age-specific, as evidenced by remyelination despite continuing exposure. No histologic alterations were observed in the brain or spinal cord and demyelinated axons were occasionally observed in the brachial plexus of some animals; in general, no alterations were observed in the liver.

### 3.4. Genotoxicity

No data on the genotoxicity of tellurium hexafluoride were found.

### 3.5. Chronic Toxicity and Carcinogenicity

No data on the chronic toxicity or carcinogenicity of tellurium hexafluoride were found.

### 3.5. Summary

Only one study of tellurium hexafluoride toxicity in animal models was found. In that study, all rabbits, guinea pigs, rats, and mice exposed to tellurium hexafluoride at 5, 10, 25, 50, or 100 ppm for 4 h died (Kimmerle 1960). All mice exposed at 5 ppm for 1 h died, whereas animals exposed at 1 ppm for 1 h survived. Repeated exposure to tellurium hexafluoride at 1 ppm for 1 h per day for 5 days resulted in no clinical signs or mortality in any species tested. Clinical signs (respiratory distress) and post-mortem findings (pulmonary edema) were consistent with severe irritation in all animals except those exposed at 1 ppm for 1 h, which exhibited only hyperpnea. A limitation of this study is that only a small number of animals were tested. No data on the developmental or reproductive toxicity, genotoxicity, or chronic toxicity or carcinogenicity following inhalation exposure to tellurium hexafluoride were found. Studies of related chemicals (tellurium and tellurium pulveratum) have reported demyelination in peripheral nerves and morphologic alterations in the brain of developing animals after oral exposure (Duckett 1970; Lampert et al. 1970; Malczewska-Toth 2012).

## 4. SPECIAL CONSIDERATIONS

### 4.1. Metabolism and Disposition

Little information on the metabolism and disposition of tellurium hexafluoride were found. Tellurium hexafluoride may be hydrolyzed in the moist respiratory tract to hydrogen fluoride and the tellurium ion or telluric acid (HSDB 2008). Tellurium is distributed through the body with higher concentrations found in the kidneys, liver, bone, brain, and testes (IPCS 1998). In the liver, hepatic metabolism creates dimethyl telluride, which is exhaled and has a garlic

odor (IPCS 1998). Tellurium is mainly excreted in the urine with small amounts exhaled as dimethyl telluride (IPCS 1998).

### 4.2. Mechanism of Toxicity

In the moist respiratory tract, tellurium hexafluoride slowly hydrolyzes into hydrogen fluoride and tellurium ion or telluric acid. Kimmerle (1960) has shown that the toxic effects of inhaled tellurium hexafluoride are consistent with severe irritation and corrosion. Hydrogen fluoride is a severe irritant to the skin, eyes, and respiratory tract. The AEGL values for hydrogen fluoride, however, are orders of magnitude higher than the AEGL values for tellurium hexafluoride, which may indicate that hydrogen fluoride does not play a major role in its toxicity. Penetration of hydrogen fluoride to the lungs produces pulmonary hemorrhage and edema and may result in death (NRC 2004a). The mechanism of toxicity of tellurium is unknown. It has been shown that tellurium inhibits squalene epoxidase, which might interfere with neurotransmission through demyelination. Demyelination has been observed in young animals but not in humans (Anthony et al. 2001).

### 4.3. Structure-Activity Relationships

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

The 1-h $LC_{50}$ values for hydrogen fluoride for the mouse range from 342 to 501 ppm (NRC 2004a). If the acute inhalation toxicity of tellurium hexafluoride was due only to hydrogen fluoride, then 1-h $LC_{50}$ values for tellurium hexafluoride should have a range of 57-84 ppm for mice. However, 100% mortality occurred in mice exposed to tellurium hexafluoride at 5 ppm for 1 h (Kimmerle 1960). The greater relative toxicity of tellurium hexafluoride might be due to the tellurium moiety and/or the slow hydrolysis rate of tellurium hexafluoride. If the slow hydrolysis rate resulted in more hydrogen fluoride being released in the lung than in the upper respiratory tract, it would result in greater pulmonary damage and likely be more lethal. Mortality in rats exposed to hydrogen fluoride at 1,300 ppm for 30 min by cannulation (to simulate mouth breathing) was 25%, whereas no mortality occurred in rats similarly exposed by nasal breathing (Stavert et al. 1991).

Few toxicity studies are available on other metal hexafluorides, such as uranium hexafluoride and selenium hexafluoride. The relevance of those compounds to tellurium hexafluoride has not been established. Tellurium hexafluoride is analogous to selenium hexafluoride in molecular structure and noble gas

configuration. Both are irritating gases that cause pulmonary edema and death. Tellurium hexafluoride was found to be more toxic in laboratory animals than selenium hexafluoride (Kimmerle 1960); although this comparison is limited by the small number of animals tested for both compounds (one rabbit, one guinea pig, two rats, and four mice). All rabbits, guinea pigs, rats, and mice exposed to selenium hexafluoride at 10 ppm for 4 h died, but survived exposure at 5 or 1 ppm. Animals exposed at 5 ppm exhibited difficulty breathing and pulmonary edema, which resolved during the follow-up period. No effects were observed in animals exposed selenium hexafluoride at 1 ppm. All rabbits, guinea pigs, rats, and mice exposed to tellurium hexafluoride at 5 ppm for 4 h died, but survived exposure at 1 ppm. Animals exposed at 1 ppm exhibited difficulty breathing and pulmonary edema, which resolved during the follow-up period. Unlike tellurium hexafluoride, uranium hexafluoride rapidly hydrolyzes to form hydrogen fluoride and uranyl fluoride (NRC 2004b); thus, the site of toxicity might be different from that of tellurium hexafluoride. Acute inhalation exposure to uranium hexafluoride results in renal damage caused by the uranium moiety (NRC 2004b). However, no evidence that the kidney is a sensitive target of tellurium hexafluoride or other tellurium compounds was found. No histologic alterations were observed in the kidneys of guinea pigs administered a single injection of tellurium oxide and no alterations in urinary glucose or albumin concentrations or urine specific gravity were observed in workers exposed to tellurium and its oxides (Steinberg et al. 1942).

### 4.4. Other Relevant Information

Although the data on the toxicity of tellurium are sparse, they suggest that it is a neurotoxicant. Somnolence was reported following accidental acute exposure to tellurium hexafluoride (Blackadder and Manderson 1975) and in workers exposed to tellurium and its oxides (Steinberg et al. 1942). Additionally, demyelination of peripheral nerves and morphologic alterations in the brain were observed in developing animals (Duckett 1970; Lampert et al. 1970; Malczewska-Toth 2012).

#### 4.4.1. Species Variability

The study by Kimmerle (1960) suggests that the acute toxicity of tellurium hexafluoride is similar between rabbits, guinea pigs, rats, and mice. Mice might be slightly more sensitive, as they died from exposure to tellurium hexafluoride that the other species survived (5 ppm for 1 h). Although this sensitivity would be expected for a corrosive and severely irritating chemical, a major limitation of the study is that it tested a small number of animals.

### 4.4.2. Susceptible Populations

The effects of tellurium hexafluoride might be exacerbated in individuals with impaired pulmonary function due to the chemical's irritant properties (NIOSH 1978). However, no information on the susceptibility of such individuals to tellurium hexafluoride relative to normal individuals was found.

Mortality data on tellurium hexafluoride suggest a steep concentration-response curve, which implies little intraspecies variability. Mortality was 100% in rabbits, guinea pigs, rats, and mice exposed to tellurium hexafluoride at 5 ppm or higher for 4 h. All mice exposed at 5 ppm for 1 h died, but survived exposure at 1 ppm for 1 h (Kimmerle 1960).

### 4.4.3. Concentration-Exposure Duration Relationship

The concentration-exposure duration relationship for many irritant and systemically acting vapors and gases may be described by the equation $C^n \times t = k$, where the exponent n ranges from 0.8 to 3.5 (ten Berge et al. 1986). In the absence of data on tellurium hexafluoride from which to derive an empirical value for n, temporal scaling was performed using default values of n = 3 when extrapolating to shorter durations and n = 1 when extrapolating to longer durations (NRC 2001).

### 4.4.4. Concurrent Exposure Issues

No concurrent exposure issues relevant to tellurium hexafluoride were found.

## 5. DATA ANALYSIS FOR AEGL-1

### 5.1. Human Data Relevant to AEGL-1

No human data relevant to developing AEGL-1 values for tellurium hexafluoride were identified.

### 5.2. Animal Data Relevant to AEGL-1

No animal data relevant to developing AEGL-1 values for tellurium hexafluoride were identified.

### 5.3. Derivation of AEGL-1 Values

AEGL-1 values are not recommended for tellurium hexafluoride because of insufficient data. Absence of AEGL-1 values does not imply that exposures below the AEGL-2 concentrations are without adverse effects.

## 6. DATA ANALYSIS FOR AEGL-2

### 6.1. Human Data Relevant to AEGL-2

No human data relevant to developing AEGL-2 values for tellurium hexafluoride were identified.

### 6.2. Animal Data Relevant to AEGL-2

Kimmerle (1960) exposed one rabbit, one guinea pig, two male white rats, and four male white mice per group to tellurium hexafluoride at 1 or 5 ppm for 1 or 4 h. Hyperpnea was observed in all animals exposed at 1 ppm for 1 h. At 5 ppm for 1 h, severe damage in the respiratory organs of the animals was found; the rabbit, guinea pigs, and rats survived the exposure but recovered very slowly. All of the mice died. Exposure to tellurium hexafluoride at 1 ppm for 4 h caused respiratory dysfunction in all animals.

In a study of the chemical tellurium, morphologic alterations of the brain were found in the fetuses of rats fed tellurium (Duckett 1970). Extrapolating the results of this study to derive AEGL values for tellurium hexafluoride was considered inappropriate.

### 6.3. Derivation of AEGL-2 Values

Data on tellurium hexafluoride are not consistent with AEGL-2 severity effects. Animals experienced hyperpnea after exposure to tellurium hexafluoride at 1 ppm for 1 h. The standing operating procedures for determining AEGL values specifies that AEGL-2 values for chemicals with steep concentrations-response curves may be estimated by dividing the AEGL-3 values by 3 (NRC 2001). Lethality data on tellurium hexafluoride demonstrates a steep-concentration response curve. All rabbits, guinea pigs, rats, and mice exposed at concentrations of 5, 10, 25, 50, or 100 ppm for 4 h died, and all mice exposed at 5 ppm for 1 h died. All animals exposed at 1 ppm for 1 or 4 h survived (Kimmerle 1960).

AEGL-2 values for tellurium hexafluoride are presented in Table 5-4, and the calculations are presented in Appendix A.

**TABLE 5-4** AEGL-2 Values for Tellurium Hexafluoride

| 10 min | 30 min | 1 h | 4 h | 8 h |
|---|---|---|---|---|
| 0.0097 ppm (0.096 mg/m$^3$) | 0.0067 ppm (0.066 mg/m$^3$) | 0.0053 ppm (0.052 mg/m$^3$) | 0.0033 ppm (0.033 mg/m$^3$) | 0.0017 ppm (0.017 mg/m$^3$) |

## 7. DATA ANALYSIS FOR AEGL-3

### 7.1. Human Data Relevant to AEGL-3

No human data relevant to deriving AEGL-3 values for tellurium hexafluoride were identified.

### 7.2. Animal Data Relevant to AEGL-3

Mortality was 100% in rabbits, guinea pigs, rats, and mice exposed for 4 h to tellurium hexafluoride at 5 ppm or higher (Kimmerle 1960); at 1 ppm, the animals survived but experienced pulmonary edema and respiratory dysfunction. For a 1-h exposure, all mice exposed at 5 ppm died; the other species survived that exposure and recovered slowly from severe damage to the respiratory organs. Animals exposed at 1 ppm for 1 h experienced hyperpnea.

### 7.3. Derivation of AEGL-3 Values

The highest concentration of tellurium hexafluoride causing no mortality in rabbits, guinea pigs, rats, and mice (1 ppm for 4 h) was used to derive AEGL-3 values (Kimmerle 1960). An interspecies uncertainty factor of 3 was applied because the four test species appeared to similarly sensitive to the acute effects of tellurium hexafluoride (Kimmerle 1960); however, that assessment is based on a small number of test animals (one to four per group). An intraspecies uncertainty factor of 3 was applied because tellurium hexafluoride is highly irritating and corrosive, and much of its toxicity is likely caused by a direct chemical effect on the tissue; that type of portal-of-entry effect is not expected to vary greatly among individuals. The steep concentration-response curve for tellurium hexafluoride implies little intraindividual variability. A modifying factor of 10 also was applied to account for the sparse database on tellurium hexafluoride and for the potential effects of tellurium. Thus, the total adjustment was 100. The concentration-exposure time relationship for many irritant and systemically-acting vapors and gases may be described by the equation $C^n \times t = k$, where the exponent n ranges from 0.8 to 3.5 (ten Berge et al. 1986). Data on tellurium hexafluoride were inadequate for determining an empirical value for n, so default values of n = 3 when extrapolating to shorter durations (10, 30, and 60 min) and n = 1 when extrapolating to longer durations (8 h) were used. The AEGL-3 values for tellurium hexafluoride are presented in Table 5-5, and the calculations are presented in Appendix A.

**TABLE 5-5** AEGL-3 Values for Tellurium Hexafluoride

| 10 min | 30 min | 1 h | 4 h | 8 h |
|---|---|---|---|---|
| 0.029 ppm (0.28 mg/m$^3$) | 0.020 ppm (0.20 mg/m$^3$) | 0.016 ppm (0.16 mg/m$^3$) | 0.010 ppm (0.10 mg/m$^3$) | 0.0050 ppm (0.049 mg/m$^3$) |

Because of the uncertainty associated with extrapolating a point-of-departure based on a 4-h exposure to a 10-min AEGL value, the 30-min AEGL-3 value is typically adopted as the 10-min value. For tellurium hexafluoride, however, this approach was not used and the 10-min value was calculated from the Kimmerle (1960) data. Several laboratory animal species were exposed to tellurium hexafluoride at 1 ppm for 1 h, and only hyperpnea, a nonlife-threatening end point, was observed in those animals.

## 8. SUMMARY OF AEGLS

### 8.1. AEGL Values and Toxicity End Points

AEGL values for tellurium hexafluoride are presented in Table 5-6. AEGL-1 values are not recommended because of insufficient data. Data were also insufficient for deriving AEGL-2 values. Because tellurium hexafluoride has been shown to have a steep concentration-response curve, AEGL-2 values were estimated by dividing the AEGL-3 values by 3. AEGL-3 values were based on the highest concentration of tellurium hexafluoride causing no deaths in laboratory animals (Kimmerle 1960).

### 8.2. Other Standards and Guidelines

AEGL values for tellurium hexafluoride are compared with other guidelines and standards for this chemical in Table 5-7. The time-weighted average exposure concentration for workers is 0.02 ppm (29 CFR Part 1910 [2006]; NIOSH 2011; ACGIH 2013). The American Conference of Governmental Industrial Hygienists established a threshold limit value – time-weighted average of 0.02 ppm (measured as tellurium) on the basis that tellurium hexafluoride is approximately 2.5 times as acutely toxic as ozone and to protect against respiratory effects (ACGIH 2001). The immediately dangerous to life or health value (NIOSH 1994) is based on the acute inhalation toxicity data from the studies by Kimmerle (1960).

**TABLE 5-6** AEGL Values for Tellurium Hexafluoride

| 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) | 0.0097 ppm (0.096 mg/m$^3$) | 0.0067 ppm (0.066 mg/m$^3$) | 0.0053 ppm (0.052 mg/m$^3$) | 0.0033 ppm (0.033 mg/m$^3$) | 0.0017 ppm (0.017 mg/m$^3$) |
| AEGL-3 (lethal) | 0.029 ppm (0.28 mg/m$^3$) | 0.020 ppm (0.20 mg/m$^3$) | 0.016 ppm (0.16 mg/m$^3$) | 0.010 ppm (0.10 mg/m$^3$) | 0.0050 ppm (0.049 mg/m$^3$) |

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

**TABLE 5-7** Standards and Guidelines for Tellurium Hexafluoride

| | Exposure Duration | | | | |
|---|---|---|---|---|---|
| Guideline | 10 min | 30 min | 1 h | 4 h | 8 h |
| AEGL-1 | NR | NR | NR | NR | NR |
| AEGL-2 | 0.0097 ppm | 0.0067 ppm | 0.0053 ppm | 0.0033 ppm | 0.0017 ppm |
| AEGL-3 | 0.029 ppm | 0.020 ppm | 0.016 ppm | 0.010 ppm | 0.0050 ppm |
| IDLH (NIOSH)[a] | – | 1 ppm | – | – | – |
| TLV-TWA (ACGIH)[b] | – | – | – | – | 0.02 ppm as Te |
| PEL-TWA (OSHA)[c] | – | – | – | – | 0.02 ppm as Te |
| REL-TWA (NIOSH)[d] | – | – | – | – | 0.02 ppm as Te |
| MAC (The Netherlands)[e] | – | – | – | – | 0.02 ppm |

[a]IDLH (immediately dangerous to life or health, National Institute for Occupational Safety and Health) (NIOSH 1994) represents the maximum concentration from which one could escape within 30 min without any escape-impairing symptoms or any irreversible health effects.
[b]TLV-TWA (threshold limit value – time-weighted average, American Conference of Governmental Industrial Hygienists) (ACGIH 2013) is the time-weighted average concentration for a normal 8-h workday and a 40-h work week, to which nearly all workers may be repeatedly exposed, day after day, without adverse effect.
[c]PEL-TWA (permissible exposure limit – time-weighted average, Occupational Health and Safety Administration) (29 CFR Part 1910 [2006]) is defined analogous to the ACGIH TLV-TWA, but is for exposures of no more than 10 h/day, 40 h/wk.
[d]REL-TWA (recommended exposure limit – time-weighted average, National Institute for Occupational Safety and Health) (NIOSH 2011) is defined analogous to the ACGIH TLV-TWA.
[e]MAC (maximaal aanvaaarde concentratie [maximal accepted concentration – peak category]) (Dutch Expert Committee for Occupational Standards, The Hague, The Netherlands (MSZW 2007) is defined analogous to the to the ACGIH TLV-TWA.

### 8.3. Data Adequacy and Research

No quantitative human data on tellurium hexafluoride are available, and only a few animal studies have been conducted. A single study of the acute toxicity of tellurium hexafluoride in rabbits, guinea pigs, rats, and mice is available (Kimmerle 1960), but only a few animals were tested and some potentially relevant end points were not evaluated. For example, humans acutely or repeatedly exposed to tellurium compounds frequently report somnolence, but the Kimmerle (1960) study did not examine that end point. A few studies of the related chemicals tellurium and tellurium pulveratum (Duckett 1970; Lampert et al. 1970; Malczewska-Toth 2012) found morphologic alterations in fetuses and demyelination in weanling rats after oral exposure; it is unknown whether reproductive and developmental toxicity would also occur following acute inhala-

tion exposure to tellurium hexafluoride. In the moist respiratory tract, tellurium hexafluoride slowly breaks down into hydrogen fluoride and tellurium; however, the contribution of the hydrolysis products to tellurium hexafluoride toxicity is unknown. No mechanistic data are available for other potential end points, including neurotoxicity and reproductive and developmental toxicity. Additional acute inhalation toxicity studies would help strengthen the basis of the AEGL values.

## 9. REFERENCES

ACGIH (American Conference of Governmental Industrial Hygienists). 2001. Documentation of the Threshold Limit Values and Biological Exposure Indices: Tellurium Hexafluoride. American Conference of Governmental Industrial Hygienists, Inc. Cincinnati, OH.

ACGIH (American Conference of Governmental Industrial Hygienists). 2013. TLVs and BEIs: Threshold Limit Values for Chemical and Physical Agents and Biological Exposure Indices. American Conference of Governmental Industrial Hygienists, Inc., Cincinnati, OH.

Amdur, M.I. 1958. Tellurium oxide: An animal study in acute toxicity. AMA Arch. Ind. Health 17(6):665-667.

Anthony, D.C., T.J. Montine, W.M. Valentine, and D.G. Graham. 2001. Toxic responses of the nervous system. P. 535-563 in Casarett & Doull's Toxicology: The Basic Science of Poisons, 6th Ed., C.D. Klaassen, ed. New York: McGraw-Hill.

Blackadder, E.S., and W.G. Manderson. 1975. Occupational absorption of tellurium: A report of two cases. Br. J. Ind. Med. 32(1):59-61.

Duckett, S. 1970. Fetal encephalopathy following ingestion of tellurium. Experientia 26(11):1239-1241.

HSDB (Hazardous Substances Data Bank). 2008. Tellurium Hexafluoride (CAS Reg. No. 7783-80-4). TOXNET, Specialized Information Services, U.S. National Library of Medicine, Bethesda, MD [online]. Available: http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB [accessed Sept. 10, 2013].

IPCS (International Programme on Chemical Safety). 1998. Tellurium Hexafluoride. UKPID Monograph [online] Available: http://www.inchem.org/documents/ukpids/ukpids/ukpid83.htm [accessed December 9, 2014].

Kimmerle, G. 1960. Comparative studies on the inhalation toxicity of sulfur-, selenium-, and tellurium-hexafluoride [in German]. Arch. Toxikol. 18:140-144.

Lampert, P., F. Garro, and A. Pentschew. 1970. Tellurium neuropathy. Acta Neuropathol. 15(4):308-317.

Malczewska-Toth, B. 2012. Phosphorus, selenium, tellurium, and sulfur. Pp. 841-884 in Patty's Toxicology, 6th Ed., P.E. Bingham, and B. Cohrssen, eds. Wiley Online Library.

MSZW (Ministerie van Sociale Zaken en Werkgelegenheid). 2007. OEL Database: Tellurium hexafluoride (as Te). The Social and Economic Council of the Netherlands, The Hague [online]. Available: http://www.ser.nl/en/grenswaarden/telluriumhexafluoride%20%20als%20te.aspx [accessed Dec. 9, 2014].

NIOSH (National Institute for Occupational Safety and Health). 1978. Occupational Health Guideline for Tellurium Hexafluoride. National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention, Atlanta, GA. September 1978

[online]. Available: http://www.cdc.gov/niosh/docs/81-123/pdfs/0588.pdf [accessed Sept. 20, 2013].

NIOSH (National Institute for Occupational Safety and Health). 1994. Documentation for Immediately Dangerous to Life and Health Concentrations (IDLHs): Tellurim hexafluoride (as Te) [online]. Available: http://www.cdc.gov/niosh/idlh/7783804.html [accessed Sept. 20, 2013].

NIOSH (National Institute for Occupational Safety and Health). 2011. NIOSH Pocket Guide to Chemical Hazards: Tellurium hexafluoride [online]. Available: http://www.cdc.gov/niosh/npg/npgd0588.html [accessed Sept. 10, 2013].

NRC (National Research Council). 1993. Guidelines for Developing Community Emergency Exposure Levels for Hazardous Substances. Washington, DC: National Academy Press.

NRC (National Research Council). 2001. Standing Operating Procedures for Developing Acute Exposure Guideline Levels for Hazardous Chemicals. Washington, DC: National Academy Press.

NRC (National Research Council). 2004a. Hydrogen fluoride. Pp. 123-197 in Acute Exposure Guideline Levels for Selected Airborne Chemicals, Vol. 4. Washington, DC: The National Academies Press.

NRC (National Research Council). 2004b. Uranium hexafluoride. Pp. 250-291 in Acute Exposure Guideline Levels for Selected Airborne Chemicals, Vol. 4. Washington, DC: The National Academies Press.

OSHA (Occupational Safety and Health Administration). 1996. Occupational Safety and Health Guideline for Tellurium Hexafluoride [online]. Available: http://www.osha.gov/SLTC/healthguidelines/telluriumhexafluoride/recognition.html [accessed Feb. 4, 2009].

Stavert, D.M., D,C. Archuleta, M.J. Behr, and B.E. Lehner. 1991. Relative acute toxicities of hydrogen fluoride, hydrogen chloride, and hydrogen bromide in nose- and pseudo-mouth-breathing rats. Fundam. Appl. Toxicol. 16(4):636-655.

Steinberg, H.H., S.C. Massari, A.C. Miner, and R. Rink. 1942. Industrial exposure to tellurium: Atmospheric studies and clinical evaluation. J. Ind. Hyg. Toxicol. 24:183-192.

ten Berge, W.F., A. Zwart, and L.M. Appelman. 1986. Concentration-time mortality response relationship of irritant and systemically acting vapours and gases. J. Hazard. Mater. 13(3):301-309.

# APPENDIX A

# DERIVATION OF AEGL VALUES

## Derivation of AEGL-1 Values

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

## Derivation of AEGL-2 Values

| | |
|---|---|
| Key study: | Kimmerle, G. 1960. Comparative studies on the inhalation toxicity of sulfur-, selenium-, and tellurium-hexafluoride [in German]. Arch. Toxikol. 18:140-144. |
| Toxicity end points: | Data were inadequate for deriving AEGL-2 values. However, the standing operating procedures for determining AEGL values specifies that AEGL-2 values for chemicals with steep concentrations-response curves may be estimated by dividing the AEGL-3 values by 3 (NRC 2001). Lethality data on tellurium hexafluoride demonstrates a steep-concentration response curve. All rabbits, guinea pigs, rats, and mice exposed at concentrations of 5, 10, 25, 50, or 100 ppm for 4 h died, and all mice exposed at 5 ppm for 1 h died. All animals exposed at 1 ppm for 1 or 4 h survived (Kimmerle 1960). |
| Calculations: | |
| 10-min AEGL-2: | 0.029 ppm ÷ 3 = 0.0097 ppm |
| 30-min AEGL-2: | 0.020 ppm ÷ 3 = 0.0067 ppm |
| 1-h AEGL-2: | 0.016 ppm÷ 3 = 0.0053 ppm |
| 4-h AEGL-2: | 0.010 ppm÷ 3 = 0.0033 ppm |
| 8-h AEGL-2: | 0.005 ppm÷ 3 = 0.0017 ppm |

## Derivation of AEGL-3 Values

| | |
|---|---|
| Key studies: | Kimmerle, G. 1960. Comparative studies on the inhalation toxicity of sulfur-, selenium-, and tellurium-hexafluoride [in German]. Arch. Toxikol. 18:140-144. |

| | |
|---|---|
| Toxicity end point: | Highest concentration causing no mortality in the guinea pig, rabbit, rat, and mouse (1 ppm for 4 h) |
| Uncertainty factors: | Interspecies: 3, because the guinea pig, rabbit, rat, and mouse appear to be similarly sensitive to the acute effects of tellurium hexafluoride; however, this assessment is based on a small number of animals.<br><br>Intraspecies: 3, because tellurium hexafluoride is highly irritating and corrosive and much of the toxicity is likely caused by a direct chemical effect on the tissues; that type of portal-of-entry effect is not expected to vary greatly among individuals. |
| Modifying factor: | 10, because of the sparse database on tellurium hexafluoride and the potential effects of tellurium |
| 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)<br>1 ppm ÷ 100 (total uncertainty factor) = 0.01 ppm<br>$(0.01 \text{ ppm})^3 \times 240 \text{ min} = 0.00024 \text{ ppm-min}$<br>$(0.01 \text{ ppm})^1 \times 240 \text{ min} = 2.4 \text{ ppm-min}$ |
| 10-min AEGL-3: | $C^3 \times 10 \text{ min} = 0.00024 \text{ ppm-min}$<br>C = 0.029 ppm |
| 30-min AEGL-3: | $C^3 \times 30 \text{ min} = 0.00024 \text{ ppm-min}$<br>C = 0.020 ppm |
| 1-h AEGL-3: | $C^3 \times 30 \text{ min} = 0.00024 \text{ ppm-min}$<br>C = 0.016 ppm |
| 4-h AEGL-3: | $C^1 \times 240 \text{ min} = 2.4 \text{ ppm-min}$<br>C = 0.010 ppm |
| 8-h AEGL-3: | $C^1 \times 480 \text{ min} = 2.4 \text{ ppm-min}$<br>C = 0.0050 ppm |

## APPENDIX B

## ACUTE EXPOSURE GUIDELINE LEVELS FOR TELLURIUM HEXAFLUORIDE

### Derivation Summary

### AEGL-1 VALUES

No AEGL-1 values were derived for tellurium hexafluoride because of insufficient data. Absence of AEGL-1 values does not imply that exposure below the AEGL concentrations are without adverse effects.

**AEGL-2 VALUES**

| 10 min | 30 min | 1 h | 4 h | 8 h |
|---|---|---|---|---|
| 0.0097 ppm | 0.0067 ppm | 0.0053 ppm | 0.0033 ppm | 0.0017 ppm |

Data adequacy: Data on tellurium hexafluoride were inadequate for deriving AEGL-2 values. However, the standing operating procedures for determining AEGL values specify that AEGL-2 values for chemicals with steep concentrations-response curves may be estimated by dividing the AEGL-3 values by 3 (NRC 2001). Lethality data on tellurium hexafluoride indicate a steep-concentration response curve. All rabbits, guinea pigs, rats, and mice exposed at concentrations of 5, 10, 25, 50, or 100 ppm for 4 h died, and all mice exposed at 5 ppm for 1 h died. All animals exposed at 1 ppm for 1 or 4 h survived (Kimmerle 1960).

**AEGL-3 VALUES**

| 10 min | 30 min | 1 h | 4 h | 8 h |
|---|---|---|---|---|
| 0.029 ppm | 0.020 ppm | 0.016 ppm | 0.010 ppm | 0.0050 ppm |

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

Test species/Strain/Number: Unspecified strains of rabbits (n = 1), guinea pigs (n = 1), rats (n = 2), and mice (n = 4)

Exposure route/Concentrations/Durations: Inhalation ; 1, 5, 10, 25, 50, 100 ppm for 4 h

Effects:
1 ppm: respiratory dysfunction, pulmonary edema
5 ppm: death after 4-24 h
10 ppm: death after 100-140 min
25 ppm: death after 60-110 min
50 ppm: death after 45-70 min
100 ppm: death after 10-30 min

End point/Concentration/Rationale: Highest concentration causing no mortality (1 ppm for 4 h)

*(Continued)*

**AEGL-3 VALUES** Continued

| |
|---|
| Uncertainty factors/Rationale:<br>Total uncertainty factor: 10<br>Interspecies: 3, because the guinea pig, rabbit, rat, and mouse appear to be similarly sensitive to the acute effects of tellurium hexafluoride; however, this assessment is based on a small number of animals.<br>Intraspecies: 3, because tellurium hexafluoride is highly irritating and corrosive and much of the toxicity is likely caused by a direct chemical effect on the tissues; that type of portal-of-entry effect is not expected to vary greatly among individuals. |
| Modifying factor: 10, because of the sparse database on tellurium hexafluoride and to account for potential effects of tellurium |
| Animal-to-human dosimetric adjustment: None |
| 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). |
| Data adequacy: Tellurium hexafluoride has a sparse database consisting of one lethality study in laboratory animals. |

## APPENDIX C

## CATEGORY PLOT FOR TELLURIUM HEXAFLUORIDE

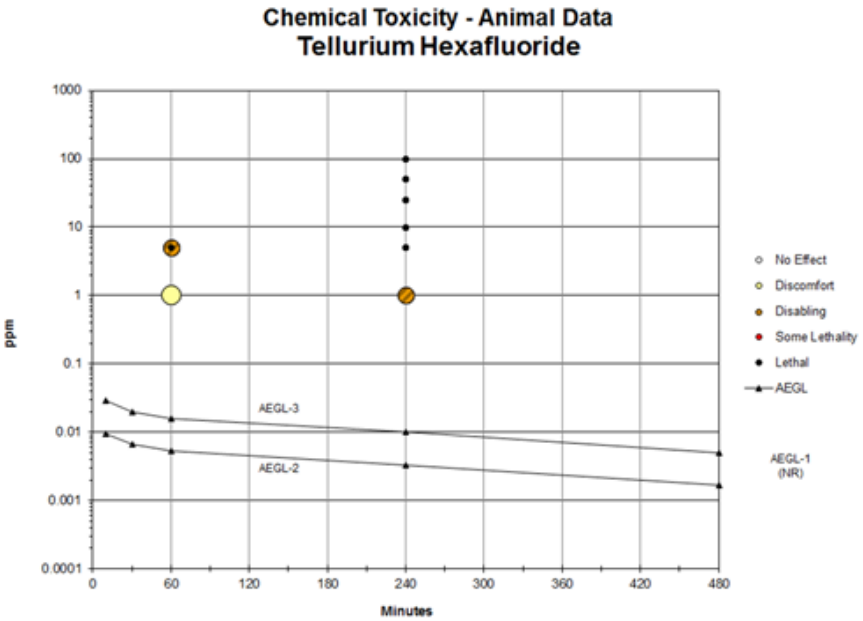


**FIGURE C-1** Category plot of toxicity data and AEGL values for tellurium hexafluoride.

**TABLE D-1** Data Used in the Category Plot for Tellurium Hexafluoride

| Source | Species | Sex | No. of Exposures | ppm | Minutes | Category | Comments |
|---|---|---|---|---|---|---|---|
| AEGL-2 | | | | 0.0097 | 10 | AEGL | |
| AEGL-2 | | | | 0.0067 | 30 | AEGL | |
| AEGL-2 | | | | 0.0053 | 60 | AEGL | |
| AEGL-2 | | | | 0.0033 | 240 | AEGL | |
| AEGL-2 | | | | 0.0017 | 480 | AEGL | |
| AEGL-3 | | | | 0.029 | 10 | AEGL | |
| AEGL-3 | | | | 0.020 | 30 | AEGL | |
| AEGL-3 | | | | 0.016 | 60 | AEGL | |
| AEGL-3 | | | | 0.010 | 240 | AEGL | |
| AEGL-3 | | | | 0.0050 | 480 | AEGL | |
| Kimmerle 1960 | Rabbit | M | 1 | 1 | 240 | 2 | Respiratory dysfunction, pulmonary edema |
| Kimmerle 1960 | Rabbit | M | 1 | 5 | 240 | 3 | Death after 8 h |
| Kimmerle 1960 | Rabbit | M | 1 | 10 | 240 | 3 | Death after 140 min |
| Kimmerle 1960 | Rabbit | M | 1 | 25 | 240 | 3 | Death after 80 min |
| Kimmerle 1960 | Rabbit | M | 1 | 50 | 240 | 3 | Death after 60 min |
| Kimmerle 1960 | Rabbit | M | 1 | 100 | 240 | 3 | Death after 15 min |
| Kimmerle 1960 | Rabbit | M | 1 | 1 | 60 | 1 | Hyperpnea |
| Kimmerle 1960 | Rabbit | M | 1 | 5 | 60 | 2 | Severe damage to respiratory organs |
| Kimmerle 1960 | Guinea pig | M | 1 | 1 | 240 | 2 | Respiratory dysfunction, pulmonary edema |
| Kimmerle 1960 | Guinea pig | M | 1 | 5 | 240 | 3 | Death after 8 h |
| Kimmerle 1960 | Guinea pig | M | 1 | 10 | 240 | 3 | Death after 140 min |

*(Continued)*

**TABLE D-1** Continued

| Source | Species | Sex | No. of Exposures | ppm | Minutes | Category | Comments |
|---|---|---|---|---|---|---|---|
| Kimmerle 1960 | Guinea pig | M | 1 | 25 | 240 | 3 | Death after 80 min |
| Kimmerle 1960 | Guinea pig | M | 1 | 50 | 240 | 3 | Death after 60 min |
| Kimmerle 1960 | Guinea pig | M | 1 | 100 | 240 | 3 | Death after 15 min |
| Kimmerle 1960 | Guinea pig | M | 1 | 1 | 60 | 1 | Hyperpnea |
| Kimmerle 1960 | Guinea pig | M | 1 | 5 | 60 | 2 | Severe damage to respiratory organs |
| Kimmerle 1960 | Rat | M | 1 | 1 | 240 | 2 | Respiratory dysfunction, pulmonary edema |
| Kimmerle 1960 | Rat | M | 1 | 5 | 240 | 3 | Death after 8 h |
| Kimmerle 1960 | Rat | M | 1 | 10 | 240 | 3 | Death after 140 min |
| Kimmerle 1960 | Rat | M | 1 | 25 | 240 | 3 | Death after 80 min |
| Kimmerle 1960 | Rat | M | 1 | 50 | 240 | 3 | Death after 60 min |
| Kimmerle 1960 | Rat | M | 1 | 100 | 240 | 3 | Death after 15 min |
| Kimmerle 1960 | Rat | M | 1 | 1 | 60 | 1 | Hyperpnea |
| Kimmerle 1960 | Rat | M | 1 | 5 | 60 | 2 | Severe damage to respiratory organs |
| Kimmerle 1960 | Mouse | M | 1 | 1 | 240 | 2 | Respiratory dysfunction, pulmonary edema |
| Kimmerle 1960 | Mouse | M | 1 | 5 | 240 | 3 | Death after 8 h |
| Kimmerle 1960 | Mouse | M | 1 | 10 | 240 | 3 | Death after 140 min |
| Kimmerle 1960 | Mouse | M | 1 | 25 | 240 | 3 | Death after 80 min |
| Kimmerle 1960 | Mouse | M | 1 | 50 | 240 | 3 | Death after 60 min |
| Kimmerle 1960 | Mouse | M | 1 | 100 | 240 | 3 | Death abate 15 min |
| Kimmerle 1960 | Mouse | M | 1 | 1 | 60 | 1 | Hyperpnea |
| Kimmerle 1960 | Mouse | M | 1 | 5 | 60 | 3 | Death between 24-36 h |

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