Acute Exposure Guideline Levels for Selected Airborne Chemicals: Volume 19

ISBN
978-0-309-36894-0

224 pages
6 x 9
PAPERBACK (2015)

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

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VOLUME 19

Committee on Acute Exposure Guideline Levels

Committee on Toxicology

Board on Environmental Studies and Toxicology

Division on Earth and Life Studies

NATIONAL RESEARCH COUNCIL
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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 between the National Academy of Sciences and the U.S. Department of Defense. 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: 978-0-309-36894-0
International Standard Book Number-10: 0-309-36894-4

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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.

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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 (1×10^{-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 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

1

Cyanide Salts[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 Cheryl Bast (Oak Ridge National Laboratory), Heather Carlson-Lynch (SRC, Inc.), Chemical Manager Ralph Gingell (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

Sodium cyanide, potassium cyanide, and calcium cyanide are simple inorganic cyanide salts with an almond-like odor. They may react with water or moist air to release toxic, corrosive, or flammable gases. Reaction with water may generate heat which will increase the concentration of hydrogen cyanide fumes in the air (HSDB 2005a,b; 2014).

Even though the cyanide salts are solids, inhalation of dusts may result in ionization in the nasal or pulmonary mucosal fluids to yield cyanide. The salts may also react with water in humid air and be inhaled as hydrogen cyanide. In both cases, there will be systemic absorption of cyanide ion, which is the toxic moiety. Cyanide inhibits cellular respiration by blocking electron transfer from cytochrome oxidase to oxygen, causing tissue hypoxia and cell death. Low concentrations or low dose rates of cyanide are tolerated by detoxification by rhodanese to thiocyanate (Kopras 2012).

In the absence of appropriate chemical-specific data on the three cyanide salts, the AEGL-1, AEGL-2, and AEGL-3 values for hydrogen cyanide (NRC 2002) were used to obtain the AEGL values for the salts. Hydrogen cyanide was used as a surrogate for data on the cyanide salts because qualitative (clinical signs) and quantitative (adjusted rat oral LD_{50} [lethal dose, 50% lethality] values) data suggest that the cyanide moiety is responsible for the acute toxicity of the cyanide salts. Thus, the concentrations of the cyanide salts that would generate hydrogen cyanide concentrations equivalent to that chemical's AEGL values was calculated. The calculations assumed a temperature of 25°C, a pressure of

760 mm Hg, and complete hydrolysis (one mole of sodium cyanide or potassium cyanide yields one mole of hydrogen cyanide, and one mole of calcium cyanide will yield two moles of hydrogen cyanide).

The calculated AEGL values for the cyanide salts are presented Table 1-1.

1. INTRODUCTION

Sodium cyanide, potassium cyanide, and calcium cyanide are simple inorganic cyanide salts with an almond-like odor. They may react with water or moist air to release toxic, corrosive, or flammable gases. Reaction with water may generate heat which will increase the concentration of hydrogen cyanide fumes in the air (HSDB 2005a,b; 2014).

Even though the salts are solids, inhalation of dusts may result in ionization in the nasal or pulmonary mucosal fluids to yield cyanide. The salts may also react with water in humid air and be inhaled as hydrogen cyanide. In both cases, there will be systemic absorption of cyanide ion, which is the toxic moiety. Cyanide inhibits cellular respiration by blocking electron transfer from cytochrome oxidase to oxygen, causing tissue hypoxia and cell death. Low concentrations or low dose rates of cyanide are tolerated by detoxification by rhodanese to thiocyanate (Kopras 2012).

TABLE 1-1 AEGL Values for Cyanide Salts[a]

Classification	10 min	30 min	1 h	4 h	8 h
Sodium Cyanide					
AEGL-1	5.0 mg/m^3	5.0 mg/m^3	4.0 mg/m^3	2.6 mg/m^3	2.0 mg/m^3
AEGL-2	34 mg/m^3	20 mg/m^3	14 mg/m^3	7.0 mg/m^3	5.0 mg/m^3
AEGL-3	54 mg/m^3	42 mg/m^3	30 mg/m^3	17 mg/m^3	13 mg/m^3
Potassium Cyanide					
AEGL-1	6.6 mg/m^3	6.6 mg/m^3	5.3 mg/m^3	3.5 mg/m^3	2.7 mg/m^3
AEGL-2	45 mg/m^3	27 mg/m^3	19 mg/m^3	9.3 mg/m^3	6.6 mg/m^3
AEGL-3	72 mg/m^3	56 mg/m^3	40 mg/m^3	23 mg/m^3	18 mg/m^3
Calcium Cyanide[b]					
AEGL-1	4.7 mg/m^3	4.7 mg/m^3	3.8 mg/m^3	2.4 mg/m^3	1.9 mg/m^3
AEGL-2	32 mg/m^3	19 mg/m^3	13 mg/m^3	6.6 mg/m^3	4.7 mg/m^3
AEGL-3	51 mg/m^3	39 mg/m^3	28 mg/m^3	16 mg/m^3	12 mg/m^3

[a]Airborne concentrations of these salts will produce the equivalent AEGL values for hydrogen cyanide.

[b]Although the adjusted rat oral LD_{50} value for calcium cyanide is much greater than would be expected on a molar basis for cyanide (suggesting that it is a less toxic compound), the production of two moles of hydrogen cyanide was assumed per mole of calcium cyanide. That assumption will yield protective AEGL values.

The rate of cyanide generation depends on ambient temperature, humidity, pH, and the particular cyanide salt; sodium and potassium cyanide behave differently than calcium cyanide. In moist air and at normal temperature, sodium and potassium cyanide slowly decompose and generate hydrogen cyanide (Gail et al. 2011). In the presence of strong acids, complete decomposition and release of hydrogen cyanide occurs (Gail et al. 2011). In dry air, both sodium and potassium cyanide are stable even at high temperatures (Gail et al. 2011).

The alkaline earth cyanides (such as calcium cyanide) are less stable than the alkali metal cyanides (sodium or potassium cyanides) (Gail et al. 2011). Alkaline earth metal cyanides decompose at high temperature, generating hydrogen cyanide. In addition, alkaline earth metal cyanides readily hydrolyze in moist air to release hydrogen cyanide (Pesce 2010; Gail et al. 2011). The amount of hydrogen cyanide released from commercially-produced calcium cyanide (for fumigation purposes) is about 50% of the weight of the cyanide in granular formulation (FAO 1965; Bond 1984).

Hydrolysis constants for sodium and potassium cyanide are similar (2.51×10^{-5} and 2.54×10^{-5}, respectively, at 25°C) (Pesce 2010); data on the hydrolysis of calcium cyanide were not found. Hydrolysis reactions for the three cyanide salts are shown below (Pesce 2010). One mole of sodium cyanide or potassium cyanide may react with water or moisture to produce a maximum of one mole of hydrogen cyanide by the following reactions:

$$NaCN + H_2O \rightarrow HCN + NaOH$$
$$KCN + H_2O \rightarrow HCN + KOH$$

One mole of calcium cyanide may react with water or moisture to produce a maximum of two moles of hydrogen cyanide by the following reaction:

$$Ca(CN)_2 + 2H_2O \rightarrow 2HCN + Ca(OH)_2$$

Sodium cyanide is a white crystalline solid, and may be prepared by heating sodium amide with carbon or by melting sodium chloride and calcium cyanamide together in an electric furnace. It is used for extracting gold and silver from ores, heat treating of metals, electroplating, various organic reactions, and the manufacturing of adiponitrile (Kopras 2012). US production of sodium cyanide was reported as "at least" 1.14×10^{11} grams in 1977, and US imports were reported as 2.77×10^{7} pounds in 1986 (HSDB 2005a).

Potassium cyanide, a white crystalline solid, is prepared by reaction of an aqueous solution of potassium hydroxide with hydrogen cyanide. It is used for fine silver plating, dyes and specialty products, and fumigation of fruit trees, ships, railway cars, and warehouses. US production information was not available; however, US imports were reported as 1,468,423 pounds in 1987 (HSDB 2005b).

Calcium cyanide is a white powder, and is prepared from lime, calcium oxide, coke, and nitrogen in an electric furnace. The commercial product is dark

gray because of the presence of carbon. It is used in the extraction of precious metal ores, adsorption of gold complexes on carbon, as a fumigant, and as a rodenticide (Kopras 2012). US production information on calcium cyanide was not available; however, US imports were reported as 468,246 pounds in 1986 (HSDB 2014).

The chemical and physical properties of the three cyanide salts are presented in Tables 1-2, 1-3, and 1-4.

TABLE 1-2 Chemical and Physical Properties of Sodium Cyanide

Parameter	Value	References
Synonyms	Cyanogran; cyanide of sodium; cymag; hydrocyanic acid sodium salt; cyanobrik; white cyanide	Kopras 2012
CAS registry no.	143-33-9	HSDB 2005a
Chemical formula	NaCN	HSDB 2005a
Molecular weight	49.0	HSDB 2005a
Physical state	White crystalline solid	HSDB 2005a
Melting point	563°C	HSDB 2005a
Boiling point	1,496°C	HSDB 2005a
Density /specific gravity	1.595 g/cm^3 at 20°C	HSDB 2005a
Solubility in water	48 g/100 mL water at 10°C; forms HCN	HSDB 2005a
Vapor pressure	1 mm Hg at 817°C	HSDB 2005a
Hydrolysis constant	2.51×10^{-5} per second at 25°C; yields calculated half-life of 7.7 h	Pesce 2010
Conversion factors	1 ppm = 2.0 mg/m^3 1 mg/m^3 = 0.50 ppm	

TABLE 1-3 Chemical and Physical Properties of Potassium Cyanide

Parameter	Value	References
Synonyms	Hydrocyanic acid potassium salt	Kopras 2012
CAS registry no.	151-50-8	HSDB 2005b
Chemical formula	KCN	HSDB 2005b
Molecular weight	65.11	HSDB 2005b
Physical state	White crystalline solid	HSDB 2005b
Melting point	634°C	HSDB 2005b
Density/specific gravity	1.55 at 20°C	HSDB 2005b
Solubility in water	100 g/100 mL water at >176°F; forms HCN	HSDB 2005b
Hydrolysis constant	2.54×10^{-5} per sec at 25°C; calculated half-life of 7.6 h	Pesce 2010
Conversion factors	1 ppm = 2.7 mg/m^3 1 mg/m^3 = 0.38 ppm	

TABLE 1-4 Chemical and Physical Properties of Calcium Cyanide

Parameter	Value	References
Synonyms	Calcyanide; cyanogas; black cyanide, aero; calcium cyanide, tech grade	Kopras 2012
CAS registry no.	592-01-8	HSDB 2014
Chemical formula	$Ca(CN)_2$	HSDB 2014
Molecular weight	92.12	HSDB 2014
Physical state	White powder, solid	HSDB 2014
Melting point	640°C (estimated by extrapolation because of decomposition)	HSDB 2014
Density/specific gravity	1.853 at 20°C	HSDB 2014
Solubility in water	Soluble in water, gradual liberation of HCN	HSDB 2014
Conversion factors	1 ppm = 3.8 mg/m^3 1 mg/m^3 = 0.27 ppm	

2. HUMAN TOXICITY DATA

No human toxicity data on sodium, potassium, or calcium cyanide were found. There are numerous reports of occupational exposure to hydrogen cyanide (see NRC 2002).

3. ANIMAL TOXICITY DATA

No animal toxicity data on sodium, potassium, or calcium cyanide were found. However, the toxicity data base for hydrogen cyanide is robust. Lethality data are available from studies of dogs, rats, mice, and rabbits, and nonlethal toxicity data are available from studies of nonhuman primates, rats, and mice (see NRC 2002).

4. SPECIAL CONSIDERATIONS

4.1. Metabolism and Disposition

Solid cyanide salts deposited on moist respiratory-tract surfaces may hydrolyze and release absorbable cyanide. Another scenario would involve atmospheric hydrolysis of metal cyanides to hydrogen cyanide vapor. Metabolism and disposition information on hydrogen cyanide is summarized in NRC (2002).

Dermal absorption of cyanide salts depends on the form of the salt and the condition of the skin. Dermal exposure to cyanide salts in solution, or exposure of moist or abraded skin to dry cyanide salts, can result in significant absorption of cyanide ion or hydrogen cyanide (Ballantyne 1987). The permeability of cyanide ion across human skin in vitro was estimated to be 3.5×10^{-4} cm/h, and the

permeability of hydrogen cyanide was 100×10^{-4} cm/h (Dugard 1987). In addition, skin exposure to very high air concentrations of hydrogen cyanide has resulted in human poisoning (Potter 1950).

4.2. Mechanism of Toxicity

Hydrogen cyanide is a systemic poison that acts on the central nervous system. Hydrogen cyanide interrupts cellular respiration by blocking electron transfer from cytochrome oxidase to oxygen. Tissue concentrations of oxygen rise, resulting in increased tissue oxygen tension and decreased unloading for oxyhemoglobin. As a consequence, oxidative metabolism may slow to a point where it cannot meet metabolic demands. This is particularly critical in the brainstem nuclei where lack of an energy source results in central respiratory arrest and death. Cyanide can inhibit many other enzymes, particularly those that contain iron or copper, but cytochrome oxidase appears to be the most sensitive enzyme. Cyanide also stimulates the chemoreceptors of the carotid and aortic bodies to produce a brief period of hyperpnea. Cardiac irregularities may occur, but death is due to respiratory arrest (Smith 1996; Kopras 2012). Brain lesions in animals have been associated with exposure to hydrogen cyanide at high concentrations (ATSDR 2006).

4.3. Structure-Activity Relationships

As noted earlier, no acute inhalation toxicity data on the cyanide salts were available. However, acute oral toxicity data suggest both qualitatively (clinical signs) and quantitatively (rat LD_{50} values) that the cyanide moiety is responsible for the acute toxicity of the cyanide salts. Cyanide-induced clinical effects are indistinguishable in humans and animals after inhalation or dermal exposure to hydrogen cyanide vapor or after oral exposure to sodium or potassium cyanide. Clinical signs include headaches, dizziness, nausea, inability to concentrate, thoracic oppression, palpitation, numbness, weakness, rapid pulse, face flushing, unconsciousness, and death (Kopras 2012).

Rat oral LD_{50} values support the contention that cyanide is the toxic moiety. The LD_{50} values for the salts and the LD_{50} values adjusted as equivalent doses of cyanide are presented in Table 1-5. The adjusted values for hydrogen, sodium, and potassium cyanide are comparable whereas the adjusted value for calcium cyanide is much greater (suggesting a less toxic compound) than would be expected on a molar basis for cyanide. The difference may be due to a slower hydrolysis rate, allowing for more efficient detoxification, relative to the other cyanide salts. (Although hydrolysis rates were not found, water solubility/reactivity is described as “forms hydrogen cyanide” for sodium and potassium cyanides [HSDB 2005a,b], and “gradually liberates hydrogen cyanide” for calcium cyanide [HSDB 2014]).

TABLE 1-5 Lethality in Rats Exposed Orally to Hydrogen Cyanide and Cyanide Salts

Compound	LD_{50}, mg/kg (sex)	Adjusted LD_{50}, mg/kg CN^-	Reference
HCN	4.2 (F)	4.1	Ballantyne 1987
NaCN	5.7 (F)	3.0	Ballantyne 1987
	15 (M)	8.0	Smyth et al. 1969
KCN	7.5 (F)	3.0	Ballantyne 1987
	10 (M)	4.0	Hayes 1967
	6 (M)	2.4	Lorke 1983
$Ca(CN)_2$	39 (M)	22	Smyth et al. 1969

4.4. Other Relevant Information

4.4.1. Concurrent Exposure Issues

Because hydrogen cyanide is the toxic moiety of all three salts, and may also be generated by other compounds, coexposure to multiple cyanide salts or other sources of cyanide will result in greater cumulative exposure to cyanide. Exposures should be expressed as cyanide ion and compared with the AEGLs expressed in the same manner to ensure that cumulative exposure is evaluated.

5. DATA ANALYSIS FOR AEGL-1

5.1. Human Data Relevant to AEGL-1

No human data relevant to developing AEGL-1 values for the cyanide salts were found.

5.2. Animal Data Relevant to AEGL-1

No animal data relevant to developing AEGL-1 values for the cyanide salts were found.

5.3. Derivation of AEGL-1 Values

In the absence of appropriate chemical-specific data for the cyanide salts, the AEGL-1 values for hydrogen cyanide (NRC 2002) were used to obtain AEGL-1 values for them. The use of hydrogen cyanide as a surrogate for the cyanide salts is deemed appropriate because qualitative (clinical signs) and quantitative (adjusted rat oral LD_{50} values) data suggest that the cyanide moiety is responsible for the acute toxicity of the cyanide salts. In addition, because hydrolysis of cyanide salts in the air or moist respiratory tract may be incomplete (whereas hydrolysis is likely complete after oral exposure due to the low pH of the stomach), the use of hydrogen cyanide as a surrogate for derivation of AEGL values is expected to be conservative.

The hydrogen cyanide AEGL-1 values were used as target values for calculating the concentrations of cyanide salt needed to generate the hydrogen cyanide AEGL values. The calculations assumed a temperature of 25°C, a pressure of 760 mm Hg, and complete hydrolysis. The AEGL-1 values for the cyanide salts are presented in Table 1-6, the calculations are presented in Appendix A, and derivation summary tables are provided in Appendix C. For comparison, the calculations and AEGL derivation summary tables for hydrogen cyanide are presented in Appendix B and Appendix D, respectively.

6. DATA ANALYSIS FOR AEGL-2

6.1. Human Data Relevant to AEGL-2

No human data relevant to developing AEGL-2 values for the cyanide salts were found.

6.2. Animal Data Relevant to AEGL-2

No animal data relevant to developing AEGL-2 values for the cyanide salts were found.

6.3. Derivation of AEGL-2 Values

In the absence of appropriate chemical-specific data for the cyanide salts, the AEGL-2 values for hydrogen cyanide (NRC 2002) were used to obtain AEGL-2 values for the title cyanide salts. The use of hydrogen cyanide as a surrogate for the cyanide salts is deemed appropriate because qualitative (clinical signs) and quantitative (adjusted rat oral LD_{50} values) data suggest that the cyanide moiety is responsible for acute toxicity of the cyanide salts. In addition, because hydrolysis of cyanide salts in the air or moist respiratory tract may be incomplete (whereas hydrolysis is likely complete after oral exposure due to the low pH of the stomach), the use of hydrogen cyanide as a surrogate for derivation of AEGL values is expected to be conservative.

The hydrogen cyanide AEGL-2 values were used as target values for calculating the concentrations of cyanide salt needed to generate the hydrogen cyanide AEGL values. The calculations assumed a temperature of 25°C, a pressure of 760 mm Hg, and complete hydrolysis. The AEGL-2 values for the cyanide salts are presented in Table 1-7, the calculations are presented in Appendix A, and derivation summary tables for the cyanide salts are provided in Appendix C. For comparison, the calculations and AEGL derivation summary tables for hydrogen cyanide are presented in Appendix B and Appendix D, respectively.

TABLE 1-6 AEGL-1 Values for Cyanide Salts[a]

Compound	10 min	30 min	1 h	4 h	8 h
Sodium cyanide	5.0 mg/m^3	5.0 mg/m^3	4.0 mg/m^3	2.6 mg/m^3	2.0 mg/m^3
Potassium cyanide	6.6 mg/m^3	6.6 mg/m^3	5.3 mg/m^3	3.5 mg/m^3	2.7 mg/m^3
Calcium cyanide[b]	4.7 mg/m^3	4.7 mg/m^3	3.8 mg/m^3	2.4 mg/m^3	1.9 mg/m^3

[a]Airborne concentrations of these salts will produce the equivalent AEGL values for hydrogen cyanide.
[b]Although the adjusted rat oral LD_{50} value for calcium cyanide is much greater than would be expected on a molar basis for cyanide (suggesting that it is a less toxic compound), the production of two moles of hydrogen cyanide was assumed per mole of calcium cyanide. That assumption will yield protective AEGL values.

TABLE 1-7 AEGL-2 Values for Cyanide Salts[a]

Compound	10 min	30 min	1 h	4 h	8 h
Sodium cyanide	34 mg/m^3	20 mg/m^3	14 mg/m^3	7.0 mg/m^3	5.0 mg/m^3
Potassium cyanide	45 mg/m^3	27 mg/m^3	19 mg/m^3	9.3 mg/m^3	6.6 mg/m^3
Calcium cyanide[b]	32 mg/m^3	19 mg/m^3	13 mg/m^3	6.6 mg/m^3	4.7 mg/m^3

[a]Airborne concentrations of these salts will produce the equivalent AEGL values for hydrogen cyanide.
[b]Although the adjusted rat oral LD_{50} value for calcium cyanide is much greater than would be expected on a molar basis for cyanide (suggesting that it is a less toxic compound), the production of two moles of hydrogen cyanide was assumed per mole of calcium cyanide. That assumption will yield protective AEGL values.

7. DATA ANALYSIS FOR AEGL-3

7.1. Human Data Relevant to AEGL-3

No human data relevant to developing AEGL-3 values for the cyanide salts were found.

7.2. Animal Data Relevant to AEGL-3

No animal data relevant to developing AEGL-3 values for the cyanide salts were found.

7.3. Derivation of AEGL-3 Values

In the absence of appropriate chemical-specific data for the title cyanides, the AEGL-3 values for hydrogen cyanide (NRC 2002) were used to obtain AEGL-3 values for the title cyanide salts. The use of hydrogen cyanide as a surrogate for the cyanide salts is deemed appropriate because qualitative (clinical signs) and quantitative (adjusted rat oral LD_{50} values) data suggest that the cyanide moiety is responsible for acute toxicity of the cyanide salts. In addition,

because hydrolysis of cyanide salts in the air or moist respiratory tract may be incomplete (whereas hydrolysis is likely complete after oral exposure due to the low pH of the stomach), the use of hydrogen cyanide as a surrogate for derivation of AEGL values is expected to be conservative.

The hydrogen cyanide AEGL-3 values were used as target values for calculating the concentrations of cyanide salt needed to generate the hydrogen cyanide AEGL values. The calculations assumed a temperature of 25°C, a pressure of 760 mm Hg, and complete hydrolysis. The AEGL-3 values for the cyanide salts are presented in Table 1-8, the calculations are presented in Appendix A, and derivation summary tables for cyanide salts are provided in Appendix C. For comparison, the calculations and AEGL derivation summary tables for hydrogen cyanide are presented in Appendix B and Appendix D, respectively.

8. SUMMARY OF AEGLS

8.1. AEGL Values and Toxicity End Points

The AEGL values for the cyanide salts are presented in Table 1-9. They are based on molar adjustments of the AEGL values for hydrogen cyanide (NRC 2002).

8.2. Comparison with Other Standards and Guidelines

Exposure standards and guidelines for the cyanide salts are presented in Table 1-10, and are expressed in terms of cyanide ion. The 10-min AEGL-1 value for the cyanide salts (2.7 mg/m^3) is in reasonably good agreement with the short-term exposure limit of 5 mg/m^3 established by the American Conference of Governmental Industrial Hygienists (ACGIH 2001, 2013) and the National Institute for Occupational Safety and Health (NIOSH 2011). Likewise, the 30-min AEGL-3 value of 22 mg/m^3 for the cyanide salts is similar to the NIOSH (1994) immediately dangerous to life or health value of 25 mg/m^3.

TABLE 1-8 AEGL-3 Values for Cyanide Salts[a]

Compound	10 min	30 min	1 h	4 h	8 h
Sodium cyanide	54 mg/m^3	42 mg/m^3	30 mg/m^3	17 mg/m^3	13 mg/m^3
Potassium cyanide	72 mg/m^3	56 mg/m^3	40 mg/m^3	23 mg/m^3	18 mg/m^3
Calcium cyanide[b]	51 mg/m^3	39 mg/m^3	28 mg/m^3	16 mg/m^3	12 mg/m^3

[a]Airborne concentrations of these salts will produce the equivalent AEGL values for hydrogen cyanide.

[b]Although the adjusted rat oral LD_{50} value for calcium cyanide is much greater than would be expected on a molar basis for cyanide (suggesting that it is a less toxic compound), the production of two moles of hydrogen cyanide was assumed per mole of calcium cyanide. That assumption will yield protective AEGL values.

TABLE 1-9 AEGL Values for Cyanide Salts[a]

Classification	10 min	30 min	1 h	4 h	8 h
Sodium Cyanide					
AEGL-1	5.0 mg/m^3	5.0 mg/m^3	4.0 mg/m^3	2.6 mg/m^3	2.0 mg/m^3
AEGL-2	34 mg/m^3	20 mg/m^3	14 mg/m^3	7.0 mg/m^3	5.0 mg/m^3
AEGL-3	54 mg/m^3	42 mg/m^3	30 mg/m^3	17 mg/m^3	13 mg/m^3
Potassium Cyanide					
AEGL-1	6.6 mg/m^3	6.6 mg/m^3	5.3 mg/m^3	3.5 mg/m^3	2.7 mg/m^3
AEGL-2	45 mg/m^3	27 mg/m^3	19 mg/m^3	9.3 mg/m^3	6.6 mg/m^3
AEGL-3	72 mg/m^3	56 mg/m^3	40 mg/m^3	23 mg/m^3	18 mg/m^3
Calcium Cyanide[b]					
AEGL-1	4.7 mg/m^3	4.7 mg/m^3	3.8 mg/m^3	2.4 mg/m^3	1.9 mg/m^3
AEGL-2	32 mg/m^3	19 mg/m^3	13 mg/m^3	6.6 mg/m^3	4.7 mg/m^3
AEGL-3	51 mg/m^3	39 mg/m^3	28 mg/m^3	16 mg/m^3	12 mg/m^3

[a]Airborne concentrations of these salts will produce the equivalent AEGL values for hydrogen cyanide.
[b]Although the adjusted rat oral LD_{50} value for calcium cyanide is much greater than would be expected on a molar basis for cyanide (suggesting that it is a less toxic compound), the production of two moles of hydrogen cyanide was assumed per mole of calcium cyanide. That assumption will yield protective AEGL values.

TABLE 1-10 Standards and Guidelines for Cyanide Salts (Expressed as CN^-)

	Exposure Duration				
Guideline	10 min	30 min	1 h	4 h	8 h
AEGL-1	2.7 mg/m^3	2.7 mg/m^3	2.1 mg/m^3	1.3 mg/m^3	1.1 mg/m^3
AEGL-2	18 mg/m^3	11 mg/m^3	7.5 mg/m^3	3.8 mg/m^3	2.7 mg/m^3
AEGL-3	29 mg/m^3	22 mg/m^3	16 mg/m^3	9.1 mg/m^3	7.0 mg/m^3
IDLH (NIOSH)[a]	–	25 mg/m^3	–	–	–
PEL-TWA (OSHA)[b]	–	–	–	–	11 mg/m^3
TLV-STEL (ACGIH)[c]	5.0 mg/m^3	–	–	–	–
REL-STEL (NIOSH)[d]	5.0 mg/m^3	–	–	–	–
MAK (Germany)[e]	–	–	–	–	2.0 mg/m^3
MAC-Peak Category (The Netherlands)[f]	10 mg/m^3 [15 min]	–	–	–	1.0 mg/m^3
CLV (Sweden)[g]	–	–	–	–	5.0 mg/m^3

[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]PEL-TWA (permissible exposure limit – time-weighted average, Occupational Safety and Health Administration) (OSHA 1978) is the time-weighted average concentrations for a 10-h workday and a 40-h workweek, to which nearly all workers may be repeatedly exposed, day after day, without adverse effect.

[c]TLV-STEL (threshold limit value – short-term exposure limit, American Conference of Governmental Industrial Hygienists) (ACGIH 2001, 2013) is defined as a 15-min time-weighted average exposure which should not be exceeded at any time during the workday even if the 8-h time-weighted average is within the threshold-limit value–time-weighted average. Exposures above the threshold-limit value–time-weighted average up to the STEL should not be longer than 15 min and should not occur more than four times per day. There should be at least 60 min between successive exposures in that range. Value is for hydrogen cyanide and sodium, potassium, and calcium cyanides (as cyanide).
[d]REL-STEL (recommended exposure limits – short-term exposure limit, National Institute for Occupational Safety and Health) (NIOSH 2011) is defined analogous to the ACGIH TLV-STEL.
[e]MAK (maximale arbeitsplatzkonzentration [maximum workplace concentration], Deutsche Forschungsgemeinschaft [German Research Association]) (DFG 2007) is the time-weighted average concentrations for a normal 8-h workday and a 40-h workweek, to which nearly all workers may be repeatedly exposed, day after day, without adverse effect.
[f]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 ACGIH-ceiling.
[g]CLV (ceiling limit value, Swedish Work Environment Authority) (SWEA 2005) is the maximum acceptable average concentration limit value (time-weighted average) for a workday. Value is for cyanides and hydrogen cyanide (as CN) total dust.

8.3. Data Adequacy and Research Needs

There are no human or animal inhalation data for sodium, potassium, or calcium cyanide. However, data suggest that the cyanide moiety is responsible for the acute toxicity of these compounds, and the hydrogen cyanide data set is fairly robust.

9. REFERENCES

ACGIH (American Conference of Governmental Industrial Hygienists). 2001. Documentation of the Threshold Limit Values and Biological Exposure Indices: Hydrogen Cyanide and Cyanide Salts, as CN. American Conference of Governmental Industrial Hygienists, Inc., Cincinnati, OH.

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

ATSDR (Agency for Toxic Substances and Disease Registry). 2006. Toxicological Profile for Cyanide. U.S. Department of Health and Human Services, Public Health Service, Agency for Toxic Substances and Disease Registry, Atlanta, GA [online]. Available: http://www.atsdr.cdc.gov/toxprofiles/tp8.pdf [accessed Nov. 19, 2014].

Ballantyne, B. 1987. Toxicology of cyanides. Pp. 41-126 in Clinical and Experimental Toxicology of Cyanides, B. Ballantyne, and T.C. Marrs, eds. Bristol: Wright.

Bond, E.J. 1984. Manual of Fumigation for Insect Control. FAO Plant Production and Protection Papers No. 54. Rome: Food and Agriculture Organization of the United

Nations [online]. Available: http://www.fao.org/docrep/X5042E/X5042E00.htm [accessed Nov. 19, 2014].

DFG (Deutsche Forschungsgemeinschaft). 2007. List of MAK and BAT Values 2007: Maximum Concentrations and Biological Tolerance Values at the Workplace. Report No. 43. Weinheim, Germany: Wiley-VCH.

Dugard, P.H. 1987. The absorption of cyanide through human skin in vitro from solutions of sodium cyanide and gaseous HCN. Pp. 127-137 in Clinical and Experimental Toxicology of Cyanides, B. Ballantyne, and T.C. Marrs, eds. Bristol: Wright.

El Ghawabi, S.H., M.A. Gaafar, A.A. El-Saharti, S.H. Ahmed, K.K. Malash, and R. Fares. 1975. Chronic cyanide exposure: A clinical, radioisotope, and laboratory study. Br. J. Ind. Med. 32(3):215-219.

FAO (Food and Agriculture Organization of the United Nations). 1965. Evaluation of the Hazards to Consumers Resulting from the Use of Fumigants in the Protection of Food. Joint Meeting of the FAO Committee on Pesticides in Agriculture and the WHO Expert Committee on Pesticide Residues, March 15-22, 1965. FAO Meeting Report No. PL/1965/10/2; WHO/Food Add/28.65. Rome: FAO.

Gail, E., S. Gos, R. Kulzer, J. Lorosch, A. Rubo, M. Sauer, R. Kellens, J. Reddy, N. Steier, and W. Hasenpusch. 2011. Cyano compounds, inorganic. In Ullmann's Encyclopedia of Industrial Chemistry. Wiley Online Library.

Grabois, B. 1954. Exposure to hydrogen cyanide in processing of apricot kernels. Monthly Review NY Department of Labor 33(September):33-36.

Hardy, H.L., W.M. Jeffries, M.M. Wasserman, and W.R. Waddell. 1950. Thiocyanate effect following industrial cyanide exposure - report of two cases. New Engl. J. Med. 242(25):968-972.

Haskell Laboratory. 1981. Inhalation Toxicity of Common Combustion Gases. Haskell Laboratory Report No. 238-81. E.I. du Pont de Nemours and Company, Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE.

Hayes, W.J. 1967. The 90-day LD_{50} and chronicity factors as a measure of toxicity. Toxicol. Appl. Pharmacol. 11:327-335.

HSDB (Hazardous Substances Data Bank). 2005a. Sodium Cyanide (CASRN 143-33-9). TOXNET Toxicology Data Network, U.S. National Library of Medicine, Bethesda, MD [online]. Available: http://toxnet.nlm.nih.gov/cgi-bin/sis [accessed Nov. 19, 2014].

HSDB (Hazardous Substances Data Bank). 2005b. Potassium Cyanide (CASRN 151-50-8). TOXNET Toxicology Data Network, U.S. National Library of Medicine, Bethesda, MD [online]. Available: http://toxnet.nlm.nih.gov/cgi-bin/sis [accessed Nov. 19, 2014].

HSDB (Hazardous Substances Data Bank). 2014. Calcium Cyanide (CASRN 592-01-8). TOXNET Toxicology Data Network, U.S. National Library of Medicine, Bethesda, MD [online]. Available: http://toxnet.nlm.nih.gov/cgi-bin/sis [accessed Nov. 19, 2014].

Kopras, E.J. 2012. Cyanides and nitriles. In Patty's Toxicology. Wiley Online Library.

Leeser, J.E., J.A. Tomenson, and D.D. Bryson. 1990. A Cross-Sectional Study of the Health of Cyanide Salt Production Workers. Report No. OHS/R/2, ICI Central Toxicology Laboratory, Macclesfield, UK. January 12, 1990.

Lorke, D. 1983. A new approach to practical acute toxicity testing. Arch. Toxicol. 54(4):275-287.

Maehly, A.C., and A. Swensson. 1970. Cyanide and thiocyanate levels in blood and urine of workers with low-grade exposure to cyanide. Int. Arch. Arbeitsmed. 27(3):195-209.

MSZW (Ministerie van Sociale Zaken en Werkgelegenheid). 2007. OEL Database: Hydrogen Cyanide. The Social and Economic Council of the Netherlands, The Hague [online]. Available: http://www.ser.nl/en/grenswaarden/hydrogen%20cyanide.aspx [accessed Nov. 19, 2014].

NIOSH (National Institute for Occupational Safety and Health). 1976. Pp. 37-114 in Criteria for a Recommended Standard. Occupational Exposure to Hydrogen Cyanide and Cyanide Salts (NaCN, KCN, and Ca(CN2)). DHEW (NIOSH) Pub. No. 77-108. PB 266 230. U.S. Department of Health, Education, and Welfare, National Institute for Occupational Safety and Health, Washington, DC.

NIOSH (National Institute for Occupational Safety and Health). 1994. Documentation for Immediately Dangerous to Life or Health Concentrations (IDLHs): Cyanides (as CN) [online]. Available: http://www.cdc.gov/niosh/idlh/cyanides.html [accessed Nov. 19, 2014].

NIOSH (National Institute for Occupational Safety and Health). 2011. NIOSH Pocket Guide to Chemical Hazards: Hydrogen Cyanide [online]. Available: http://www.cdc.gov/niosh/npg/npgd0333.html [accessed Nov. 19, 2014].

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). 2002. Hydrogen Cyanide. Pp. 211-276 in Acute Exposure Guideline Levels for Selected Airborne Chemicals, Vol. 2. Washington, DC: The National Academies Press.

OSHA (Occupational Health and Safety Administration). 1978. Occupational Health Guideline for Hydrogen Cyanide. U.S. Department of Health and Human Services and U.S. Department of Labor. September 1978 [online]. Available; http://www.cdc.gov/niosh/docs/81-123/pdfs/0333.pdf [accessed Nov. 20, 2014].

Pesce, L.D. 2010. Cyanides. In Kirk-Othmer Encyclopedia of Chemical Technology. Wiley Online Library.

Potter, L. 1950. The successful treatment of two recent cases of cyanide poisoning. Br. J. Ind. Med. 7(3):125-130.

Purser, D.A. 1984. A bioassay model for testing the incapacitating effects of exposure to combustion product atmospheres using cynomolgus monkeys. J. Fire Sci. 2:20-36.

Purser, D.A., P. Grimshaw, and K.R. Berrill. 1984. Intoxication by cyanide in fires: A study in monkeys using polyacrylonitrile. Arch. Environ. Health 39(6):394-400.

Smith, R.P. 1996. Toxic responses of the blood. Pp. 335-354 in Casarett and Doull's Toxicology: The Basic Science of Poisons, 5th Ed., C.D. Klaassen, ed. New York: McGraw-Hill.

Smyth, H.F., C.P. Carpenter, C.S. Weil, U.C. Pozzani, J.A. Striegel, and J.S. Nycum. 1969. Range-finding toxicity data: List VII. Am. Ind. Hyg. Assoc. J. 30(5):470-476.

SWEA (Swedish Work Environment Authority). 2005. Cyanides, and hydrogen cyanides (as CN). Pp. 27 in Occupational Exposure Limit Values and Measures against Air Contaminants. AFS 2005:17 [online]. Available: http://www.av.se/dokument/inenglish/legislations/eng0517.pdf [accessed Nov. 20, 2014].

APPENDIX A

DERIVATION OF AGEL VALUES FOR CYANIDE SALTS

Derivation of AEGL-1 Values

The AEGL-1 values for hydrogen cyanide were used as target values for calculating the concentrations of the cyanide salt needed to generate the hydrogen cyanide AEGL values. The calculations assumed a temperature of 25°C, a pressure of 760 mm Hg, and complete hydrolysis (one mole of sodium cyanide or potassium cyanide will yield one mole of hydrogen cyanide, and one mole of calcium cyanide will yield two moles of hydrogen cyanide).

Sodium Cyanide

10-min AEGL-1:
2.5 ppm ÷ 1 = 2.5 ppm
2.5 ppm × 49.0 ÷ 24.5 = 5.0 mg/m^3

30-min AEGL-1:
2.5 ppm ÷ 1 = 2.5 ppm
2.5 ppm × 49.0 ÷ 24.5 = 5.0 mg/m^3

1-h AEGL-1:
2.0 ppm ÷ 1 = 2.0 ppm
2.0 ppm × 49.0 ÷ 24.5 = 4.0 mg/m^3

4-h AEGL-1:
1.3 ppm ÷ 1 = 1.3 ppm
1.3 ppm × 49.0 ÷ 24.5 = 2.6 mg/m^3

8-h AEGL-1:
1.0 ppm ÷ 1 = 1.0 ppm
1.0 ppm × 49.0 ÷ 24.5 = 2.0 mg/m^3

Potassium Cyanide

10-min AEGL-1:
2.5 ppm ÷ 1 = 2.5 ppm
2.5 ppm × 65.1 ÷ 24.5 = 6.6 mg/m^3

30-min AEGL-1:
2.5 ppm ÷ 1 = 2.5 ppm
2.5 ppm × 65.1 ÷ 24.5 = 6.6 mg/m^3

1-h AEGL-1:
2.0 ppm ÷ 1 = 2.0 ppm
2.0 ppm × 65.1 ÷ 24.5 = 5.3 mg/m^3

4-h AEGL-1:
1.3 ppm ÷ 1 = 1.3 ppm
1.3 ppm × 65.1 ÷ 24.5 = 3.5 mg/m^3

8-h AEGL-1:
1.0 ppm ÷ 1 = 1.0 ppm
1.0 ppm × 65.1 ÷ 24.5 = 2.7 mg/m^3

Calcium Cyanide

10-min AEGL-1: 2.5 ppm ÷ 2 = 1.25 ppm
1.25 ppm × 92.1 ÷ 24.5 = 4.7 mg/m^3

30-min AEGL-1: 2.5 ppm ÷ 2 = 1.25 ppm
1.25 ppm × 92.1 ÷ 24.5 = 4.7 mg/m^3

1-h AEGL-1: 2.0 ppm ÷ 2 = 1.0 ppm
1.0 ppm × 92.1 ÷ 24.5 = 3.8 mg/m^3

4-h AEGL-1: 1.3 ppm ÷ 2 = 0.65 ppm
0.65 ppm × 92.1 ÷ 24.5 = 2.4 mg/m^3

8-h AEGL-1: 1.0 ppm ÷ 2 = 0.50 ppm
0.50 ppm × 92.1 ÷ 24.5 = 1.9 mg/m^3

Derivation of AEGL-2 Values

The AEGL-2 values for hydrogen cyanide were used as target values for calculating the concentrations of the cyanide salt needed to generate the hydrogen cyanide AEGL values. The calculations assumed a temperature of 25°C, a pressure of 760 mm Hg, and complete hydrolysis (one mole of sodium cyanide or potassium cyanide will yield one mole of hydrogen cyanide, and one mole of calcium cyanide will yield two moles of hydrogen cyanide).

Sodium Cyanide

10-min AEGL-2: 17 ppm ÷ 1 = 17 ppm
17 ppm × 49.0 ÷ 24.5 = 34 mg/m^3

30-min AEGL-2: 10 ppm ÷ 1 = 10 ppm
10 ppm × 49.0 ÷ 24.5 = 20 mg/m^3

1-h AEGL-2: 7.1 ppm ÷ 1 = 7.1 ppm
7.1 ppm × 49.0 ÷ 24.5 = 14 mg/m^3

4-h AEGL-2: 3.5 ppm ÷ 1 = 3.5 ppm
3.5 ppm × 49.0 ÷ 24.5 = 7.0 mg/m^3

8-h AEGL-2: 2.5 ppm ÷ 1 = 2.5 ppm
2.5 ppm × 49.0 ÷ 24.5 = 5.0 mg/m^3

Potassium Cyanide

10-min AEGL-2: 17 ppm ÷ 1 = 17 ppm
17 ppm × 65.1 ÷ 24.5 = 45 mg/m^3

30-min AEGL-2: 10 ppm ÷ 1 = 10 ppm
10 ppm × 65.1 ÷ 24.5 = 27 mg/m^3

1-h AEGL-2: 7.1 ppm ÷ 1 = 7.1 ppm
7.1 ppm × 65.1 ÷ 24.5 = 19 mg/m^3

4-h AEGL-2: 3.5 ppm ÷ 1 = 3.5 ppm
3.5 ppm × 65.1 ÷ 24.5 = 9.3 mg/m^3

8-h AEGL-2: 2.5 ppm ÷ 1 = 2.5 ppm
2.5 ppm × 65.1 ÷ 24.5 = 6.6 mg/m^3

Calcium Cyanide

10-min AEGL-2: 17 ppm ÷ 2 = 8.5 ppm
8.5 ppm × 92.1 ÷ 24.5 = 32 mg/m^3

30-min AEGL-2: 10 ppm ÷ 2 = 5 ppm
5 ppm × 92.1 ÷ 24.5 = 19 mg/m^3

1-h AEGL-2: 7.1 ppm ÷ 2 = 3.55 ppm
3.55 ppm × 92.1 ÷ 24.5 = 13 mg/m^3

4-h AEGL-2: 3.5 ppm ÷ 2 = 1.75 ppm
1.75 ppm × 92.1 ÷ 24.5 = 6.6 mg/m^3

8-h AEGL-2: 2.5 ppm ÷ 2 = 1.25 ppm
1.25 ppm × 92.1 ÷ 24.5 = 4.7 mg/m^3

Derivation of AEGL-3 Values

The AEGL-3 values for hydrogen cyanide were used as target values for calculating the concentrations of the cyanide salt needed to generate the hydrogen cyanide AEGL values. The calculations assumed a temperature of 25°C, a pressure of 760 mm Hg, and complete hydrolysis (one mole of sodium cyanide or potassium cyanide will yield one mole of hydrogen cyanide, and one mole of calcium cyanide will yield two moles of hydrogen cyanide).

Sodium Cyanide

10-min AEGL-3: 27 ppm ÷ 1 = 27 ppm
27 ppm × 49.0 ÷ 24.5 = 54 mg/m^3

30-min AEGL-3: 21 ppm ÷ 1 = 21 ppm
21 ppm × 49.0 ÷ 24.5 = 42 mg/m^3

1-h AEGL-3: 15 ppm ÷ 1 = 15 ppm
15 ppm × 49.0 ÷ 24.5 = 30 mg/m^3

4-h AEGL-3: 8.6 ppm ÷ 1 = 8.6 ppm
8.6 ppm × 49.0 ÷ 24.5 = 17 mg/m^3

8-h AEGL-3: 6.6 ppm ÷ 1 = 6.6 ppm
6.6 ppm × 49.0 ÷ 24.5 = 13 mg/m^3

Potassium Cyanide

10-min AEGL-3: 27 ppm ÷ 1 = 27 ppm
27 ppm × 65.1 ÷ 24.5 = 72 mg/m^3

30-min AEGL-3: 21 ppm ÷ 1 = 21 ppm
21 ppm × 65.1 ÷ 24.5 = 56 mg/m^3

1-h AEGL-3: 15 ppm ÷ 1 = 15 ppm
15 ppm × 65.1 ÷ 24.5 = 40 mg/m^3

4-h AEGL-3: 8.6 ppm ÷ 1 = 8.6 ppm
8.6 ppm × 65.1 ÷ 24.5 = 23 mg/m^3

8-h AEGL-3: 6.6 ppm ÷ 1 = 6.6 ppm
6.6 ppm × 65.1 ÷ 24.5 = 18 mg/m^3

Calcium Cyanide

10-min AEGL-3: 27 ppm ÷ 2 = 13.5 ppm
13.5 ppm × 92.1 ÷ 24.5 = 51 mg/m^3

30-min AEGL-3: 21 ppm ÷ 2 = 10.5 ppm
10.5 ppm × 92.1 ÷ 24.5 = 39 mg/m^3

1-h AEGL-3: 15 ppm ÷ 2 = 7.5 ppm
7.5 ppm × 92.1 ÷ 24.5 = 28 mg/m^3

4-h AEGL-3: 8.6 ppm ÷ 2 = 4.3 ppm
4.3 ppm × 92.1 ÷ 24.5 = 16 mg/m^3

8-h AEGL-3: 6.6 ppm ÷ 2 = 3.3 ppm
3.3 ppm × 92.1 ÷ 24.5 = 12 mg/m^3

APPENDIX B

DERIVATION OF THE AEGL VALUES FOR HYDROGEN CYANIDE (NRC 2002)

Derivation of AEGL-1 Values

Key studies:	Leeser et al. 1990
Supporting studies:	Hardy et al. 1950; Grabois 1954; Maehly and Swensson 1970; El Ghawabi et al. 1975
Toxicity end point:	No adverse effect in healthy adult humans occupationally exposed at geometric mean concentration of ≤1 [range 0.01-3.3 ppm, personal samplers (up to 6 ppm, area samples)] or 5 ppm; mild headache in adult humans occupationally exposed at 8 ppm. The exposure duration was considered to be 8 h.
Uncertainty factor:	An uncertainty factor was not applied to the Leeser et al. (1990) 1-ppm concentration because it is the lowest NOAEL. A factor of 3 for intraspecies differences was applied to the supporting studies because no susceptible populations were identified. The uncertainty factor was applied to the 8-h 5 ppm and 8 ppm concentrations, which resulted in concentrations close to the 8-h 1-ppm concentration in the Leeser et al. (1990) study.
Time scaling:	$C^3 \times t = k$ (conservative time-scaling relationship because, the relationship between concentration and exposure duration for the headache effect is unknown). An 8-h 1 ppm concentration was used as the starting point for time scaling.
Calculations:	$(C^3 \div \text{uncertainty factors}) \times t = k$ $(1 \text{ ppm})^3 \times 480 \text{ min} = 480 \text{ ppm-min}$
10-min AEGL-1:	$(480 \text{ ppm-min}/10 \text{ min})^{1/3} = 3.6 \text{ ppm}$ Because 3.6 ppm is above the highest exposure concentration in the Leeser et al. (1990) study, as measured by personal monitors, the 10-min value was set equal to the 30-min value.
30-min AEGL-1:	$(480 \text{ ppm-min} \div 30 \text{ min})^{1/3} = 2.5 \text{ ppm}$
1-h AEGL-1:	$(480 \text{ ppm-min} \div 60 \text{ min})^{1/3} = 2.0 \text{ ppm}$

4-h AEGL-1: $(480 \text{ ppm-min} \div 240 \text{ min})^{1/3} = 1.3 \text{ ppm}$

8-h AEGL-1: 1.0 ppm

Derivation of AEGL-2 Values

Key study: Purser 1984

Toxicity end point: Slight central nervous system depression in monkeys inhaling 60 ppm for 30 min.

Time scaling: $C^2 \times t = k$ (this document; based on regression analysis of incapacitation and lethality data for the monkey)

Uncertainty factors: 2 for interspecies differences
3 for intraspecies variability
Total uncertainty factor: 6

Calculations: $(C^2 \div \text{uncertainty factors}) \times t = k$
$(60 \text{ ppm} \div 6)^2 \times 30 \text{ min} = 3{,}000 \text{ ppm-min}$

10-min AEGL-2: $(3{,}000 \text{ ppm-min} \div 10 \text{ min})^{1/2} = 17 \text{ ppm}$

30-min AEGL-2: $60 \text{ ppm} \div 6 = 10 \text{ ppm}$

1-h AEGL-2: $(3{,}000 \text{ ppm-min} \div 60 \text{ min})^{1/2} = 7.1 \text{ ppm}$

4-h AEGL-2: $(3{,}000 \text{ ppm-min} \div 240 \text{ min})^{1/2} = 3.5 \text{ ppm}$

8-h AEGL-2: $(3{,}000 \text{ ppm-min} \div 480 \text{ min})^{1/2} = 2.5 \text{ ppm}$

Derivation of AEGL-3 Values

Key study: Haskell Laboratory 1981

Toxicity end point: 15-min LC_{01} of 138 ppm in the rat
30-min LC_{01} of 127 ppm in the rat
1-h LC_{01} of 88 ppm in the rat
LC_{01} derived by probit analysis

Time scaling: $C^{2.6} \times t = k$ (this document; based on the Haskell Laboratory [1981] rat dataset)

Uncertainty factors: 2 for interspecies
3 for intraspecies
Total uncertainty factor: 6

Calculations:	$(C^{2.6} \div \text{uncertainty factors}) \times t = k$ $(138 \text{ ppm} \div 6)^{2.6} \times 15 \text{ min} = 52{,}069.5 \text{ ppm-min}$ $(127 \text{ ppm} \div 6)^{2.6} \times 30 \text{ min} = 83{,}911 \text{ ppm-min}$ $(88 \text{ ppm} \div 6)^{2.6} \times 60 \text{ min} = 64{,}656.6 \text{ ppm-min}$
10-min AEGL-3:	$(52{,}069.5 \text{ ppm-min} \div 10 \text{ min})^{1/2.6} = 27 \text{ ppm}$
30-min AEGL-3:	$127 \text{ ppm} \div 6 = 21 \text{ ppm}$
1-h AEGL-3:	$88 \text{ ppm} \div 6 = 15 \text{ ppm}$
4-h AEGL-3:	$(64{,}656.6 \text{ ppm-min} \div 240 \text{ min})^{1/2.6} = 8.6 \text{ ppm}$
8-h AEGL-3:	$(64{,}656.6 \text{ ppm-min} \div 480 \text{ min})^{1/2.6} = 6.6 \text{ ppm}$

APPENDIX C

ACUTE EXPOUSRE GUIDELINES FOR CYANIDE SALTS

Derivation Summary

AEGL-1 VALUES

10 min	30 min	1 h	4 h	8 h
Sodium cyanide				
5.0 mg/m^3	5.0 mg/m^3	4.0 mg/m^3	2.6 mg/m^3	2.0 mg/m^3
Potassium cyanide				
6.6 mg/m^3	6.6 mg/m^3	5.3 mg/m^3	3.5 mg/m^3	2.7 mg/m^3
Calcium cyanide				
4.7 mg/m^3	4.7 mg/m^3	3.8 mg/m^3	2.4 mg/m^3	1.9 mg/m^3

Key reference: NRC (National Research Council). 2002. Hydrogen cyanide. Pp. 211-276 in Acute Exposure Guideline Levels for Selected Airborne Chemicals, Volume 2. Washington, DC: The National Academies Press.

End point/Concentration/Rationale: AEGL-1 values for hydrogen cyanide were used to obtain AEGL-1 values for the three cyanide salts. The use of hydrogen cyanide as a surrogate for the cyanide salts is deemed appropriate because qualitative (clinical signs) and quantitative (adjusted rat oral LD_{50} values) data suggest that the cyanide moiety is responsible for the acute toxicity of the cyanide salts. The hydrogen cyanide AEGL-1 values were used as target values for calculating the concentrations of cyanide salt needed to generate the hydrogen cyanide AEGL values. The calculations assumed a temperature of 25°C, a pressure of 760 mm Hg, and complete hydrolysis.

Molar adjustment factor:
1 (sodium cyanide and potassium cyanide); 2 (calcium cyanide)

Data adequacy: AEGL-1 values for the cyanide salts were derived by analogy to the AEGL-1 values for hydrogen cyanide. The database on hydrogen cyanide is robust. The adjusted rat oral LD_{50} value for calcium cyanide is much greater than would be expected on a molar basis for cyanide (suggesting that it is a less toxic compound). However, the production of two moles of hydrogen cyanide was assumed per mole of calcium cyanide. That assumption will yield protective AEGL values.

AEGL-2 VALUES

10 min	30 min	1 h	4 h	8 h
Sodium cyanide				
34 mg/m^3	20 mg/m^3	14 mg/m^3	7.0 mg/m^3	5.0 mg/m^3
Potassium cyanide				
45 mg/m^3	27 mg/m^3	19 mg/m^3	9.3 mg/m^3	6.6 mg/m^3
Calcium cyanide				
32 mg/m^3	19 mg/m^3	13 mg/m^3	6.6 mg/m^3	4.7 mg/m^3

Key reference: NRC (National Research Council). 2002. Hydrogen cyanide. Pp. 211-276 in Acute Exposure Guideline Levels for Selected Airborne Chemicals, Volume 2. Washington, DC: The National Academies Press.

(Continued)

AEGL-2 VALUES Continued

End point/Concentration/Rationale: AEGL-2 values for hydrogen cyanide were used to obtain AEGL-2 values for the three cyanide salts. The use of hydrogen cyanide as a surrogate for the cyanide salts is deemed appropriate because qualitative (clinical signs) and quantitative (adjusted rat oral LD_{50} values) data suggest that the cyanide moiety is responsible for acute toxicity of the cyanide salts. The hydrogen cyanide AEGL-2 values were used as target values for calculating the concentrations of cyanide salt needed to generate the hydrogen cyanide AEGL values. The calculations assumed a temperature of 25°C, a pressure of 760 mm Hg, and complete hydrolysis.

Molar adjustment factor:
1 (sodium cyanide and potassium cyanide); 2 (calcium cyanide)

Data adequacy: AEGL-2 values for the cyanide salts were derived by analogy to the AEGL-2 values for hydrogen cyanide. The database on hydrogen cyanide is robust. The adjusted rat oral LD_{50} value for calcium cyanide is much greater than would be expected on a molar basis for cyanide (suggesting that it is a less toxic compound). However, the production of two moles of hydrogen cyanide was assumed per mole of calcium cyanide. That assumption will yield protective AEGL values.

AEGL-3 VALUES

10 min	30 min	1 h	4 h	8 h
Sodium cyanide				
54 mg/m^3	42 mg/m^3	30 mg/m^3	17 mg/m^3	13 mg/m^3
Potassium cyanide				
72 mg/m^3	56 mg/m^3	40 mg/m^3	23 mg/m^3	18 mg/m^3
Calcium cyanide				
51 mg/m^3	39 mg/m^3	28 mg/m^3	16 mg/m^3	12 mg/m^3

Key reference: NRC (National Research Council). 2002. Hydrogen cyanide. Pp. 211-276 in Acute Exposure Guideline Levels for Selected Airborne Chemicals, Volume 2. Washington, DC: The National Academies Press.

End point/Concentration/Rationale: AEGL-3 values for hydrogen cyanide were used to obtain AEGL-3 values for the three cyanide salts. The use of hydrogen cyanide as a surrogate for the cyanide salts is deemed appropriate because qualitative (clinical signs) and quantitative (adjusted rat oral LD_{50} values) data suggest that the cyanide moiety is responsible for acute toxicity of the cyanide salts. The hydrogen cyanide AEGL-3 values were used as target values for calculating the concentrations of cyanide salt needed to generate the hydrogen cyanide AEGL values. The calculations assumed a temperature of 25°C, a pressure of 760 mm Hg, and complete hydrolysis.

Molar adjustment factor:
1 (sodium cyanide and potassium cyanide)
2 (calcium cyanide)

Data adequacy: AEGL-3 values for the cyanide salts were derived by analogy to the AEGL-3 values for hydrogen cyanide. The database on hydrogen cyanide is robust. The adjusted rat oral LD_{50} value for calcium cyanide is much greater than would be expected on a molar basis for cyanide (suggesting that it is a less toxic compound). However, the production of two moles of hydrogen cyanide was assumed per mole of calcium cyanide. That assumption will yield protective AEGL values.

APPENDIX D

ACUTE EXPOUSRE GUIDELINES FOR HYDROGEN CYANIDE

Derivation Summary (NRC 2002)

AEGL-1 VALUES FOR HYDROGEN CYANIDE

10 min	30 min	1 h	4 h	8 h
2.5 ppm (2.8 mg/m^3)	2.5 ppm (2.8 mg/m^3)	2.0 ppm (2.2 mg/m^3)	1.3 ppm (1.4 mg/m^3)	1.0 ppm (1.1 mg/m^3)

Key reference: Leeser, J.E., J.A. Tomenson, and D.D. Bryson. 1990. A Cross-sectional Study of the Health of Cyanide Salt Production Workers. Report No. OHS/R/2. ICI Central Toxicology Laboratory, Macclesfield, U.K.

Supporting references: (1) El Ghawabi, S.H., M.A. Gaafar, A.A. El-Saharti, S.H. Ahmed, K.K. Malash, and R. Fares. 1975. Chronic cyanide exposure: A clinical, radioisotope, and laboratory study. Br.. J. Ind. Med. 32(3):215-219.

(2) Grabois, B. 1954. Exposure to hydrogen cyanide in processing of apricot kernels. Monthly Review NY Department of Labor, 33(September):33-36.

(3) Maehly, A.C., and A. Swensson. 1970. Cyanide and thiocyanate levels in blood and urine of workers with low-grade exposure to cyanide. Int. Arch. Arbeitsmed. 27(3):195-209.

(4) Hardy, H.L., W.M. Jeffries, M.M. Wasserman, and W.R. Waddell. 1950. Thiocyanate effect following industrial cyanide exposure - report of two cases. New Engl. J. Med. 242(25):968-972.

Test species/Strain/Number:
Occupational exposures/63 employees, mean age 44.7 (Leeser et al. 1990)
Occupational exposures/36 workers (El Ghawabi et al. 1975)
Occupational exposures/five factories (Grabois 1954)
Occupational exposures/94 workers (Maehly and Swensson 1970)
Occupational exposures/factories (Hardy et al. 1950)

Exposure route/Concentrations/Durations: Inhalation/geometric mean exposure of ≤1 ppm (range, 0.01-3.3 ppm; personal samplers), up to 6 ppm (area samples)/mean service years, 16.5 (Leeser et al. 1990); inhalation/average exposure 8 ppm/5-15 y (El Ghawabi et al. 1975); inhalation/5 ppm/unknown (Hardy et al. 1950; Grabois 1954; Maehly and Swensson 1970).

Effects: No exposure related adverse symptoms or health effects (surveys and medical examinations taken in spring and fall of year) (Leeser et al. 1990); mild headache, other symptoms (El Ghawabi et al. 1975); no effects reported (Hardy et al. 1950; Grabois 1954; Maehly and Swensson 1970).

End point/Concentration/Rationale: 1 ppm from the Leeser (1990) study; 8 ppm from the El Ghawabi et al. (1975) study; or 5 ppm from the Hardy et al. (1950), Grabois (1954), and Maehly and Swensson (1970) studies were considered no-adverse-effect to mild effect concentrations for an 8-h workday. The NRC adjusted the chronic 8 ppm value of El Ghawabi et al. (1975) to a 1-h exposure for healthy adults.

Uncertainty Factors/Rationale:
Total uncertainty factor: 3
Interspecies: Not applicable

(Continued)

AEGL-1 Continued

Intraspecies: 3, an uncertainty factor was not applied to the Leeser et al.(1990) 1 ppm concentration, as it is the lowest NOAEL. A factor of 3 was applied to the supporting studies as no specific susceptible populations were identified in monitoring studies or during the clinical use of nitroprusside solutions to control hypertension. The detoxifying enzyme rhodanese is present in all individuals including newborns. Application of the uncertainty factor to the El Ghawabi et al. (1975; as adjusted by the NRC) and Grabois (1954) data results in a value close to the 8-h 1 ppm concentration in the Leeser et al. (1990) study.

Modifying factor: Not applicable

Animal-to-human dosimetric Adjustment: Not applicable

Time scaling: Because of the long-term exposure duration of the key studies, the conservative time-scaling value of n = 3 (k = 480 ppm^3-min) was applied when scaling to shorter exposure durations. The starting point for time scaling was an 8-h concentration of 1 ppm.

Data adequacy: The preponderance of data from the key studies supports an 8-h no-effect concentration of 1 ppm. The Leeser et al. (1990) study encompassed subjective symptoms as well as extensive medical examinations. The occupational monitoring study of El Ghawabi et al. (1975), in which it is believed that workers inhaling a mean concentration of 8 ppm may suffer mild headaches, supports the safety of the derived values. The values are also supported by a NIOSH (1976) report in which 5 ppm was identified as a no-effect concentration in the Grabois et al. (1954) occupational study. Additional monitoring studies support the values.

AEGL-2 VALUES FOR HYDROGEN CYANIDE

10 min	30 min	1 h	4 h	8 h
17 ppm (19 mg/m^3)	10 ppm (11 mg/m^3)	7.1 ppm (7.8 mg/m^3)	3.5 ppm (3.9 mg/m^3)	2.5 ppm (2.8 mg/m^3)

Key references: (1) Purser, D.A. 1984. A bioassay model for testing the incapacitating effects of exposure to combustion product atmospheres using cynomolgus monkeys. J. Fire Sci. 2:20-36.
(2) Purser, D.A., P. Grimshaw and K.R. Berrill. 1984. Intoxication by cyanide in fires: A study in monkeys using polyacrylonitrile. Arch. Environ. Health 39(6):393-400.

Test species/Strain/Sex/Number: Cynomolgus monkeys, 4 per exposure group (sex not stated)

Exposure route/Concentrations/Durations: Inhalation, 60, 100, 102, 123, 147, or 156 ppm for 30 min

Effects: (30-min exposures)
60 ppm - increased respiratory minute volume and slight changes in EEGs near end of exposure
100 ppm - incapacitation (semi-conscious state) in 19 min
102 ppm - incapacitation in 16 min
123 ppm - incapacitation in 15 min
147 ppm - incapacitation in 8 min
156 ppm - incapacitation in 8 min

(Continued)

AEGL-2 Continued

End point/Concentration/Rationale: The 30-min exposure to 60 ppm, a NOAEL, was chosen because the next higher tested concentration, 100 ppm, resulted in incapacitation within the 30-min exposure period.

Uncertainty factors/Rationale:
Total uncertainty factor: 6
Interspecies: 2–The monkey is an appropriate model for humans, the small size and higher respiratory rate of the monkey may result in more rapid uptake and greater sensitivity than in humans.
Intraspecies: 3–No specific susceptible populations were identified during monitoring studies or during the clinical use of nitroprusside solutions to control hypertension. The detoxifying enzyme rhodanese is present in all individuals including newborns.

Modifying Factor: Not applicable

Animal-to-human dosimetric adjustment: Insufficient data.

Time scaling: $C^n \times t = k$, where n = 2 and k = 3,000 ppm-min on the basis of regression analysis of time-concentration relationships for both incapacitation times of 8 to 19 min and lethality data (3-60 min) for the monkey.

Data adequacy: Although human data are limited to primarily occupational monitoring studies, the data base on animal studies is good. The test atmosphere in the key study was supplied via a face mask to the restrained test subjects; restrained animals have been shown to be more sensitive than unrestrained animals to inhaled toxicants. Relative species sensitivity to inhaled HCN may be related to breathing rate. Compared to rodents, the slower breathing rate of humans and monkeys may make them less sensitive to the effects of HCN.
The following two supporting studies were located:
1. A 30-min exposure of rats to 55 ppm resulted in changes in lung phospholipids and lung dynamics. Use of an uncertainty factor of 6 results in a 30-min AEGL-2 of 9.2 ppm, which is similar to the AEGL value.
2. Humans inhaling mean concentrations of 10 or 15 ppm in electroplating or silver-reclaiming factories for up to 15 y reported symptoms including headache, fatigue, effort dyspnea, and syncopes. There was no evidence that these symptoms occurred on the first day of employment.

AEGL-3 VALUES FOR HYDROGEN CYANIDE

10 min	30 min	1 h	4 h	8 h
27 ppm (30 mg/m^3)	21 ppm (23 mg/m^3)	15 ppm (17 mg/m^3)	8.6 ppm (9.7 mg/m^3)	6.6 ppm (7.3 mg/m^3)

Key reference: Haskell Laboratory. 1981. Inhalation Toxicity of Common Combustion Gases. Haskell Laboratory Report No. 238-81. E.I. du Pont de Nemours and Company, Haskell Laboratory, Newark, DE.

Test species/Strain/Sex/Number: Crl:CD male rats, 10/exposure group

Exposure route/Concentrations/Durations: Inhalation
273, 328, 340, 353, 441, 493, or 508 ppm for 5 min
110, 175, 188, 204, 230, 251, 283, or 403 ppm for 15 min
128, 149, 160, 183, 222, or 306 ppm for 30 min
76, 107, 154, 183, or 222 ppm for 60 min

(Continued)

AEGL-3 Continued

Effects (LC_{01} values were calculated by Haskell Laboratory using probit analysis):
5-min LC_{01}: 283 ppm
15-min LC_{01}: 138 ppm
30-min LC_{01}: 127 ppm
60-min LC_{01}: 88 ppm

End point/Concentration/Rationale:
The LC_{01}, the threshold for lethality, was used as the basis for the derivation of the AEGL-3.
The 15-min LC_{01} was used to calculate the 10 min value; the 30-min LC_{01} was used for the 30-min value; and the 60-min LC_{01} was used to derive the 1-, 4- and 8-h AEGL-3 values.

Uncertainty factors/Rationale:
Total uncertainty factor: 6
Interspecies: 2 - LC_{50} values for the same exposure durations for several species (rat, mouse, and rabbit) were within a factor of approximately 1.5 of each other. Based on relative respiration rates, humans are expected to be less sensitive than rodents. The mechanism is the same for all species.
Intraspecies: 3 - No specific susceptible populations were identified during monitoring studies or during the clinical use of nitroprusside solutions to control hypertension. The detoxifying enzyme rhodanese is present in all individuals, including newborns.

Modifying factor: Not applicable

Animal-to-human dosimetric adjustment: Insufficient data.

Time scaling: $C^n \times t = k$, where n = 2.6 was derived from empirical data and used in a regression analysis of time-concentration relationships for rat LC_{50} values conducted at time periods of 5, 15, 30, and 60 min in the key study. However, the 15-, 30-, and 60-min values were calculated directly from the empirical (LC_{01}) data. The k value of 52,069.5 $ppm^{2.6}$-min, based on the 15-min LC_{01}, was used for the 10-min value and the k value of 64,656.6 $ppm^{2.6}$-min, based on the 1-h LC_{01}, was used for the 4- and 8-h AEGL-3 values.

Data adequacy: The study was well conducted. The HCN concentrations were continuously monitored using infrared spectrophotometry and validated by gas chromatography.
One supporting study was located: exposure of rats to 30 ppm for 24 h resulted in lung congestion but no deaths. Use of a total uncertainty factor of 6 and extrapolation across time to 30 min results in a 30-min AEGL-3 of 22 ppm which is similar to the derived value of 21 ppm.