Acute Exposure Guideline Levels for Selected Airborne Chemicals

VOLUME 16

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

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

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

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

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

in that series. AEGL documents for selected aliphatic nitriles, benzonitrile, methacrylonitrile, allyl alcohol, hydrogen selenide, ketene, and tear gas are each published as an appendix in this report. The committee concludes that the AEGLs developed in these appendixes are scientifically valid conclusions based on the data reviewed by NAC and are consistent with the NRC guideline reports. AEGL reports for additional chemicals will be presented in subsequent volumes.

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

The interim reports of the committee that led to this report were reviewed in draft form by individuals selected for their diverse perspectives and technical expertise, in accordance with procedures approved by the NRC's Report Review Committee. The purpose of this independent review is to provide candid and critical comments that will assist the institution in making its published report as sound as possible and to ensure that the report meets institutional standards for objectivity, evidence, and responsiveness to the study charge. The review comments and draft manuscript remain confidential to protect the integrity of the deliberative process. We wish to thank the following individuals for their review of the committee interim reports, which summarize the committee's conclusions and recommendations for improving NAC's AEGL documents for selected aliphatic nitriles (interim reports 19b and 21b), benzonitrile (interim reports 19b and 21b), methacrylonitrile (interim reports 19a, 20a, and 21a), allyl alcohol (interim reports 10, 12, 14, 18, and 21a), hydrogen selenide (interim report 16), ketene (interim reports 17 and 21a), and tear gas (interim reports 19a and 21a): Deepak Bhalla (Wayne State University), Harvey Clewell (The Hamner Institutes for Health Sciences), Jeffrey Fisher (U.S. Food and Drug Administration), Sidney Green (Howard University), David Gaylor (Gaylor and Associates, LLC), Sam Kacew (University of Ottawa), A. Wallace Hayes (Harvard School of Public Health), Rogene Henderson (Lovelace Respiratory Research Institute [retired]), James McDougal (Wright State University [retired]), Charles Reinhardt (DuPont Haskell Laboratory [retired]), Andrew Salmon (California Environmental Protection Agency), Kenneth Still (Portland State University), Joyce Tsuji (Exponent, Inc.), Bernard Wagner (New York University Medical Center [retired]), and Judith Zelikoff (New York University).

Although the reviewers listed above have provided many constructive comments and suggestions, they were not asked to endorse the conclusions or recommendations, nor did they see the final draft of this volume before its release. The review of interim reports was overseen by David Gaylor (Gaylor and

Associates, LLC), Robert Goyer (University of Western Ontario [retired]), and David H. Moore (Battelle Memorial Institute). Appointed by the NRC, they were responsible for making certain that an independent examination of the interim reports was carried out in accordance with institutional procedures and that all review comments were carefully considered. Responsibility for the final content of this report rests entirely with the authoring committee and the institution.

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

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Acute Exposure Guideline Levels for Selected Airborne Chemicals

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

This report is the sixteenth 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 fifteen 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). This report is the sixteenth volume in that series. AEGL documents for selected aliphatic nitriles, benzonitrile, methacrylonitrile, allyl alcohol, hydrogen selenide, ketene, and tear gas are each published as an appendix in this report. The committee concludes that the AEGLs developed in these appendixes are scientifically valid conclusions based on the data reviewed by NAC and are consistent with the NRC guideline reports. AEGL reports for additional chemicals will be presented in subsequent volumes.

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.

Appendixes

5

Hydrogen Selenide[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

[1]This document was prepared by the AEGL Development Team composed of Carol Wood (Oak Ridge National Laboratory), Heather Carlson-Lynch (SRC, Inc.), and Chemical Managers Nancy Kim (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).

effects. However, the effects are not disabling and are transient and reversible upon cessation of exposure.

AEGL-2 is the airborne concentration (expressed as ppm or mg/m^3) of a substance above which it is predicted that the general population, including susceptible individuals, could experience irreversible or other serious, long-lasting adverse health effects or an impaired ability to escape.

AEGL-3 is the airborne concentration (expressed as ppm or mg/m^3) of a substance above which it is predicted that the general population, including susceptible individuals, could experience life-threatening health effects or death.

Airborne concentrations below the AEGL-1 represent exposure concentrations that could produce mild and progressively increasing but transient and nondisabling odor, taste, and sensory irritation or certain asymptomatic, nonsensory effects. With increasing airborne concentrations above each AEGL, there is a progressive increase in the likelihood of occurrence and the severity of effects described for each corresponding AEGL. Although the AEGL values represent threshold concentrations for the general public, including susceptible subpopulations, such as infants, children, the elderly, persons with asthma, and those with other illnesses, it is recognized that individuals, subject to idiosyncratic responses, could experience the effects described at concentrations below the corresponding AEGL.

SUMMARY

Hydrogen selenide is a gas with a disagreeable odor at room temperature. It is formed by the reaction of acids or water with metal selenides (Malczewska-Toth 2012). Although elemental selenium has a wide variety of uses in industry, agriculture, and pharmaceuticals (ATSDR 2003), hydrogen selenide has no commercial use (Malczewska-Toth 2012).

Hydrogen selenide is highly irritating to the respiratory tract and effects progress to pulmonary edema, bronchitis, and bronchial pneumonia (Glover 1970; IPCS 1987; Malczewska-Toth 2012). Initial effects in exposed workers are signs of respiratory irritation, include tearing, running nose, coughing, sneezing, and chest tightness. The compound is oxidized to elemental selenium when it comes into contact with mucus membranes and appears as a red precipitate (Dudley and Miller 1937, 1941; Glover 1970; Zwart and Arts 1989). A distinct garlic odor of the breath has been reported in people accidentally exposed to selenium or selenium compounds and is most likely the result of the excretion of dimethyl selenide in expired air (ATSDR 2003).

No reports of human death after exposure to hydrogen selenide were found in the literature. AIHA (1989) reports an odor threshold of 0.3 ppm for hydrogen selenide. Olfactory fatigue occurs quickly at that concentration, and anecdotal reports indicate that workers exposed to hydrogen selenide at concentrations greater than 1.5 ppm experienced nasal and throat irritation that was

severe enough that they could not remain at work, but that workers were able to tolerate 0.3 ppm for several minutes without noticeable effects (Dudley and Miller 1941).

Dudley and Miller (1937, 1941) performed a series of experiments in which groups of 16-32 guinea pigs (sex and strain not specified) were exposed whole body to various concentrations of hydrogen selenide for 10-480 min and monitored for 30 days. Concentration-related clinical signs of toxicity at concentrations greater than 6.3 ppm included pawing at the nose and eyes, copious mucus from the nasal passages, and difficulty breathing. Marked weight loss was apparent, with recovery in survivors beginning 8 days after exposure. Animals that died within 48 h exhibited respiratory and circulatory failure, whereas those dying after 5 days or later had few acute respiratory symptoms but exhibited bronchial pneumonia for extended periods. The calculated 1-h LC_{50} (lethal concentration, 50% lethality) was 3.6 ppm, and 100% lethality occurred at 6.0 ppm. The main finding during histopathologic examination was fatty deposition in the liver and, to a lesser extent, in the kidney; splenic enlargement due to hyperplasia of the lymphoid tissue was also found. Hepatic lesions, but no increase in mortality, were observed at concentrations as low as 1.2 ppm for 30-60 min and the lesions generally resolved 17-20 days after exposure.

Lethality studies were conducted in pairs of Wistar rats exposed nose-only to various concentrations of hydrogen selenide for different durations, followed by a 14-day observation period (Zwart and Arts 1989; Zwart et al. 1992). In one experiment, no deaths occurred after exposure at 117 ppm for 4 or 15 min, but one animal died after exposure for 7.5 min; thus, 117 ppm for 15 min or less might be a threshold for death. In another experiment, groups of five male and five female Wistar rats were exposed to hydrogen selenide at 47-74 ppm for 1 h. Most deaths occurred within 2 days after exposure. Concentration-related clinical signs observed after exposure was stopped included piloerection, red discoloration of the fur, cyanosis, half-closed eyes, red nasal discharge, mouth breathing, moist or dry rales, and apnea. Surviving animals had body weight loss or reduced weight gain throughout the observation period. For example, at 47 ppm, no deaths occurred but four males and two females lost weight throughout the 14-day observation period. Necropsy revealed gas in the stomach or intestines of animals that died during the study and red discolored, atelectatic, edematous, or spongy, swollen, and/or spotted lungs with irregular surface in almost all decedents and survivors. A 1-h LC_{50} of 72 ppm was calculated (Zwart and Arts 1989; Zwart et al. 1992). Examination of the data used to calculate the 1-h LC_{50} shows a steep dose-response curve (0% mortality at 47 ppm, 20% at 71 ppm, and 60% at 74 ppm).

AEGL-1 values are not recommended for hydrogen selenide, because no animal or human data on appropriate end points were found. Data were insufficient to calculate the level of distinct odor awareness for the chemical because the basis of the reported odor threshold of 0.3 ppm was not documented.

Data were also insufficient to calculate AEGL-2 values for hydrogen selenide. In the absence of specific data for determining an AEGL-2 value, one-third of the AEGL-3 values can be used to establish AEGL-2 values (NRC 2001). This approach is justified because the lethality data in rats indicate a steep concentration-response relationship.

AEGL-3 values for hydrogen selenide were based on an estimated LC_{01} of 33 ppm, obtained by a log-probit analysis of data from experiments in Wistar rats (Zwart and Arts 1989; Zwart et al. 1992). Values were scaled using the equation $C^n \times t = k$, where n ranges from 0.8 to 3.5 (ten Berge et al. 1986). A value of n = 2.5 was calculated by probit analysis of all of the available lethality data in the rat. A total uncertainty factor of 100 was applied (10 for interspecies differences and 10 for intraspecies variability). The intraspecies factor of 10 was selected to address uncertainty about the mechanism of action for the marked body-weight loss exhibited by some surviving rats and whether this reflected a moribund state. An interspecies factor of 10 was used, because data were available in only two species and the limited data suggest that the rat might not be the most sensitive species.

AEGL values for hydrogen selenide are presented in Table 5-1.

1. INTRODUCTION

Hydrogen selenide is a gas with a disagreeable odor at room temperature. It has a density greater than that of air and is formed by the reaction of acids or water with metal selenides (Malczewska-Toth 2012). Although elemental selenium has a wide variety of uses in industry, agriculture, and pharmaceuticals (ATSDR 2003), hydrogen selenide has no commercial use (Malczewska-Toth 2012).

Hydrogen selenide is highly irritating to the respiratory tract with effects progressing to pulmonary edema, bronchitis, and bronchial pneumonia (Glover 1970; Malczewska-Toth 2012). The compound is oxidized to elemental selenium when it comes into contact with mucus membranes, and appears as a red precipitate (Dudley and Miller 1937, 1941; Glover 1970; Zwart and Arts 1989). The breath of people accidentally exposed to selenium or selenium compounds has been reported to have a distinct garlic odor, most likely the result of excretion of dimethyl selenide in expired air (ATSDR 2003).

The chemical and physical properties of hydrogen selenide are listed in Table 5-2.

2. HUMAN TOXICITY DATA

2.1. Acute Lethality

No reports of human lethality following exposure to hydrogen selenide were found in the available literature.

TABLE 5-1 AEGL Values for Hydrogen Selenide

Classification	10 min	30 min	1 h	4 h	8 h	End Point (Reference)
AEGL-1 (nondisabling)	NR[a]	NR[a]	NR[a]	NR[a]	NR[a]	Insufficient data
AEGL-2 (disabling)	0.22 ppm (0.73 mg/m^3)	0.15 ppm (0.48 mg/m^3)	0.11 ppm (0.37 mg/m^3)	0.064 ppm (21 mg/m^3)	0.048 ppm (0.16 mg/m^3)	One-third of the AEGL-3 values
AEGL-3 (lethal)	0.67 ppm (2.2 mg/m^3)	0.44 ppm (1.5 mg/m^3)	0.33 ppm (1.1 mg/m^3)	0.19 ppm (0.63 mg/m^3)	0.14 ppm (0.48 mg/m^3)	Calculated 1-h LC_{01} in rats (Zwart and Arts 1989; Zwart et al. 1992)

[a]Not recommended. Absence of an AEGL-1 value does not imply that exposure below the AEGL-2 value is without adverse effects.
Abbreviations: LC_{01}, lethal concentration, 1% lethality; NR, not recommended.

TABLE 5-2 Chemical and Physical Properties of Hydrogen Selenide

Parameter	Value	Reference
Synonyms	Dihydrogen selenide, selenium hydride, selenium dihydride, selane	ATSDR 2003
CAS registry no.	7783-07-5	O'Neil et al. 2006
Chemical formula	H_2Se	
Molecular weight	80.98	O'Neil et al. 2006
Physical state	Colorless gas	ATSDR 2003
Melting point	-65.73°C	O'Neil et al. 2006
Boiling point	-41.3°C	O'Neil et al. 2006
Liquid density (water = 1)	2.12 at -42°C/4°C	O'Neil et al. 2006
Solubility in water	377 mL/100 mL at 4°C	O'Neil et al. 2006
Vapor density (air = 1)	2.80	Yaws 2001
Vapor pressure	9,120 mm Hg (12 atm) at 30.8°C	ATSDR 2003; O'Neil et al. 2006
Conversion factors	1 ppm = 3.3 mg/m^3 1 mg/m^3 = 0.3 ppm	NIOSH 2011

2.2. Nonlethal Toxicity

Odor thresholds for hydrogen selenide are reported to range from 0.0005 to 3.6 ppm, with irritation reported at 1.8 ppm; the odor was described as decayed horseradish (Ruth 1986). AIHA (1989) lists the odor threshold as 0.3 ppm. Olfactory fatigue occurs quickly at this concentration (Dudley and Miller 1941).

2.2.1. Case Reports

Dudley and Miller (1941) reported that workers exposed to concentrations of hydrogen selenide greater than 1.5 ppm experienced nasal and throat irritation that was so severe that they could not remain at work. Workers were able to tolerate 0.3 ppm for several minutes without noticeable effects. However, these observations were reported in the discussion section of the paper without a citation or information on any associated sampling or analysis.

Twenty-five workers engaged in various metal etching, buffering, and polishing operations were exposed to hydrogen selenide in a large workroom (Buchan 1947). A reaction of selenious acid in the ink with metal was identified as the source of the hydrogen selenide. The breath of all of the exposed workers had a distinct garlic odor, but five had recently eaten food containing garlic. Only five complained of symptoms, including nausea, vomiting, metallic taste in the mouth, dizziness, extreme lassitude, and fatigue. No correlation was found between symptoms and urinary concentrations of selenium. Air samples were taken at six sites in the room; although a visible precipitate was observed on the filter paper, the measured concentration of hydrogen selenide did not exceed the detection limit of 0.2 ppm for the titrometric method. Additional details of the analytic methods were not described. However, the possibility that the highest concentrations were reached close to the breathing zone of the workers was noted by the authors. A review chapter describing this study (Glover et al. 1979) reported that "Five cases of subacute industrial selenosis were reported as due to exposure to less than 0.07 mg/m^3 of H_2Se"; however, that concentration appears to be an erroneous conversion from the detection limit of 0.2 ppm (the correct conversion would be 0.7 mg/m^3).

Other early reports of symptoms in workers exposed to hydrogen selenide have been summarized by Glover (1970) and IPCS (1987). Initial effects are of respiratory irritation and include tearing, running nose, coughing, sneezing, and tightness of the chest. A latent period of several hours may follow, after which pulmonary edema occurs. Affected workers all had complete recovery, but no exposure concentrations were measured. A chemist exposed to a "high concentration" of hydrogen selenide developed hyperglycemia that was controllable by increasing doses of insulin (Rosenfeld and Beath 1964; Malczewska-Toth 2012).

Banerjee et al. (1997) described effects in 31 workers exposed to "toxic fumes" produced during refining or recovery of scrap metal. The initial clinical presentation included intense cough, suffocation, burning, severe water discharge from eyes, cyanosis, tachypnea, tachycardia, and severe bronchospasm. Most workers recovered within 7 days; however, four with respiratory diseases associated with heavy smoking (one with acute respiratory distress syndrome, one with bilateral emphysema, two with chronic obstructive pulmonary disease) were treated for more than 3 weeks. Blood selenium concentrations did not correlate with symptoms; only four samples had selenium concentrations in the range of 71-189 μg/L on the first day. Selenium was confirmed in soil and wall-scratch samples from the incident site but no exposures could be determined.

Workers were exposed to selenium fume while smelting scrap aluminum contaminated with metallic selenium (Clinton 1947). A reddish cloud was released into the plant when the contents of a furnace were stirred in preparation for pouring; no concentrations were measured and the author estimated that no worker was exposed for more than 2 min. All exposed workers had intense irritation of the eyes, nose, and throat and headache developed several hours later. In addition, one worker with potentially higher exposure developed severe dyspnea 8-12 h after the accident. All workers appeared completely well in 3 days.

A 24-year old male was accidentally exposed to hydrogen selenide while transferring the gas from one cylinder to another (Schecter et al. 1980). Immediate symptoms included burning of the eyes and throat and was followed by coughing and wheezing. He was hospitalized 18 h later due to recurrent cough and dyspnea. Chest X-ray revealed pneumomediastinum and subcutaneous emphysema. Results of most pulmonary function tests returned to predicted levels within 30 days of the accident. However, abnormalities in flows at 50% and 25% of vital capacity persisted for up to 3 years.

A female college student was exposed to hydrogen selenide gas at least once a week for one year while working in a research laboratory (Alderman and Bergin 1986). She complained of chronic diarrhea and abdominal pain, had conjunctivitis and nasal stuffiness, and six dental caries had recently developed. She also had granular conjunctivitis, breath with a distinct garlic-like odor, and prominent transverse ridges of the fingernails. Chronic selenosis was diagnosed, which resolved after exposure ended. No exposure measurements were made in the research laboratory.

Another report described exposure of a researcher once a week for 2 years to selenium vapors produced by evaporation of pure selenium in an evacuated container (Ducloux et al. 1976). Symptoms included eczema of the face, weakness, and bronchitis. No other details were given.

2.2.2. Epidemiologic Studies

No epidemiologic studies of exposure to hydrogen selenide were found.

2.3. Neurotoxicity

No information regarding the neurotoxicity of hydrogen selenide in humans was found.

2.4. Developmental and Reproductive Toxicity

No information regarding the developmental or reproductive toxicity of hydrogen selenide in humans was found.

2.5. Genotoxicity

No information regarding the genotoxicity of hydrogen selenide in humans was found.

2.6. Carcinogenicity

No information regarding the carcinogenicity of hydrogen selenide in humans was found. A study of smelter workers found that those who died of lung cancer had lower selenium concentrations than either controls or workers who died of other causes (Gerhardsson et al. 1986). EPA (1993) has judged that selenium and selenium compounds are not classifiable as to their carcinogenicity in humans because of inadequate human data and inadequate evidence of carcinogenicity in animals. However, the agency found the evidence on selenium sulfide to be sufficient for classifying it as a probable human carcinogen classification.

2.7. Summary

Hydrogen selenide is highly irritating to the respiratory tract with effects progressing to pulmonary edema, bronchitis, and bronchial pneumonia (Glover 1970; Malczewska-Toth 2012). Irritation occurs at or below the odor threshold (Ruth 1986).

3. ANIMAL TOXICITY DATA

3.1. Acute Lethality

3.1.1. Guinea Pigs

Dudley and Miller (1937, 1941) performed a series of experiments in which groups of 16 or 32 guinea pigs (sex and strain not specified) were exposed whole body to various concentrations of hydrogen selenide (0.001- 0.57 mg/L or 0.3-171 ppm) for 10, 30, 60, 120, 240, or 480 min and were monitored for 30 days. Chamber atmospheres were calibrated prior to exposures and analytic concentrations were measured by weighing precipitated selenium from air samples. Clinical signs of toxicity from exposure at concentrations of 0.021 mg/L (6.3 ppm) or higher included pawing at the nose and eyes, copious mucus from the nasal passages, and difficulty breathing. At concentrations less than 0.021 mg/L (6.3 ppm) for up to 8 h, nasal discharge was less marked and severe ocular and nasal irritation were not observed; difficulty breathing was not observed until 24 h after exposure. Decomposition of the chemical by the mucus in the nasal passages resulted in a deposit of red, amorphous selenium on the nose and head of the animals. Marked weight loss was apparent with recovery in sur-

vivors beginning 8 days after exposure. Animals that died within 48 h exhibited respiratory and circulatory failure whereas those that died after 5 days or later had few acute respiratory symptoms but exhibited bronchial pneumonia for extended periods. More importantly, even for concentrations greater than the LC_{50}, the majority of deaths occurred more than 5 days after exposure; the peak occurred at 8-10 days, which likely corresponded to evidence of hepatic damage (see discussion of histopathologic findings below).

The investigators did not report LC_{50} values; however, on the basis of the lethality data from the study, LC_{50} values were calculated to be 0.34, 0.020, 0.012, 0.012, 0.012, and 0.0054 mg/ L (102, 6.0, 3.6, 3.6, 3.6, and 1.6 ppm) for 10, 30, 60, 120, 240, and 480 min, respectively. A few animals (1-3) died in each of the control groups, so the reliability of these data and the calculated LC_{50} values is uncertain. Regardless, a marked increase in deaths (resulting in more than 35% lethality) was consistently seen at 3.3-3.6 ppm for durations of 30-240 min.

Histopathologic examinations were performed on the animals used in the lethality studies (Dudley and Miller 1937, 1941), but severity scores were not determined. The main finding was fatty deposition in the liver and, to a lesser extent, in the kidney. Splenic enlargement due to hyperplasia of the lymphoid tissue was also found. Hepatic lesions, but no increase in mortality, were observed at concentrations as low as 1.3 ppm for 30-60 min. Fatty changes became progressively more severe for up to 10 days and generally resolved by 17-20 days after exposure. Slight to moderate thickening of the alveolar wall was found in the lung of almost all animals and acute pneumonia that progressed to bronchopneumonia occurred in about half of the animals. Most importantly, the severity of the pathologic lesions was more closely related to the amount of time between exposure and death than to the concentration or duration of exposure.

3.1.2. Rats

Two lethality studies were conducted in Wistar rats exposed nose-only to various concentrations of hydrogen selenide for different durations followed by a 14-day observation period (Zwart and Arts 1989; Zwart et al. 1992). The mortality results are summarized in Table 5-3. Test atmospheres were measured by atomic absorption spectrometry. In the first experiment (Study A or C × t study), groups of one male and one female rat were exposed at concentrations of 0.13-2.9 g/m^3 (39-870 ppm) for durations of 4-120 min. At 0.39 g/m^3 (117 ppm), no deaths occurred following exposures for 4 and 15 min, but one animal died during the observation period following exposure for 7.5 min; thus, 117 ppm for 15 min or less may be a threshold for death. Nearly all animals exposed to hydrogen selenide at 78 ppm or greater for 30 min or more died. At a concentration of 39 ppm, no animals died following exposure for up to 60 min, but one of two died following exposure for 84 or 120 min. Most deaths occurred within 2 days

after exposure. Concentration-related clinical signs included piloerection, red discoloration of the fur, cyanosis, half-closed eyes, red nasal discharge, mouth breathing, moist or dry rales, and apnea. For animals exposed at 39 ppm, "breathing problems" recurred during week 2 of the observation period. Surviving animals had body weight loss or reduced weight gain throughout the observation period. Necropsy revealed gas in the stomach or intestines of animals that died during the study and red discolored, atelectatic, edematous, or spongy, swollen, and/or spotted lungs with irregular surface in almost all decedents and survivors. The authors reported a 1-h LC_{50} of 0.18 g/m^3 (54 ppm).

In the second experiment (Study B or 1-h LC_{50} study), groups of five male and five female Wistar rats were exposed nose-only to hydrogen selenide at 0.155, 0.235, or 0.245 g/m^3 (47, 71, or 74 ppm) for 1 h. Clinical signs, effects on body weight, and gross findings were similar to those described above for the first experiment. At 0.155 g/m^3 (47 ppm), four males and two females had body weight loss throughout the 14-day observation period. A 1-h LC_{50} of 0.24 g/m^3 (72 ppm) was calculated (Zwart and Arts 1989; Zwart et al. 1992). Examination of the data used to calculate the 1-h LC_{50} shows a steep concentration-response curve (see Table 5-3).

On the basis of marked body weight loss among survivors (which suggested the animals were moribund) during the observation periods of both experiments, the investigators postulated that the LC_{50} estimates would have been lower if the observation periods had been longer. However, extending the observation period was not considered ethical due to the condition of the animals. Zwart and Arts (1989) suggested that animals that lost weight during days 8-14 of the observation period could be considered "dead", and estimated that this approach would yield a 1-h LC_{50} of 0.06-0.07 g/m^3 (18-21 ppm).

TABLE 5-3 Lethality in Rats Exposed to Hydrogen Selenide

Concentration	4-20 min	30 min	60 min	120 min
Study A (C × t study)				
0.13 g/m^3 (39 ppm)	NR	0/2	0/2	1/2
0.26 g/m^3 (78 ppm)	NR	2/2	2/2	2/2
0.39 g/m^3 (117 ppm)	1/6	2/2	2/2	NR
1.41 g/m^3 (423 ppm)	10/10	NR	NR	NR
2.90 g/m^3 (870 ppm)	8/8	2/2	NR	NR
Study B (1-h LC_{50} study)				
155 g/m^3 (47 ppm)	NR	NR	0/10	NR
235 g/m^3 (71 ppm)	NR	NR	2/10	NR
245 g/m^3 (74 ppm)	NR	NR	6/10	NR

Abbreviations: LC_{50}, lethal concentration, 50% lethality; NR, not reported.
Source: Zwart and Arts 1989; Zwart et al. 1992.

3.2. Nonlethal Toxicity

Groups of five young, female albino rats were exposed to selenium fumes produced by passing a current through tungsten wire wound in a cone and filled with chips of selenium (Hall et al. 1951). The exposure concentration, particle size, and chemical form were not specified. Exposures were for 2-16 min and animals were killed 1-16 days following exposure. At necropsy, lung weights were increased and hemorrhage with scattered emphysematous and atelectatic areas were observed. Little evidence of repair was apparent up to 16 days after exposure.

3.3. Neurotoxicity

No evidence of a narcotic or anesthetic effect was seen in guinea pigs exposed to lethal concentrations of hydrogen selenide for up to 8 h (Dudley and Miller 1937, 1941).

3.4. Developmental and Reproductive Toxicity

No information on the developmental or reproductive toxicity of hydrogen selenide in animals was found. Selenium or selenium compounds have produced defects in the chick when applied to the air cell, and decreased live births and pup size in mice when administered orally or by injection; no adverse effects have been found in hamsters or monkeys (Shepard 2010).

3.5. Genotoxicity

No information on the genotoxicity of hydrogen selenide was found. Sodium selenite and sodium selenide, which are metabolized to hydrogen selenide, induced DNA single-strand breaks and growth inhibition in a mouse mammary carcinoma cell line (Lu et al. 1995). Hydrogen selenide was not measured in the culture medium.

3.6. Chronic Toxicity and Carcinogenicity

No information on the chronic toxicity or carcinogenicity of hydrogen selenide in laboratory animals was found. In studies of selenium sulfide and Selsun (2.5% selenium sulfide), no evidence of carcinogenicity was found following dermal application of either compound to the skin of male and female ICR mice three times per week for 86-88 weeks (NTP 1980 a,b). However, these studies were considered inadequate because of their short duration due to the limited lifetime of the test stain of mice.

3.7. Summary

Lethality studies in guinea pigs and rats show a steep concentration-response relationship for hydrogen selenide. Clinical signs in both species were indicative of severe irritation and pulmonary lesions were observed at necropsy. Exposures at high concentrations for a short duration resulted in death from pulmonary edema. In contrast, deaths in studies with longer durations occurred over a relatively flat concentration range and were most likely secondary to hepatic damage. Effects in the liver were identified in guinea pigs but these lesions resolved in surviving animals. Livers from rats were not examined microscopically.

4. SPECIAL CONSIDERATIONS

4.1. Metabolism and Disposition

No information on the metabolism and disposition of hydrogen selenide was found. However, the absorption, distribution, metabolism, and excretion of selenium have been reviewed elsewhere (Sunde 1990; ATSDR 2003); salient information is briefly reviewed in this section. In the dog, inhaled selenious acid aerosol was rapidly and almost completely absorbed whereas the metal aerosol was less rapidly absorbed. Selenium from both aerosols was distributed similarly to the liver, kidney, spleen, and heart and had a biologic half-life of 30-40 days; the main route of excretion was via the urine (Weissman et al. 1983). Results from inhalation studies of selenious acid or selenium aerosols in the rat confirm that, once absorbed, selenium from both compounds is distributed and excreted in an identical manner (Medinsky et al. 1981).

In blood, selenium is rapidly taken up by erythrocytes and metabolized to a form that binds to plasma proteins (Lee et al. 1969; Gasiewicz and Smith 1978). The uptake and release was shown to be dependent on glutathione and resulted in depletion of erythrocyte glutathione (Gasiewicz and Smith 1978). When some other forms of selenium are metabolized, hydrogen selenide may be formed as an intermediate through reduction of a selenopersulfide by glutathione reductase (Gasiewicz and Smith 1978). A brief review of selenium metabolic pathways indicates the intermediate formation of hydrogen selenide from inorganic forms of selenium (Lu et al. 1995). Hydrogen selenide formed in this manner may either be incorporated into cellular selenoproteins or further metabolized by methylation before elimination. Methylation of selenium results in the formation of dimethyl selenide, the compound found in exhaled air that is likely responsible for the garlic-breath odor commonly reported in exposed persons (ATSDR 2003). Selenium is excreted in the urine, feces, and expired air (ATSDR 2003).

4.2. Mechanism of Toxicity

The mechanism of toxicity (including pulmonary edema and marked body weight loss) following acute exposure to hydrogen selenide is unknown.

The mechanism of toxicity of selenium and selenium compounds is likely to vary depending on the individual compound (IPCS 1987; ATSDR 2003). One possible mechanism for selenium toxicity is via alteration of enzyme activities, such as inactivation of sulfhydryl enzymes or the succinic dehydrogenase system, interference with glutathione metabolism, or substitution for sulfur in biomolecules (IPCS 1987; ATSDR 2003). Whether these effects may contribute to the toxic effects of hydrogen selenide is unknown.

Examination of the lethality data in guinea pigs (Dudley and Miller 1937, 1941) and rats (Zwart and Arts 1989; Zwart et al. 1992) suggests that hydrogen selenide may exert effects via at least two distinct mechanisms of toxicity. For guinea pigs, it appears that exposures at high concentrations for a short duration result in death due to pulmonary edema as a result of severe irritation. Clinical signs of irritation were observed in the animals. This part of the concentration-response curve is very steep. In contrast, deaths in studies with longer durations occurred over a relatively flat concentration range and were most likely secondary to liver damage. As noted earlier in Section 3.1.1, most deaths occurred more than 5 days after exposure when hepatic damage was greatest. Glutathione depletion by high concentrations of selenium may play a contributing role in the observed hepatic damage.

In Figure 5-1, LC_{50} values for guinea pigs with respect to exposure duration are compared with data on partial lethality in rats (only a 1-h LC_{50} was available for rats). The observation that deaths occur at a threshold concentration at longer durations is also suggested to some degree by data from rats (Zwart and Arts 1989; Zwart et al. 1992); however, the small number of rats (2/concentration) exposed for durations other than 60 min limit the confidence in lethality data for other time points.

4.3. Structure Activity Relationships

Toxicities of the various selenium compounds vary widely depending on the individual compound; hydrogen selenide is one of the most toxic due to its irritant properties (ATSDR 2003).

4.4. Other Relevant Information

4.4.1. Species Variability

Data on hydrogen selenide were available for only two species. Estimated 1-h LC_{50} values for the guinea pig and rat were 3.6 and 72 ppm, respectively. Although these two values suggest significant species differences, other differ-

ences (including whole-body vs. nose-only exposure, different analytic techniques, and differences in the post-exposure observation duration) between the studies make it difficult to draw direct comparisons between the LC_{50}s. Furthermore, in the guinea pig studies, one to three control animals died, raising additional questions as to the reliability of the data. The guinea pig study, which was conducted more than 70 years ago, involved whole body exposures (Dudley and Miller 1937, 1941) that could have resulted in oral exposure to elemental selenium from grooming, as well as percutaneous absorption. The higher total dose from all routes of exposure could have contributed to the hepatic lesions and delayed deaths in guinea pigs. In the more recent rat study, the animals were exposed nose-only (Zwart and Arts 1989; Zwart et al. 1992), eliminating potential exposure by other routes. In addition, the guinea pig study measured concentrations of hydrogen selenide by weighing precipitated selenium, whereas the rat study used atomic absorption spectrometry. Direct measurement of the test atmospheres is probably a more accurate method of determining exposure concentrations. Finally, the guinea pigs were observed for up to 30 days, whereas the rats were observed for only 14 days. All but a few of the guinea pig deaths occurred within the first 15 days in the 1-h study, indicating that the increased observation period probably had limited impact on the value of the LC_{50}; however, a longer observation period in the rat study might also have lead to a slightly lower LC_{50} value. In summary, while the available data suggest that the guinea pig may be more sensitive to hydrogen selenide, conclusions are difficult to draw because of the differences in the exposures, analytic techniques, and observation periods used in the two studies.

4.4.2. Susceptible Populations

In the experiments with guinea pigs (Dudley and Miller 1937, 1941), no significant differences in death rates were found between young animals (body weights 189-283 g) and older animals (body weights 451-701 g) or between males and females exposed to hydrogen selenide.

Epidemiologic studies of populations living in areas with high dietary intakes of selenium suggest that children are less susceptible to selenium intoxication than adults, as 97% of selenosis cases are in individuals more than 18 years of age (ATSDR 2003).

4.4.3. Concentration-Exposure Duration Relationship

As discussed in Section 4.2 and shown in Figure 2-1, lethality data from studies of guinea pigs and the rats suggest two possible mechanisms of action: one that is operant at high concentrations with brief exposures and one that is operant at lower concentrations with longer exposures. Although limited, the data indicate that the first mechanism exhibits a steep concentration-time relationship with a strong time component, whereas the mechanism at lower concen-

trations and longer durations appears to be primarily dependent on concentration. These concentration-time relationships may be explained by the postulated mechanisms of toxicity; exposure at high concentrations results in severe irritation and causes death by pulmonary edema, whereas the liver can compensate for exposure at lower concentrations and of a long duration, and only when a threshold concentration is exceeded are mortalities seen.

The observed concentration-exposure duration relationships pose a challenge in identifying a suitable approach for time scaling AEGL values. AEGL values are scaled to the various durations from experimentally derived values using the equation $C^n \times t = k$, where C = concentration, t = time, k is a constant, and the value of n ranges from 0.8 to 3.5 (ten Berge et al. 1986). Zwart and Arts (1989) derived a value for n (b_1/b_2) of 1.98 from probit analysis of lethality data (Study A, which examined the time and concentration [C × t] relationship for hydrogen selenide) in rats using both concentration and time as variables.

An argument could be made for making separate estimates of n for the two distinct concentration-duration relationships suggested by the guinea pig and rat data; however, many of the data points for shorter exposure durations were associated with 100% mortality, and the numbers of animals (n = 2) in the groups were too small to provide a reliable estimate of n. An alternative to the n value estimated by Zwart and Arts (1989) can be calculated by probit analysis of the combined lethality data from Study A and Study B (1-h LC_{50}study, which used 10 rats/concentration). The value of n is 2.5 on the basis of the combined data. This estimate makes use of the more robust lethality data from Study B, in addition to the data on the concentration-time relationship from Study A. Although this estimate for n might yield lower concentrations than the data might suggest when extrapolating from longer to shorter durations, such extrapolations will be conservative. Furthermore, the empirical value of 2.5 is close to the default value of 3 that is used to extrapolate from longer to shorter durations in the absence of data to estimate an empirical value of n.

4.4.4. Concurrent Exposure Issues

Total body burden of selenium would potentially be of concern only for chronic hydrogen selenide exposures. No other concurrent exposure issues for acute exposures were identified.

5. DATA ANALYSIS FOR AEGL-1

5.1. Summary of Human Data Relevant to AEGL-1

No human data for calculating AEGL-1 values for hydrogen selenide were available. Dudley and Miller (1941) reported anecdotally that workers were able to tolerate a concentration of 0.3 ppm for several minutes without noticeable effects. According to the authors, olfactory fatigue occurred quickly at this con-

centration. However, the report did not provide a citation for this observation, nor any information on sampling or analysis of workplaces to support the statement.

5.2. Summary of Animal Data Relevant to AEGL-1

No animal data for calculating AEGL-1 values for hydrogen selenide were available.

5.3. Derivation of AEGL-1 Values

AEGL-1 values are not recommended for hydrogen selenide. No human or animal data on appropriate end points were available. Data for calculating the level of distinct odor awareness for hydrogen selenide were insufficient because the reported odor threshold of 0.3 ppm was based on an anecdotal report.

6. DATA ANALYSIS FOR AEGL-2

6.1. Summary of Human Data Relevant to AEGL-2

No human data for calculating AEGL-2 values for hydrogen selenide were available. Dudley and Miller (1941) reported that workers exposed at concentrations greater than 1.5 ppm experienced nasal and throat irritation severe enough that they could not remain at work. The duration of exposure was not reported, so it was assumed that effects were immediate. However, as noted earlier, the statements by Dudley and Miller (1941) were not supported by a citation or any information on sampling or analysis of workplaces.

6.2. Summary of Animal Data Relevant to AEGL-2

In lethality studies of hydrogen selenide, histopathologic examinations were performed on guinea pigs (Dudley and Miller 1937, 1941), but severity scores were not specified. The main finding was fatty deposition in the liver and, to a lesser extent, in the kidney; splenic enlargement due to hyperplasia of the lymphoid tissue was also found. Hepatic lesions, but no increase in mortality, were observed at concentrations as low as 1.3 ppm for 30-60 min. Fatty changes became progressively more severe for up to 10 days and generally resolved with 17-20 days after exposure.

6.3. Derivation of AEGL-2 Values

Data for calculating AEGL-2 values were not available. Hepatic lesions in the guinea pig resolved if the exposure was not lethal. According to the AEGL

standing operating procedures (NRC 2001), in the absence of specific data for determining an AEGL-2 value, one-third of the AEGL-3 values can be used to establish AEGL-2 values. This approach is justified because the lethality data indicate a steep concentration-response curve, as discussed in Section 4.4.3. AEGL-2 values for hydrogen selenide are presented in Table 5-4.

7. DATA ANALYSIS FOR AEGL-3

7.1. Summary of Human Data Relevant to AEGL-3

No reports of human lethality following exposure to hydrogen selenide were found.

7.2. Summary of Animal Data Relevant to AEGL-3

Data relevant to determining AEGL-3 values for hydrogen selenide include those from guinea pig (Dudley and Miller 1937, 1941) and rat (Zwart and Arts 1989; Zwart et al. 1992) lethality studies. As described in Section 4.4.1, the guinea pig lethality data (Dudley and Miller 1937, 1941) had a number of uncertainties because the exposures were whole-body instead of nose-only (leading to potential oral and dermal exposure in addition to inhalation), less precise analytic methods to estimate exposure concentrations, and unexplained mortalities in the controls. Consequently, the rat lethality studies were selected for deriving AEGL-3 values.

In the rat studies of 60-min exposures, no animals died at 47 ppm, but 2/10 died at 71 ppm and 6/10 died at 74 ppm. Most deaths occurred within 2 days after exposure. Concentration-related clinical signs included piloerection, red discoloration of the fur, cyanosis, half-closed eyes, red nasal discharge, mouth breathing, moist or dry rales, and apnea. Most surviving animals had body weight loss throughout the observation period. Necropsy revealed gas in the stomach and intestines of premature decedents and red discolored, atelectatic, edematous, or spongy, swollen, and spotted lungs with irregular surface in almost all decedents and survivors.

7.3. Derivation of AEGL-3 Values

To derive AEGL-3 values for hydrogen selenide, two options were considered for identifying a point of departure and time-scaling value. For time scaling, the equation $C^n \times t = k$ was used, where n ranges from 0.8 to 3.5 (ten Berge et al. 1986). For the first option, the point of departure was an LC_{01} of 66 ppm (calculated by log-probit analysis) and n was 2.0, on the basis of data from the 1-h LC_{50} experiment (Zwart and Arts 1989). However, calculation of AEGL

TABLE 5-4 AEGL-2 Values for Hydrogen Selenide

10 min	30 min	1 h	4 h	8 h
0.22 ppm (0.73 mg/m^3)	0.15 ppm (0.48 mg/m^3)	0.11 ppm (0.37 mg/m^3)	0.064 ppm (0.21 mg/m^3)	0.048 ppm (0.16 mg/m^3)

values on the basis of those estimates results in a predicted LC_{01} of 47 ppm at 120 min, which is inconsistent with data that show that a lower concentration of 39 ppm resulted in 1/2 deaths after 120 min of exposure (Zwarts and Art 1989). Thus, it appears that this approach would not be adequately protective.

The second option involved combining data from two experiments to estimate the point of departure and the value of n. The two experiments were a C × t study (Zwarts et al. 1992) and 1-h LC_{50} study (Zwarts and Arts 1989). From the combined data, an LC_{01} of 33 ppm and an n of 2.5 are estimated. This approach yields a 120-min LC_{01} of 25 ppm, which is below the observed lethal concentration of 40 ppm. The combined data were analyzed in total (28 observations) and after excluding data at 1,410 mg/m^3 and higher; mortality was 100% (2/2) at those concentrations, so the data provided little value to the analysis. Both analyses yielded the same 1-h LC_{01} and n value. A total uncertainty factor of 100 was applied. A factor of 10 for interspecies differences was used because data were available only on two species and the limited data indicate that the rat may not be the most sensitive (see Section 4.4.1). A value of 10 for intraspecies variability was applied because of uncertainty with respect to the mechanism of action for the marked body weight loss exhibited by some surviving rats in the second week of observation, and uncertainty as to whether this body weight loss reflected a moribund state. AEGL-3 values for hydrogen selenide are presented in Table 5-5.

8. SUMMARY OF AEGL VALUES

8.1. AEGL Values and Toxicity End Points

AEGL values for hydrogen selenide are summarized in Table 5-6. AEGL-1 values are not recommended because symptoms in workers have been reported at concentrations at or below the odor threshold and because values based on irritation may not account for the delayed onset of pulmonary edema. Data on hydrogen selenide were inadequate for calculating AEGL-2 values, so estimates were made taking one-third of the AEGL-3 values. For AEGL-3 values, a 1-h LC_{01} calculated from mortality data in rats was used to derive values.

8.2. Comparison with Other Standards and Guidelines

Standards and guidance levels for workplace and community exposures to hydrogen selenide are presented in Table 5-7. The concentration that is immediately dangerous to life and health (IDLH) is 1 ppm (NIOSH 1994), which is

higher than the 30-min AEGL-3 value of 0.44 ppm. The supporting documentation of the IDLH value indicates that it is based on acute inhalation data in humans, and cites Dudley and Miller (1941) and Glover et al. (1979) but does not provide details of the derivation.

TABLE 5-5 AEGL-3 Values for Hydrogen Selenide

10 min	30 min	1 h	4 h	8 h
0.67 ppm (2.2 mg/m^3)	0.44 ppm (1.5 mg/m^3)	0.33 ppm (1.1 mg/m^3)	0.19 ppm (0.63 mg/m^3)	0.14 ppm (0.48 mg/m^3)

TABLE 5-6 AEGL Values for Hydrogen Selenide

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)	0.22 ppm (0.73 mg/m^3)	0.15 ppm (0.48 mg/m^3)	0.11 ppm (0.37 mg/m^3)	0.064 ppm (0.21 mg/m^3)	0.048 ppm (0.16 mg/m^3)
AEGL-3 (lethal)	0.67 ppm (2.2 mg/m^3)	0.44 ppm (1.5 mg/m^3)	0.33 ppm (1.1 mg/m^3)	0.19 ppm (0.63 mg/m^3)	0.14 ppm (0.48 mg/m^3)

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

TABLE 5-7 Standards and Guidelines for Hydrogen Selenide

	Exposure Duration				
Guideline	10 min	30 min	1 h	4 h	8 h
AEGL-1	NR	NR	NR	NR	NR
AEGL-2	0.22 ppm	0.15 ppm	0.11 ppm	0.064ppm	0.048 ppm
AEGL-3	0.67 ppm	0.44 ppm	0.33 ppm	0.19 ppm	0.14 ppm
ERPG-1 (AIHA)[a]			Not appropriate		
ERPG-2 (AIHA)			0.2 ppm		
ERPG-3 (AIHA)			2.0 ppm		
IDLH (NIOSH)[b]		1 ppm as Se			
TLV-TWA (ACGIH)[c]					0.05 ppm as Se
REL-TWA (NIOSH)[d]					0.05 ppm as Se
PEL-TWA (OSHA)[e]					0.05 ppm as Se
MAK (Germany)[f]					0.006 ppm
MAC (The Netherlands)[g]					0.025 ppm

[a]ERPG (emergency response planning guidelines, American Industrial Hygiene Association [AIHA 2002, 2013]).
ERPG-1 is the maximum airborne concentration below which it is believed nearly all individuals could be exposed for up to 1 h without experiencing other than mild, transient adverse health effects or without perceiving a clearly defined objectionable odor.

ERPG-2 is the maximum airborne concentration below which it is believed nearly all individuals could be exposed for up to 1 h without experiencing or developing irreversible or other serious health effects or symptoms that could impair an individual's ability to take protection action.
ERPG-3 is the maximum airborne concentration below which it is believed nearly all individuals could be exposed for up to 1 h without experiencing or developing life-threatening health effects.
[b]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.
[c]TLV-TWA (threshold limit value - time weighted average, American Conference of Governmental Industrial Hygienists) (ACGIH 2001, 2012) is the time-weighted average concentration 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.
[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, but is for exposures of no more than 10 h/day, 40 h/week.
[e]PEL-TWA (permissible exposure limit - time weighted average, Occupational Safety and Health Administration) (29 CFR 1910.1000 [2006]) is defined analogous to the ACGIH TLV-TWA.
[f]MAK (maximale arbeitsplatzkonzentration [maximum workplace concentration]) (Deutsche Forschungsgemeinschaft [German Research Association] (DFG 2012) is defined analogous to the ACGIH TLV-TWA.
[g]MAC (maximaal aanvaaarde concentratie [maximum accepted concentration]) Dutch Expert Committee for Occupational Standards, The Netherlands (MSZW 2004), is defined analogous to the ACGIH TLV-TWA.

The emergency response planning guidelines (ERPGs) for hydrogen selenide are slightly higher than the corresponding AEGL values. AIHA (2002, 2013) derived an ERPG-3 of 2 ppm, noting that this value is higher than a concentration associated with acute intoxication of five workers (citing Buchan 1947) but well below the 1-h LC_{50} values of 51-72 ppm in rats (based on Zwart and Arts 1989 and Zwart et al. 1992). The ERPG-2 of 0.2 ppm was based on the statements by Dudley and Miller (1941) that 0.3 ppm was tolerated by healthy workers without irritation for several minutes and that 1.5 ppm was irritating to the eye and nose. An ERPG-1 was not set because the ERPG-2 was below the odor threshold of 0.3 ppm (AIHA 2002, 2013).

The current occupational exposure limit reported by the American Conference of Governmental Industrial Hygienists (ACGIH), the Occupational Safety and Health Administration (OSHA), the National Institute for Occupational Safety and Health, and German Research Association is 0.05 ppm (as selenium) whereas the value reported by The Netherlands is 0.025 ppm (RTECS 2009). Documentation for the ACGIH threshold limit value indicates only that the value was set to "minimize the potential for irritation, gastrointestinal effects, and the onset of chronic hydrogen selenide-related disease" (ACGIH 2001). The

OSHA standard for hydrogen selenide was derived in 1978, but the supporting documentation (29 CFR 1910.1000 [2006]) does not describe how the value was derived.

In addition to the guidelines presented in Table 5-7, the state of California has adopted 0.002 ppm (0.005 mg/m^3) as the acute reference exposure level for hydrogen selenide (CalEPA 2007). This concentration is based on data from studies in guinea pigs by Dudley and Miller (1937, 1941).

8.3. Data Adequacy and Research Needs

Little human or animal data on hydrogen selenide are available. Although symptoms in humans were well described, case reports did not include reliable exposure concentrations. Two well-conducted animal lethality studies were available, but the study in guinea pigs suffered from a variety of limitations, including potential exposure via multiple routes, use of a more uncertain analytic technique to estimate exposure concentrations, and unexplained control mortalities (see Section 4.4.1). Thus, it is difficult to draw conclusions regarding species differences (if any).

9. REFERENCES

ACGIH (American Conference of Government and Industrial Hygienists). 2001. Hydrogen selenide (CAS Reg. No. 7783-07-5). Documentation of the Threshold Limit Values and Biological Exposure Indices, 7th Ed. American Conference of Government and Industrial Hygienists, Cincinnati, OH.

ACGIH (American Conference of Government and Industrial Hygienists). 2012. Hydrogen selenide (CAS Reg. No. 7783-07-5). P. 35 in TLVs and BEIs Based on the Documentation of the Threshold Limit Values for Chemical Substances and Physical Agents & Biological Exposure Indices. American Conference of Government and Industrial Hygienists, Cincinnati, OH.

AIHA (American Industrial Hygiene Association). 1989. P. 20 in Odor Thresholds for Chemicals with Established Occupational Health Standards. Fairfax, VA: American Industrial Hygiene Association.

AIHA (American Industrial Hygiene Association). 2002. Emergency Response Planning Guidelines: Hydrogen selenide. Fairfax, VA: American Industrial Hygiene Association.

AIHA (American Industrial Hygiene Association). 2013. P. 26 in ERPG/WEEL Handbook. American Industrial Hygiene Association [online]. Available: https://www.aiha.org/get-involved/AIHAGuidelineFoundation/EmergencyResponsePlanningGuidelines/Documents/2013ERPGValues.pdf [accessed Jan. 3, 2014].

Alderman, L.C., and J.J. Bergin. 1986. Hydrogen selenide poisoning: An illustrative case with review of the literature. Arch. Environ. Health 41(6):354-358.

ATSDR (Agency for Toxic Substances and Disease Registry). 2003. Toxicological Profile for Selenium. U.S. Department of Health and Human Services, Public Health Service, Agency for Toxic Substances and Disease Registry, Atlanta, GA. September 2003 [online]. Available: http://www.atsdr.cdc.gov/toxprofiles/tp92.pdf [accessed Jan. 3, 2014].

Banerjee, B.D., S. Dwivedi, and S. Singh. 1997. Acute hydrogen selenide gas poisoning admissions in one of the hospitals in Delhi, India: Case report. Hum. Exp. Toxicol. 16(5):276-278.

Buchan, R.F. 1947. Industrial selenosis; A review of the literature, report of five cases and a general bibliography. Occup. Med. 3(5):439-456.

CalEPA (California Environmental Protection Agency). 2007. Acute Reference Exposure Level (RELs). Air Toxicology and Epidemiology, Office of Environmental Health Hazard Assessment, California Environmental Protection Agency [online]. Available: http://oehha.ca.gov/air/allrels.html [accessed Jan. 3, 2014]

Clinton, M. 1947. Selenium fume exposure. J. Ind. Hyg. Toxicol. 29(4):225.

DFG (Deutsche Forschungsgemeinschaft). 2012. Substance Overview for Hydrogen Selenide. The MAK Collection for Occupational Health and Safety. Wiley [online]. Available: http://onlinelibrary.wiley.com/doi/10.1002/3527600418.mbe778307/full [accessed Jan. 3, 2014].

Ducloux, J.P., B. Ducloux, P. Frantz, and V. Vincent. 1976. Recording a selenium intoxication. Review of the literature. Acta Pharmacol. Toxicol. 41(suppl. 2):427.

Dudley, H.C., and J.W. Miller. 1937. Toxicology of selenium. IV. Effects of exposure to hydrogen selenide. Public Health Rep. 52(36):1217-1231.

Dudley, H.C., and J.W. Miller. 1941. Toxicology of selenium. VI. Effects of subacute exposure to hydrogen selenide. J. Ind. Hyg. Toxicol. 23(10):470-477.

EPA (U.S. Environmental Protection Agency). 1993. Selenium and Compounds (CAS Reg. No. 7782-49-2). Carcinogenicity Assessment, Integrated Risk Information System, U.S. Environmental Protection Agency [online]. Available: http://www.epa.gov/iris/subst/0472.htLC [accessed Aug. 17, 2012].

Gasiewicz, T.A., and J.C. Smith. 1978. The metabolism of selenite by intact rat erythrocytes *in vitro*. Chem. Biol. Interact. 21(2-3):299-313.

Gerhardsson, L., D. Brune, G.F. Nordberg, and P.O. Wester. 1986. Selenium and other trace elements in lung tissue in smelter workers relationship to the occurrence of lung cancer. Acta Pharmacol. Toxicol. 59(suppl. 7):256-259.

Glover, J.R. 1970. Selenium and its industrial toxicology. IMS Ind. Med. Surg. 39(1):50-54.

Glover J., O. Levander, J. Parizek, and V. Vouk. 1979. Selenium. Pp. 555-557 in Handbook on the Toxicology of Metals, L. Friberg, G.F. Norberg, and V. Vouk, eds. Amsterdam: Elsevier/North Holland Biomedical Press.

Hall, R.H., S. Laskin, P. Frank, E.A. Maynard, and H.C. Hodge. 1951. Preliminary observations on toxicity of elemental selenium. AMA Arch. Ind. Hyg. Occup. Med. 4(5):458-464.

IPCS (International Programme on Chemical Safety). 1987. Selenium. Environmental Health Criteria 58. World Health Organization, Geneva, Switzerland [online]. Available: http://www.inchem.org/documents/ehc/ehc/ehc58.htm [accessed Jan. 2, 2014].

Lee, M., A. Dong, and J. Yano. 1969. Metabolism of ^{75}Se-selenite by human whole blood *in vitro*. Can. J. Biochem. 47(8):791-797.

Lu, J., C. Jiang, M. Kaeck, H. Ganther, S. Vadhanavikit, C. Ip, and H. Thompson. 1995. Dissociation of the genotoxic and growth inhibitory effects of selenium. Biochem. Pharmacol. 50(2):213-219.

Malczewska-Toth, B. 2012. Phosphorus, selenium, tellurium, and sulfur. Pp. 841-884 in Patty's Industrial Hygiene and Toxicology. New York: Wiley.

Medinsky, M.A., R.G. Cuddihy, W.C. Griffith, and R.O. McClellan. 1981. A simulation model describing the metabolism of inhaled and ingested selenium compounds. Toxicol. Appl. Pharmacol. 59(1):54-63.

MSZW (Ministerie van Sociale Zaken en Werkgelegenheid). 2004. Nationale MAC-lijst 2004: Seleen en verbindingen. Den Haag: SDU Uitgevers [online]. Available: http://www.lasrook.net/lasrookNL/maclijst2004.htm [accessed Jan. 3, 2014].

NIOSH (National Institute for Occupational Safety and Health). 1994. Documentation for Immediately Dangerous to Life or Health Concentrations (IDLHs): Hydrogen Selenide (as Se). U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, Cincinnati, OH [online]. Available: http://www.cdc.gov/niosh/idlh/7783075.html [accessed Aug. 17, 2012].

NIOSH (National Institute for Occupational Safety and Health). 2011. NIOSH Pocket Guide to Chemical Hazards: Hydrogen Selenide. U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, Cincinnati, OH [online]. Available: http://www.cdc.gov/niosh/npg/npgd0336.html [accessed Aug. 17, 2012].

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. P. 43 in Standing Operating Procedures for Developing Acute Exposure Guideline Levels for Hazardous Chemicals. Washington, DC: National Academy Press.

NTP (National Toxicology Program). 1980a. Bioassay of Selenium Sulfide (Dermal Study) for Possible Carcinogenicity. Technical Report No. 197. NTP No. 80-18. U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health, National Cancer Institute, Bethesda, MD, and National Toxicology Program, Research Triangle Park, NC [online]. Available: http://ntp.niehs.nih.gov/ntp/htdocs/LT_rpts/TR197.pdf [accessed Jan. 2, 2014].

NTP (National Toxicology Program). 1980b. Bioassay of Selsun for Possible Carcinogenicity. Technical Report No. 199. NTP No. 80-19. U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health, National Cancer Institute, Bethesda, MD, and National Toxicology Program, Research Triangle Park, NC [online]. Available: http://ntp.niehs.nih.gov/ntp/htdocs/LT_rpts/tr199.pdf [accessed Jan. 2, 2014].

O'Neil, M.J., P.E. Heckelman, C.B. Koch, and K.J. Roman, eds. 2006. Hydrogen selenide. P. 831inThe Merck Index: An Encyclopedia of Chemicals, Drugs, and Biologicals, 14th Ed. Whitehouse Station, NJ: Merck.

Rosenfeld, I., and O.A. Beath. 1964. Selenium: Geobotany, Biochemistry, Toxicity, and Nutrition. New York: Academic Press. 411 pp.

RTECS (Registry of Toxic Effects of of Chemical Substances). 2009. Hydrogen selenide. RTECS No. MX1050000 [online]. Available: http://www.cdc.gov/niosh-rtecs/MX100590.html [accessed Jan. 3, 2014].

Ruth, J.H. 1986. Odor thresholds and irritation levels of several chemical substances: A review. Am. Ind. Hyg. Assoc. J. 47(3):A142-A151.

Schecter, A., W. Shanske, A. Stenzler, H. Quintilian, and H. Steinberg. 1980. Acute hydrogen selenide inhalation. Chest 77(4):554-555.

Shepard, T.H. 2010. P. 383 in Catalog of Teratogenic Agents, 13th Ed. Baltimore, MD: The Johns Hopkins University Press.

Sunde, R.A. 1990. Molecular biology of selenoproteins. Annu. Rev. Nutr. 10:451-474.

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.

Weissman, S.H., R.G. Cuddihy, and M.A. Medinsky. 1983. Absorption, distribution, and retention of inhaled selenious acid and selenium metal aerosols in beagle dogs. Toxicol. Appl. Pharmacol. 67(3):331-337.

Yaws, C.L., ed. 2001. Pp. 404-407 in Matheson Gas Data Book, 7th Ed. New York: McGraw-Hill.

Zwart, A., and J.H.E. Arts. 1989. Acute (1-hour) Inhalation Toxicity Study with Hydrogen Selenide in Rats. Report No. V 89.463. Zeist, The Netherlands: TNO-CIVO Institutes.

Zwart, A., J.H. Arts, W.J. ten Berge, and L.M. Appleman. 1992. Alternative acute inhalation toxicity testing by determination of the concentration-time-mortality relationship: Experimental comparison with standard LC_{50} testing. Regul. Toxicol. Pharmacol. 15(3):278-290.

APPENDIX A

DERIVATION OF AEGL VALUES

Derivation of AEGL-1 Values

AEGL-1 values for hydrogen selenide are not recommended. No animal or human data on appropriate end points were found. A level of distinct odor awareness could not be calculated because the reported odor threshold of 0.3 ppm was not documented. In addition, AEGL-1 values based on irritation may not account for delayed onset of pulmonary edema.

Derivation of AEGL-2 Values

In the absence of relevant data to derive AEGL-2 values and because hydrogen selenide has a steep concentration-response relationship, AEGL-3 values were divided by 3 to estimate AEGL-2 values (NRC 2001).

Calculations:

10-min AEGL-2:	0.67 ppm ÷ 3 = 0.22 ppm
30-min AEGL-2:	0.44 ppm ÷ 3 = 0.15 ppm
1-h AEGL-2:	0.33 ppm ÷ 3 = 0.11 ppm
4-h AEGL-2:	0.19 ppm ÷ 3 = 0.064 ppm
8-h AEGL-2:	0.14 ppm ÷ 3 = 0.048 ppm

Derivation of AEGL-3

Key studies:	Zwart, A., and J.H.E. Arts. 1989. Acute (1-hour) Inhalation Toxicity Study with Hydrogen Selenide in rats. Report No. V 89.463. Zeist, The Netherlands: TNO-CIVO Institutes.
	Zwart, A., J.H.E. Arts, W.J. ten Berge, and L.M. Appleman. 1992. Alternative acute inhalation toxicity testing by determination of the concentration-time-mortality relationship: Experimental comparison with standard LC_{50} testing. Regul. Toxicol. Pharmacol. 15(3):278-290.
Toxicity end point:	1-h LC_{01} of 33 ppm, calculated by log-probit analysis of the combined lethality data from the two experiments in rats (1-h LC_{50} study and C × t study).

Time scaling:	$C^n \times t = k$ (n = 2.5, based on probit analysis of the combined lethality data)
Uncertainty factors:	10 for interspecies differences 10 for intraspecies variability
Modifying factor:	None
Calculations:	
10-min AEGL-3:	$C^{2.5} \times 0.167$ h = 6,255.829 ppm-h C = (6,255.829 ppm-h ÷ 0.167 h)$^{1/2.5}$ = 67.04 ppm 67.04 ÷ 100 = 0.67
30-min AEGL-3:	$C^{2.5} \times 0.5$ h = 6,255.829 ppm-h C = (6,255.829 ppm-h ÷ 0.5 h)$^{1/2.5}$ = 43.54 ppm 43.54 ÷ 100 = 0.44
1-h AEGL-3:	C = 33 ppm 33 ÷ 100 = 0.33 ppm
4-h AEGL-3:	$C^{2.5} \times 4$ h = 6,255.829 ppm-h C = (6,255.829 ppm-h ÷ 4 h)$^{1/2.5}$ = 18.95 18.95 ÷ 100 = 0.19 ppm
8-h AEGL-3:	$C^{2.5} \times 8$ h = 6,255.829 ppm-h C = (6,255.829 ppm-h ÷ 8 h)$^{1/2.5}$ = 14.36 ppm 14.36 ÷ 100 = 0.14

APPENDIX B

DERIVATION SUMMARY FOR HYDROGEN SELENIDE

AEGL-1 VALUES

AEGL-1 values for hydrogen selenide are not recommended because of insufficient data. No animal or human data on appropriate end points were found. A level of distinct odor awareness could not be calculated because the reported odor threshold of 0.3 ppm was not documented. In addition, AEGL-1 values may not account for pulmonary edema, which may occur from exposures resulting in irritation after a latency period.

AEGL-2 VALUES

10 min	30 min	1 h	4 h	8 h
0.22 ppm	0.15 ppm	0.11ppm	0.064 ppm	0.048 ppm

Data adequacy: No data with appropriate end points for deriving AEGL-2 values were available. Therefore, one-third of the AEGL-3 values were used to estimate AEGL-2 values (NRC 2001).

AEGL-3 VALUES

10 min	30 min	1 h	4 h	8 h
0.67 ppm	0.44 ppm	0.33 ppm	0.19 ppm	0.14 ppm

Key references:
Zwart, A., and J.H.E. Arts. 1989. Acute (1-h) Inhalation Toxicity Study with Hydrogen Selenide in Rats. Report No. V 89.463. Zeist, The Netherlands: TNO-CIVO Institutes.
Zwart, A., J.H.E. Arts, W.J. ten Berge, and L.M. Appleman. 1992. Alternative acute inhalation toxicity testing by determination of the concentration-time-mortality relationship: Experimental comparison with standard LC_{50} testing. Regul. Toxicol. Pharmacol. 15(3):278-290.

Test species/Strain/Number: Rat (males and females), Wistar, 2-10 per group

Exposure route/Concentrations/Durations: Nose-only; 39-870 ppm; 4-120 min

Effects: Mortality (incidence); clinical signs of irritation occurred at all concentrations
≥ 423 ppm for ≥4 min: 2/2
117 ppm for 4 min: 0/2
117 ppm for 7.5 min: 1/2
117 ppm for 15 min: 0/2
117 ppm for 30 min: 2/2
78 ppm for 30 min: 2/2
39 ppm for 30 min: 0/2
39 ppm for 42 min: 0/2
117 ppm for 60 min: 2/2
78 ppm for 60 min: 2/2
74 ppm for 60 min: 6/10

71 ppm for 60 min: 2/10
47 ppm for 60 min: 0/10
39 ppm for 60 min: 0/2
78 ppm for 60 min: 2/2
78 ppm for 84 min: 2/2
39 ppm for 84 min: 1/2
39 ppm for 120 min: 1/2
78 ppm for 120 min: 2/2

End point/Concentration/Rationale: LC_{01} of 33 ppm, calculated by log-probit analysis of combined data from the two studies

Uncertainty factors/Rationale:
Total uncertainty factor: 100
Interspecies: 10; data are available in only two species, and the rat is not the most sensitive species
Intraspecies: 10; although the steepness of concentration-response relationship indicates little individual variation, this factor was applied to account for the uncertainty with respect to the mechanism for and long-term implications of marked body weight loss in surviving rats

Modifying factor: None

Animal-to-human dosimetric adjustment: Not applicable

Time scaling: $C^n \times t = k$ where $n = 2.5$. Empirical value of n calculated from log probit analysis of rat lethality data combined from the two studies.

Data adequacy: Limited data are available for hydrogen selenide. AEGL-3 values were based on a well-conducted and documented study. Exposures were by nose-only administration, which eliminated potential confounding exposure routes.

APPENDIX C

CATEGORY PLOT FOR HYDROGEN SELENIDE

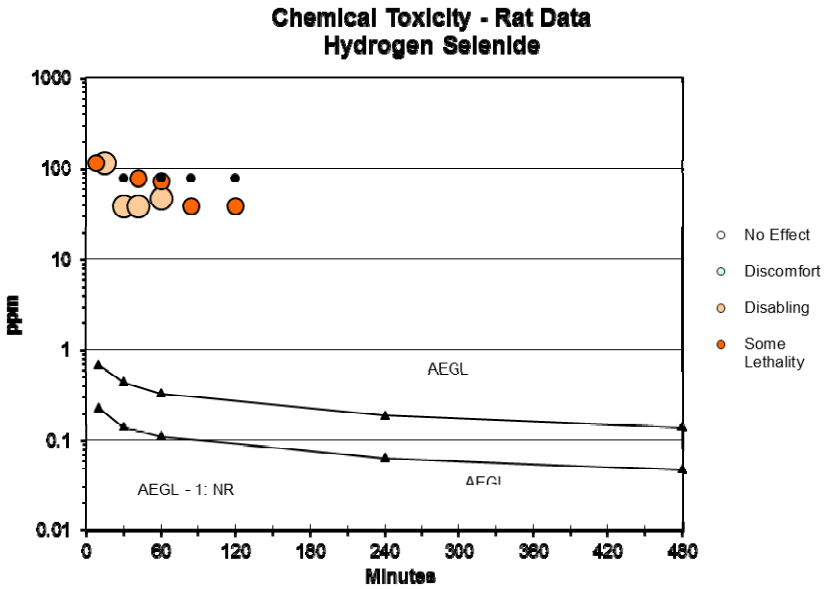

FIGURE C-1 Category plot of toxicity data and AEGL values for hydrogen selenide. Note: There are no documented human data on hydrogen selenide; anectodal information reported by Dudley and Miller (1941) is considered unreliable because no citation was provided nor did the authors indicate sampling or analysis methods to supporting their statements. Guinea pig data are not included because a large number of deaths occurred in the control groups for this study.

TABLE C-1 Data Used in Category Plot for Hydrogen Selenide

Source	Species	Sex	No. exposures	ppm	Minutes	Category	Effect
AEGL-1				NR	10	AEGL	
AEGL-1				NR	30	AEGL	
AEGL-1				NR	60	AEGL	
AEGL-1				NR	240	AEGL	
AEGL-1				NR	480	AEGL	
AEGL-2				0.22	10	AEGL	
AEGL-2				0.14	30	AEGL	
AEGL-2				0.11	60	AEGL	
AEGL-2				0.064	240	AEGL	
AEGL-2				0.048	480	AEGL	
AEGL-3				0.67	10	AEGL	
AEGL-3				0.44	30	AEGL	
AEGL-3				0.33	60	AEGL	
AEGL-3				0.19	240	AEGL	
AEGL-3				0.14	480	AEGL	
	Rat	M/F	1	117	7.5	SL	Mortality 1/2
	Rat	M/F	1	117	15	2	Pilerection, red discoloration of fur, blue discoloration of limbs, half-closed eyes, red nasal discharge, mouth breathing, moist or dry rales, apnea, body weight loss

(Continued)

TABLE C-1 Continued

Source	Species	Sex	No. exposures	ppm	Minutes	Category	Effect
	Rat	M/F	1	39	30	2	Clinical signs as above
	Rat	M/F	1	78	30	3	Mortality 2/2
	Rat	M/F	1	39	42	2	Clinical signs as above
	Rat	M/F	1	78	42	SL	Mortality1/2
	Rat	M/F	1	47	60	2	Clinical signs as above
	Rat	M/F	1	72	60	SL	LC_{50}
	Rat	M/F	1	78	60	3	Mortality 2/2
	Rat	M/F	1	39	84	SL	Mortality 1/2
	Rat	M/F	1	78	84	3	Mortality 2/2
	Rat	M/F	1	39	120	SL	Mortality 1/2
	Rat	M/F	1	78	120	3	Mortality 2/2

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