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Acute Exposure Guideline Levels for Selected Airborne Chemicals

VOLUME 15

Committee on Acute Exposure Guideline Levels

Committee on Toxicology

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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 fifteenth volume

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

in that series. AEGL documents for ethyl mercaptan, methyl mercaptan, phenyl mercaptan, tert-octyl mercaptan, lewisite, methyl isothiocyanate, and selected monoisocyanates 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 ethyl mercaptan (interim reports 19a, 20a, and 21a), methyl mercaptan (interim reports 15, 19a, 20a, and 21a), phenyl mercaptan (interim reports 19a, 20a, and 21a), tert-octyl mercaptan (interim reports 19a, 20a, and 21a), lewisite (interim reports 19a and 21a), methyl isothiocyanate (interim reports 20a and 21a), and selected monoisocyantes (interim reports 20a, 20b, 21a): Harvey Clewell (The Hamner Institutes for Health Sciences), Jeffrey Fisher (U.S. Food and Drug Administration), 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], and Judith Zelikoff (New York University).

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

ments 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

Contents

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

This report is the fifteenth 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 fourteen 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, 2013). This report is the fifteenth volume in that series. AEGL documents for ethyl mercaptan, methyl mercaptan, phenyl mercaptan, tert-octyl mercaptan, lewisite, methyl isothiocyanate, and selected monoisocyanates are each published as an appendix in this report. The committee concludes that the AEGLs developed in these appendixes are scientifically valid conclusions based on the data reviewed by NAC and are consistent with the NRC guideline reports. AEGL reports for additional chemicals will be presented in subsequent volumes.

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Appendixes

4

tert-Octyl Mercaptan[1]

Acute Exposure Guideline Levels

PREFACE

Under the authority of the Federal Advisory Committee Act (FACA) P.L. 92-463 of 1972, the National Advisory Committee for Acute Exposure Guideline Levels for Hazardous Substances (NAC/AEGL Committee) has been established to identify, review, and interpret relevant toxicologic and other scientific data and develop AEGLs for high-priority, acutely toxic chemicals.

AEGLs represent threshold exposure limits for the general public and are applicable to emergency exposure periods ranging from 10 minutes (min) to 8 hours (h). Three levels—AEGL-1, AEGL-2, and AEGL-3—are developed for each of five exposure periods (10 and 30 min and 1, 4, and 8 h) and are distinguished by varying degrees of severity of toxic effects. The three AEGLs are defined as follows:

AEGL-1 is the airborne concentration (expressed as parts per million or milligrams per cubic meter [ppm or mg/m^3]) of a substance above which it is predicted that the general population, including susceptible individuals, could experience notable discomfort, irritation, or certain asymptomatic, nonsensory effects. However, the effects are not disabling and are transient and reversible upon cessation of exposure.

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

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

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

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

SUMMARY

tert-Octyl mercaptan is a colorless liquid with a disagreeable odor. It is used in polymer modification and as a lubricant additive. It is generally prepared via acid-catalyzed synthesis. It is moderately irritating to the eyes, and may cause headache, nausea, vomiting, and central nervous system (CNS) effects, resulting in dizziness, convulsions, unconsciousness, and respiratory depression (HSDB 2006).

Data were insufficient to derive AEGL-1 values for tert-octyl mercaptan. Therefore, AEGL-1 values are not recommended.

Data on tert-octyl mercaptan were also insufficient to derive AEGL-2 values. In the absence of appropriate chemical-specific data, AEGL-3 values were divided by 3 to derive AEGL-2 values for tert-octyl mercaptan. This approach is justified by the chemical's steep concentration-response curve for lethality in rats.

AEGL-3 values were based on a 4-h $BMCL_{05}$ (benchmark concentration, 95% confidence limit with 5% response) value for tert-octyl mercaptan of 11.5 ppm, calculated from combined data on female rats (Temple University 1982). This concentration is considered a threshold for lethality and is based on the most sensitive test animals (females). An intraspecies uncertainty factor of 3 was applied and is considered sufficient because the point of departure is based on data from the more sensitive female animals and the steep concentration-response curve for lethality suggests limited intraindividual variability. An interspecies uncertainty factor of 3 was also applied because the limited data suggest

no difference in species sensitivity between rats and mice. Therefore, the total uncertainty factor was 10. Values were scaled across time using the equation $C^n \times t = k$, where default values of n = 3 when extrapolating to shorter durations and n = 1 when extrapolating to longer durations were used to derive values protective of human health (NRC 2001). The 30-min AEGL-3 value was adopted as the 10-min value because of the uncertainty in extrapolating a 4-h point of departure to a 10-min value.

AEGL values for tert-octyl mercaptan are presented in Table 4-1.

1. INTRODUCTION

tert-Octyl mercaptan is a colorless liquid with a disagreeable odor. It is used in polymer modification and as a lubricant additive. It is generally prepared via acid-catalyzed synthesis. It is moderately irritating to the eyes, and may cause headache, nausea, vomiting, and CNS effects, resulting in dizziness, convulsions, unconsciousness, and respiratory depression (HSDB 2006).

The chemical and physical properties of tert-octyl mercaptan are presented in Table 4-2.

2. HUMAN TOXICITY DATA

2.1. Acute Lethality

Human lethality data on tert-octyl mercaptan were not found.

2.2. Nonlethal Toxicity

Human nonlethal toxicity data on tert-octyl mercaptan were not found. No odor threshold data were available either.

2.3. Case Reports

No case reports on tert-octyl mercaptan were found.

2.4. Developmental and Reproductive Effects

Data on the developmental and reproductive toxicity of tert-octyl mercaptan in humans were not available.

2.5. Genotoxicity

No information regarding the genotoxicity of tert-octyl mercaptan in humans was available.

TABLE 4-1 AEGL Values for tert-Octyl Mercaptan

Classification	10 min	30 min	1 h	4 h	8 h	End Point (Reference)
AEGL-1[a] (nondisabling)	NR	NR	NR	NR	NR	Insufficient data
AEGL-2 (disabling)	0.77 ppm (4.6 mg/m^3)	0.77 ppm (4.6 mg/m^3)	0.60 ppm (3.6 mg/m^3)	0.40 ppm (2.4 mg/m^3)	0.19 ppm (1.1 mg/m^3)	One-third the AEGL-3 values.
AEGL-3 (lethal)	2.3 ppm (14 mg/m^3)	2.3 ppm (14 mg/m^3)	1.8 ppm (11 mg/m^3)	1.2 ppm (7.2 mg/m^3)	0.58 ppm (3.5 mg/m^3)	Threshold for lethality ($BMCL_{05}$) in female rats (Temple University 1982)

[a]The absence of AEGL-1 values does not imply that concentrations below AEGL-2 values will be without effect.
Abbreviations: $BMCL_{05}$, benchmark concentration, 95% confidence limit with 5% response; NR, not recommended.

TABLE 4-2 Chemical and Physical Data on tert-Octyl Mercaptan

Parameter	Value	Reference
Synonyms	tert-octanethiol; 2-methyl-2-heptanethiol; 2-pentanethiol, 2,4,4-trimethyl-	HSDB 2006
CAS registry no.	141-59-3	HSDB 2006
Chemical formula	$C_8H_{18}S$	HSDB 2006
Molecular weight	146.30	HSDB 2006
Physical state	Colorless liquid	HSDB 2006
Boiling point	154 -166°C	HSDB2006
Flash point	43°C	Shertzer 2001
Density/specific gravity	0.848 at 15.5°C	HSDB 2006
Relative vapor density	5.0 (air = 1)	HSDB 2006
Solubility in water	31 mg/L at 25°C	HSDB 2006
Saturated vapor concentration (neat)	6,842 ppm (41,052 mg/m^3)	Calculated
Vapor pressure	5.20 mm Hg at 25°C	HSDB 2006
Conversion factors in air	1 ppm = 6.0 mg/m^3 1 mg/m^3 = 0.17 ppm	

2.6. Carcinogenicity

No information was available regarding the carcinogenicity of tert-octyl mercaptan in humans.

2.7. Summary

No human data on tert-octyl mercaptan were found.

3. ANIMAL TOXICITY DATA

3.1. Acute Lethality

3.1.1. Rats

Fairchild and Stokinger (1958) exposed groups of five Wistar-derived male rats (body weight 180 -220g) to tert-octyl mercaptan at 38, 40, 44, 55, 64, 78, or 110 ppm (analytic concentrations) for up to 4 h, followed by a 15-day observation period. Vapor was generated by either bubbling a stream of nitrogen gas through a midget fritted-glass bubbler, which contained liquid tert-octyl mercaptan, or by passage of nitrogen into a borosilicate glass nebulizer containing the tert-octyl mercaptan. Target concentrations were maintained in an 18-L glass chamber by varying the ratio of air flow volume and tert-octyl mercaptan containing compressed nitrogen. Tert-octyl mercaptan concentrations during exposure periods were measured by absorption of vapors in either isopropyl alcohol or acetone containing an excess of silver nitrate and titrating the uncombined silver amperometrically. Chamber concentrations during tests were uniform after the first 30 min; mean variation was approximately 4%. Clinical signs included respiratory stimulation, followed by CNS stimulation initially characterized by a "threshold effect" consisting of localized minimal convulsive movements in the form of repeated facial and ear twitches. Seizures were observed at all concentrations; the severity, frequency, and latency period for the onset of seizures were concentration related. Propulsive and retropulsive thrusts of the trunk were also observed, followed by circumscribed clonic convulsions of the forebody and forelimbs, resulting in a sitting position while pawing in the air. These effects were followed by generalized clonic seizures of the forelimbs and hindlimbs that caused a loss of upright position. Exophthalmus with conjunctival congestion and salivation accompanied the seizures. Muscle relaxation, irregular labored breathing, and coma preceded death. An LC_{50} (lethal concentration, 50% lethality) value of 51 ppm was calculated by the investigators. A BMC_{01} of 34.4 ppm and $BMCL_{05}$ of 31.8 ppm were also calculated. Mortality data from this study are presented in Table 4-3.

Groups of five male and five female Sprague-Dawley rats were exposed to tert-octyl mercaptan at 0, 7, 15, 19, 29, 59, 71, or 110 ppm for 4 h, followed by a 14-day observation period (Temple University 1982). Exposures were conducted in an 11.4-ft^3 stainless-steel chamber. Vapor was generated by heating liquid tert-octyl mercaptan and passing air through at a constant rate. Chamber delivery system parameters were set at values calculated to produce target chamber concentrations. Analyses of tert-octyl mercaptan concentrations in the test atmospheres were performed by colorimetric titration four to 20 times during each 4-h exposure.

Clinical signs were noted in females at concentrations of 19 ppm and higher. The animals seized the wire mesh bottom of the exposure chamber with their teeth and claws, their backs were arched and tails extended, and they remained rigidly in this position until death or until the survivors were pried loose by the investigator. Salivation and a final convulsive leap were sometimes observed. Clinical signs included tremors and prostration in two of five males exposed at 71 ppm and all males exposed at 110 ppm. Animals that survived the first 24 h after exposure also survived until the end of the 14-day observation period. All surviving rats gained weight by the end of the observation period, and gross necropsy revealed no abnormalities. LC_{50} values of 33 ppm (males and females combined), 59 ppm (males), and 17 ppm (females) were calculated by the investigators. BMC_{01} values of 59.7 ppm (males) and 13.8 ppm (females) ppm and $BMCL_{05}$ values of 52 ppm (males) and 11.3 ppm (females) were also calculated. Mortality data from this study are presented in Table 4-4.

TABLE 4-3 Mortality in Wistar Rats Exposed to tert-Octyl Mercaptan for 4 Hours

Concentration (ppm)	Mortality	Comments
38	0/5	Seizures within 45 min to 1.5 h; average of 2 mild seizures
40	1/6	Seizures within 45 min to 1.5 h
44	1/5	Seizures within 45 min to 1.5 h
55	3/5	Seizures within 45 min to 1.5 h
64	5/5	Seizures within 20-30 min, at intervals of several minutes; all dead within 3 h, 10 min
78	6/6	Seizures within 20-30 min, at intervals of several minutes; all dead within 2 h, 50 min
110	6/6	Seizures within 10-15 min, at close intervals (2-3 min apart); all dead within 2 h, 45 min
LC_{50}		51 ppm (46.5-54.5 ppm)
$BMCL_{05}$		31.8 ppm
BMC_{01}		34.4 ppm

Abbreviations: BMC_{01}, benchmark concentration with 1% response; $BMCL_{05}$, benchmark concentration, 95% lower confidence limit with 5% response; LC_{50}, lethal concentration, 50% lethality.
Source: Adapted from Fairchild and Stokinger 1958.

TABLE 4-4 Mortality in Sprague-Dawley Rats Exposed to tert-Octyl Mercaptan for 4 Hours

	Mortality		
Concentration (ppm)	Male	Female	Combined
0	0/5	0/5	0/10
7 ± 0.7	0/5	0/5	0/10
15 ± 3.0	0/5	1/5	1/10
19 ± 3.0	0/5	5/5	5/10
29 ± 2.0	0/5	5/5	5/10
59 ± 3.0	0/5	5/5	5/10
71 ± 1.0	4/5	5/5	9/10
110 ± 3.0	5/5	5/5	10/10
LC_{50}	59 ppm	17 ppm	33 ppm (16-66 ppm)
$BMCL_{05}$	52 ppm	11.3 ppm	4.8 ppm
BMC_{01}	59.7 ppm	13.8 ppm	4.6 ppm

Abbreviations: BMC_{01}, benchmark concentration with 1% response; $BMCL_{05}$, benchmark concentration, 95% lower confidence limit with 5% response; LC_{50}, lethal concentration, 50% lethality.
Source: Temple University 1982.

Because of the results of the study above indicated that females are much more sensitive than male rats to acute lethality from tert-octyl mercaptan, another study was conducted in female rats. Groups of 10 female Sprague-Dawley rats were exposed to tert-octyl mercaptan at 12, 14, 17, 18, or 19 ppm for 4 h, followed by a 14-day observation period (Temple University 1982). The experimental methods were similar to those described for the previous study. Tremors and clonic convulsions were observed in all test groups. All animals that survived the first 24 h after exposure also survived until the end of the observation period. No signs of hemorrhage or other signs of visible pathology were found in rats that died. At the end of the 14-day observation period, 19 of 21 surviving rats gained weight, and gross necropsy revealed no abnormalities. An LC_{50} value of 17 ppm (15-19 ppm) was calculated by the investigators. A BMC_{01} value of 10.7 ppm and $BMCL_{05}$ value of 10.1 ppm was also calculated. Mortality data from this study are presented in Table 4-5.

When the data on female rats presented in Tables 4-4 and 4-5 are combined to calculate benchmark levels, a 4-h $BMCL_{05}$ of 11.5 ppm and BMC_{01} of 14.7 ppm result (see Appendix C). Combining the data is acceptable because the data sets are from the same laboratory and used similar experimental methods.

Groups of five male and five female Charles River CD rats were exposed to tert-octyl mercaptan at 23, 24, 25, 73, 77, or 79 ppm (nominal concentrations) for 4 h, followed by a 14-day observation period (Amoco 1979). Exposures were conducted in a 160-L cubical, stainless steel and glass chamber. Test vapors

were generated by passing air at a rate of 10 L/min through a round-bottom flask containing tert-octyl mercaptan in a heating jacket. Chamber concentrations were calculated from the ratio of the rate of vapor dissemination to the rate of total chamber airflow. Clinical signs included convulsions, with females affected more frequently and with greater severity than males; clinical signs were observed at 73 ppm or higher in males and at 24 ppm or higher in females. All surviving rats lost weight on day 1 post-exposure compared with pre-exposure values. Male survivors gained weight by the end of the observation period; however, female survivors only maintained their body weight. Rats dying during exposure had red- or pink-colored lungs or lungs with red patches or scattered red pin points at necropsy. No gross pathologic effects were noted in animals killed at the end of the observation period. LC_{50} values of 50 ppm (males and females combined), 79 ppm (males), and 24 ppm (females) were calculated by the investigators. BMC_{01} values of 65.9 ppm (males) and 21.5 ppm (females) ppm and $BMCL_{05}$ values of 63.9 ppm (males) and 21.0 ppm (females) were also calculated. Data from this study are presented in Table 4-6.

A group of 10 male Wistar rats was exposed to tert-octyl mercaptan at 330 ppm (nominal concentration) and observed until death (Pharmacology Research Inc. 1970). All of the rats died; deaths occurred within 19, 22, 26, 27, 30, 32, 40, and 49 min of exposure. Clinical signs included muscular spasms, violent clonic convulsions, prostration, and terminal dyspnea.

Fairchild and Stokinger (1958) administered tert-octyl mercaptan by oral gavage in ethanol, intraperitoneal injection, or dermal application to Wistar-derived male rats, followed by 15-day observation periods. An oral LD_{50} (lethal dose, 50% lethality) of 85.3 mg/kg, an intraperitoneal LD_{50} of 12.9 mg/kg, and a dermal LD_{50} of 1,954 mg/kg were reported.

TABLE 4-5 Mortality in Female Sprague-Dawley Rats Exposed to tert-Octyl Mercaptan for 4 Hours

Concentration (ppm)	Mortality
12 ± 0.6	1/10
14 ± 0.5	3/10
17 ± 1.4	5/10
18 ± 0.7	10/10
19 ± 1.7	10/10
LC_{50}	17 ppm (15-19 ppm)
$BMCL_{05}$	10.1 ppm
BMC_{01}	10.7 ppm

Abbreviations: BMC_{01}, benchmark concentration with 1% response; $BMCL_{05}$, benchmark concentration, 95% lower confidence limit with 5% response; LC_{50}, lethal concentration, 50% lethality.
Source: Temple University 1982.

TABLE 4-6 Mortality in Charles-River Rats Exposed to tert-Octyl Mercaptan for 4 Hours

	Mortality		
Concentration (ppm)	Male	Female	Combined
23	0/5	0/5	0/10
24	0/5	1/5	1/10
25	0/5	5/5	5/10
73	0/5	5/5	5/10
77	4/5	5/5	9/10
79	5/5	5/5	10/10
LC_{50}	79 ppm	24 ppm	50 ppm
$BMCL_{05}$	63.9 ppm	21.0 ppm	*
BMC_{01}	65.9 ppm	21.5 ppm	*

Abbreviations: BMC_{01}, benchmark concentration with 1% response; $BMCL_{05}$, benchmark concentration, 95% lower confidence limit with 5% response; LC_{50}, lethal concentration, 50% lethality.
*P-value <0.1; therefore, not reported.
Source: Amoco 1979.

Nine of 10 rats administered tert-octyl mercaptan at 50 mg/kg in sesame oil by stomach tube died within 30-143 min after intubation (Pharmacology Research Inc. 1970). The surviving rat was observed for 5 days. Clinical signs included muscular spasms, violent clonic convulsions, prostration, and terminal dyspnea.

3.1.2. Mice

Fairchild and Stokinger (1958) exposed groups of 10 Swiss-derived male mice (body weight 25 -28 g) to tert-octyl mercaptan at 38, 40, 44, 55, 64, or 78 ppm (analytic concentrations) for up to 4 h, followed by a 15-day observation period. Vapor was generated and the test chamber analyzed in the same manner as the study in rats. Clinical signs in the mice were similar to those described for the rat in Section 3.1.1. An LC_{50} value of 47 ppm was calculated by the investigators. A BMC_{01} of 34.4 ppm and $BMCL_{05}$ of 33.6 ppm were also calculated. Mortality data from this study are presented in Table 4-7.

Groups of five male MF1 mice were exposed to tert-octyl mercaptan at 42, 58, 84, 117, or 167 ppm (nominal concentrations) for 1 h, followed by a 6-day observation period (Pharmacology Research Inc. 1969). Clinical signs were noted at all test concentrations and included hypertonicity, hypersensitivity, and multiple clonic-tonic convulsions. Mortality was 0/5, 2/5, 4/5, 5/5, and 5/5 at concentrations of 42, 58, 84, 117, and 167 ppm, respectively. All deaths occurred during exposure. An LC_{50} value of 69 ppm was calculated by the investigators. A BMC_{01} of 37.6 ppm and $BMCL_{05}$ of 28.4 ppm were also calculated. No further details were available.

TABLE 4-7 Mortality in Male Swiss Mice Exposed to tert-Octyl Mercaptan for 4 Hours

Concentration (ppm)	Mortality	Comments
38	0/10	–
40	2/10	–
44	4/10	–
55	9/10	–
64	10/10	All dead within 3 h
78	10/10	All dead within 1 h, 35 min
LC_{50}		47 ppm (45.3-48.7 ppm)
$BMCL_{05}$		33.6 ppm
BMC_{01}		34.4 ppm

Abbreviations: BMC_{01}, benchmark concentration with 1% response; $BMCL_{05}$, benchmark concentration, 95% lower confidence limit with 5% response; LC_{50}, lethal concentration, 50% lethality.
Source: Adapted from Fairchild and Stokinger 1958.

3.1.3. Rabbits

Fairchild and Stokinger (1958) administered single dermal applications of tert-octyl mercaptan at 213, 427, or 854 mg/kg to groups of two New Zealand white rabbits, followed by a 72-h observation period. Both rabbits in the 854-mg/kg group died within 8 h, and none of the rabbits in the 213- or 427-mg/kg groups died.

Ten albino rabbits were administered a single dermal application of tert-octyl mercaptan at 200 mg/kg for 4 h, followed by a 5-day observation period (Pharmacology Research Inc. 1970). No mortality or signs of toxicity were observed, and animals had normal body weight gain.

3.1.4. Summary of Animal Lethality Data

Inhalation lethality studies of tert-octyl mercaptan in rats and mice are available. Lethality data suggest a steep concentration-response curve for tert-octyl mercaptan. In studies of male rats exposed to tert-octyl mercaptan for 4 h, mortality was 0% at 38 ppm and 100% at 64 ppm (Fairchild and Stokinger 1958), 0% at 59 ppm and 80% at 71 ppm (Temple University 1982), and 0% at 73 ppm and 100% at 79 ppm (Amoco 1979). In a study of female rats exposed to tert-octyl mercaptan for 4 h, mortality was10% at 12 ppm and 100% at 18 ppm. In mice exposed for 4 h, mortality was 0% at 38 ppm and 100% at 64 ppm (Fairchild and Stokinger 1958). Rat data suggest that females are much more sensitive to tert-octyl mercaptan than males; calculated 4-h LC_{50} values were 59 ppm for male rats and 17 ppm for female rats in one study (Temple University 1982) and 79 ppm for males and 24 ppm for females in another (Amoco 1979).

Clinical signs were indicative of CNS stimulation followed by central depression and finally death from respiratory failure.

3.2. Nonlethal Toxicity

No animal data on the nonlethal toxicity of tert-octyl mercaptan were found.

3.3. Developmental and Reproductive Effects

No animal developmental and reproductive data on tert-octyl mercaptan were found.

3.4. Genotoxicity

No genotoxicity data on were found.

3.5. Carcinogenicity

No carcinogenicity data on tert-octyl mercaptan were found.

4. SPECIAL CONSIDERATIONS

4.1. Metabolism and Disposition

Metabolism and disposition data for tert-octyl mercaptan were not available.

4.2. Mechanism of Toxicity

Most mercaptans act similarly to hydrogen sulfide and cyanide by interrupting electron transport through inhibition of cytochrome oxidase, and general signs of acute mercaptan poisoning are indicative of central depression and respiratory paralysis, followed by death from respiratory failure (NIOSH 1978). However, data suggest that tert-octyl mercaptan acts differently because an initial effect of CNS stimulation is observed. Fairchild and Stokinger (1958) reported that the stimulatory effects of tert-octyl mercaptan were typical of other CNS stimulants such as picrotoxin and metrazol, and that the compound appeared to act at various levels of the cerebrospinal axis. Convulsive seizures were spontaneous in origin (not triggered by external stimuli), and tert-octyl mercaptan had an analeptic action on the higher CNS centers, as evidenced by the fact that subconvulsant doses stimulated the respiratory and vasomotor centers (Fairchild and Stokinger 1958). The analeptic action was demonstrated by the ability of tert-octyl mercaptan to counteract depression produced by barbiturates. Even though the CNS stimulation is unique to tert-octyl mercaptan, the

final result of acute toxicity is similar to other mercaptans: the CNS stimulation was followed by central depression and then death from respiratory failure.

4.3. Structure-Activity Relationships

Acute intraperitoneal, oral, and inhalation data in rats and inhalation data in mice suggest that tert-octyl mercaptan is more toxic than other mercaptans tested (with the exception of phenyl mercaptan) and more toxic than hydrogen sulfide (see Table 4-8).

4.4. Species Variability

Although data are limited, acute lethality studies suggest that rats and mice have similar sensitivity to the lethal effects of tert-octyl mercaptan. The 4-h LC_{50} is 51 ppm in male rats and 47 ppm in male mice (Fairchild and Stokinger 1958).

4.5. Gender Variability

Experimental data in rats (see Tables 4-4 and 4-5) suggest that females are more sensitive than males to the toxic effects of tert-octyl mercaptan (Amoco 1979; Temple University 1982).

4.6. Temporal Extrapolation

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

5. DATA ANALYSIS FOR AEGL-1

5.1. Human Data Relevant to AEGL-1

No human data on tert-octyl mercaptan relevant deriving AEGL-1 values were available.

5.2. Animal Data Relevant to AEGL-1

No animal data on tert-octyl mercaptan relevant to deriving of AEGL-1 values were available.

TABLE 4-8 Comparative Toxicity of Mercaptans

Compound	Rat Intraperitoneal LD_{50} (mg/kg)	Rat Oral LD_{50} (mg/kg)	4-h Inhalation LC_{50} (ppm)		Reference
			Rats	Mice	
Hydrogen sulfide	–	–	444	–	Tansy et al. 1981
Methyl mercaptan	–	–	675	1,664	Horiguchi 1960 (mice); Tansy et al. 1981(rats)
Ethyl mercaptan	226	682	4,420	2,770	Fairchild and Stokinger 1958
Propyl mercaptan	515	1,790	7,200	4,010	Fairchild and Stokinger 1958
Isobutyl mercaptan	917	7,168	>25,000	>25,000	Fairchild and Stokinger 1958
tert-Butyl mercaptan	590	4,729	22,200	16,500	Fairchild and Stokinger 1958
n-Butyl mercaptan	399	1,500	4,020	2,500	Fairchild and Stokinger 1958
n-Hexyl mercaptan	396	1,254	1,080	528	Fairchild and Stokinger 1958
Phenyl mercaptan	9.8	46.2	33	28	Fairchild and Stokinger 1958
Benzyl mercaptan	373	493	>235	178	Fairchild and Stokinger 1958
tert-Octyl mercaptan	*12.9*	*83.5*	*51 (males)*	*47 (males)*	Fairchild and Stokinger 1958

5.3. Derivation of AEGL-1 Values

AEGL-1 values for tert-octyl mercaptan are not recommended because of insufficient data.

6. DATA ANALYSIS FOR AEGL-2

6.1. Human Data Relevant to AEGL-2

No human data on tert-octyl mercaptan relevant to deriving of AEGL-2 values were found.

6.2. Animal Data Relevant to AEGL-2

No animal data on tert-octyl mercaptan relevant to deriving AEGL-2 values were found.

6.3. Derivation of AEGL-2 Values

In the absence of appropriate chemical-specific data, AEGL-3 values were divided by 3 to derive AEGL-2 values for tert-octyl mercaptan. This approach is justified because of the steep concentration-response curve for lethality. (See Section 7.3 for description of lethality data that demonstrates the steepness.) AEGL-2 values were presented in Table 4-9, and calculations are presented in Appendix A.

The AEGL-2 values are considered protective for the following reasons. No effects (clinical signs or mortality) were noted in male or female rats exposed to tert-octyl mercaptan at 7 ppm for 4 h (Temple University 1982), and a slightly higher concentration of 12 ppm caused clinical signs (tremors and clonic convulsions) in 90% and mortality in 10% of the female rats (Temple University 1982). If 7 ppm was used as a point of departure and the same time-scaling procedure and uncertainty factors were applied as described earlier, the resulting values (1.4 for the 10- and 30-min, 1.1 ppm for the 1-h, 0.70 ppm for the 4-h, and 0.35 for the 8-h values) would be slightly higher than the AEGL-2 values.

7. DATA ANALYSIS FOR AEGL-3

7.1. Human Data Relevant to AEGL-3

No human data on tert-octyl mercaptan relevant to deriving AEGL-3 values were available.

7.2. Animal Data Relevant to AEGL-3

A 4-h LC_{50} value of 51 ppm was calculated by Fairchild and Stokinger (1958) for Sprague-Dawley rats; a BMC_{01} of 34.4 ppm and $BMCL_{05}$ of 31.8 ppm were also calculated from this study.

In another study of Sprague-Dawley rat (Temple University 1982), 4-h LC_{50} values of 33 ppm (males and females combined), 59 ppm (males), and 17 ppm (females) were calculated by the investigators; BMC_{01} values of 59.7 ppm (males) and 13.8 ppm (females) and $BMCL_{05}$ values of 52 ppm (males) and 11.3 ppm (females) were also calculated. In a follow-up study with female Sprague-Dawley rats (Temple University1982), a 4-h LC_{50} value of 17 ppm (15-19 ppm) was calculated by the investigators; a BMC_{01} value of 10.7 ppm and $BMCL_{05}$ value of 10.1 ppm were also calculated. Combining the female rat data from the original and follow-up studies yields a 4-h $BMCL_{05}$ of 11.5 ppm and BMC_{01} of 14.7 ppm.

In a study with Charles River rats (Amoco 1979), 4-h LC_{50} values of 50 ppm (males and females combined), 79 ppm (males), and 24 ppm (females) were calculated by the investigators; BMC_{01} values of 65.9 ppm (males) and 21.5 ppm (females) ppm and $BMCL_{05}$ values of 63.9 ppm (males) and 21.0 ppm (females) were also calculated.

TABLE 4-9 AEGL-2 Values for tert-Octyl Mercaptan

10 min	30 min	1 h	4 h	8 h
0.77 ppm (4.6 mg/m^3)	0.77 ppm (4.6 mg/m^3)	0.60 ppm (3.6 mg/m^3)	0.40 ppm (2.4 mg/m^3)	0.19 ppm (1.1 mg/m^3)

In a mouse study (Fairchild and Stokinger 1958), a 4-h LC_{50} value of 47 ppm was calculated by the investigators; a BMC_{01} of 34.4 ppm and $BMCL_{05}$ of 33.6 ppm were also calculated. In another mouse study (Pharmacology Research Inc. 1970), a 1-h LC_{50} value of 69 ppm was calculated by the investigators; a BMC_{01} of 37.6 ppm and $BMCL_{05}$ of 28.4 ppm were also calculated.

7.3. Derivation of AEGL-3 Values

The 4-h $BMCL_{05}$ value of 11.5 ppm calculated from the combined female rat data (Atochem 1982) was used as the point of departure for AEGL-3 values. That concentration is considered a threshold for lethality based on the most sensitive test animals (females). This point of departure was chosen over the most conservative benchmark value calculated from a single study (10.1 ppm) because the statistical goodness-of-fit was much greater for the combined data set ($p = 0.86$) than for a single data set ($p = 0.15$). An intraspecies uncertainty factor of 3 was applied and was considered sufficient because the point of departure is based on data from the more sensitive female rats. Calculated 4-h LC_{50} values were 59 ppm for male rats and 17 ppm for female rats in one study (Temple University 1982) and 79 ppm for males and 24 ppm for females in another (Amoco 1979). Also, the steep concentration-response curve implies limited intraindividual variability. In studies of male rats exposed to tert-octyl mercaptan for 4 h, mortality was 0% at 38 ppm and 100% at 64 ppm (Fairchild and Stokinger 1958), 0% at 59 ppm and 80% at 71 ppm (Temple University 1982), and 0% at 73 ppm and 100% at 79 ppm (Amoco 1979). In a study of female rats exposed to tert-octyl mercaptan for 4 h, mortality was10% at 12 ppm and 100% at 18 ppm. In mice exposed for 4 h, mortality was 0% at 38 ppm and 100% at 64 ppm (Fairchild and Stokinger 1958). An interspecies uncertainty factor of 3 was applied because the limited data suggest no difference in species sensitivity between rats and mice (the 4-h LC_{50} is 51 ppm for male rats and 47 ppm for male mice [Fairchild and Stokinger 1958]). Therefore, the total uncertainty factor was 10. Values were scaled across time using the equation $C^n \times t = k$, where default values of $n = 3$ when extrapolating to shorter durations and $n = 1$ when extrapolating to longer durations were used to derive values protective of human health (NRC 2001). The 30-min AEGL-3 value was adopted as the 10-min value because of the uncertainty in extrapolating a 4-h point of departure to a 10-min value.

AEGL-3 values for tert-octyl mercaptan are presented in Table 4-10, and calculations are provide in Appendix A.

8. SUMMARY OF AEGLs

8.1. AEGL Values and Toxicity End Points

AEGL-1 values are not recommended for tert-octyl mercaptan because of insufficient data. AEGL-2 values were derived by dividing the AEGL-3 values by 3, and the AEGL-3 values were based on a threshold for lethality in female rats ($BMCL_{05}$). AEGL values for tert-octyl mercaptan are presented in Table 4-11.

8.2. Comparisons with Other Standards and Guidelines

There are no other exposure standards or guidelines for tert-octyl mercaptan.

8.3. Data Adequacy and Research Needs

Human data on tert-octyl mercaptan are limited. Additional data on toxicity in females in species other than rats would be helpful.

TABLE 4-10 AEGL-3 Values for tert-Octyl Mercaptan

10 min	30 min	1 h	4 h	8 h
2.3 ppm (14 mg/m^3)	2.3 ppm (14 mg/m^3)	1.8 ppm (11 mg/m^3)	1.2 ppm (7.2 mg/m^3)	0.58 ppm (3.5 mg/m^3)

TABLE 4-11 AEGL Values for tert-Octyl Mercaptan

Classification	10 min	30 min	1 h	4 h	8 h
AEGL-1[a] (nondisabling)	NR	NR	NR	NR	NR
AEGL-2 (disabling)	0.77 ppm (4.6 mg/m^3)	0.77 ppm (4.6 mg/m^3)	0.60 ppm (3.6 mg/m^3)	0.40 ppm (2.4 mg/m^3)	0.19 ppm (1.1 mg/m^3)
AEGL-3 (lethal)	2.3 ppm (14 mg/m^3)	2.3 ppm (14 mg/m^3)	1.8 ppm (11 mg/m^3)	1.2 ppm (7.2 mg/m^3)	0.58 ppm (3.5 mg/m^3)

Abbreviation: NR, not recommended.
[a]The absence of AEGL-1 values does not imply that concentrations below AEGL-2 values will be without effect.

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APPENDIX A

DERIVATION OF AEGL VALUES FOR TERT-OCTYL MERCAPTAN

Derivation of AEGL-1 Values

AEGL-1 values are not recommended for tert-octyl mercaptan because of insufficient data.

Derivation of AEGL-2 Values

In the absence of relevant data to derive AEGL-2 values and because tert-octyl mercaptan has a steep concentration-response curve, AEGL-3 values were divided by 3 to estimate a threshold for inability to escape.

10-min AEGL-2:	2.3 ppm ÷ 3 = 0.77 ppm
30-min AEGL-2:	2.3 ppm ÷ 3 = 0.77 ppm
1-h AEGL-2:	1.8 ppm ÷ 3 = 0.60 ppm
4-h AEGL-2:	1.2 ppm ÷ 3 = 0.40 ppm
8-h AEGL-2:	0.58 ppm ÷ 3 = 0.19 ppm

Derivation of AEGL-3 Values

Key study:	Temple University. 1982. Initial Submission: Final Report on a Study to Establish an LC_{50} Concentration of t-Octyl Mercaptan in Adult Sprague-Dawley Rats of Both Sexes (Final), September 17, 1982. Submitted to EPA by Atochem North America, Inc., King of Prussia, PA with Cover Letter Dated 12/23/91. EPA Document No, 88920000497. Microfiche No. OTS0534950.
Toxicity end point:	4-h threshold for lethality in female rats, $BMCL_{05}$ of 11.5 ppm
Time scaling:	$C^n \times t = k$ (default values of n = 3 for extrapolating to shorter durations and n = 1 for extrapolating to longer durations); time scaling not performed for the 10-min AEGL-3 because of the uncertainty in extrapolating a 4-h point of departure to a 10-min value. $(11.5 \text{ ppm})^1 \times 4 \text{ h} = 46 \text{ ppm-h}$ $(11.5 \text{ ppm})^3 \times 4 \text{ h} = 6{,}084 \text{ ppm-h}$

Uncertainty factors:	3 for interspecies differences 3 for intraspecies variability
Modifying factor:	Not applicable
Calculations:	
10-min AEGL-3:	2.3 ppm (30-min AEGL-3 value adopted)
30-min AEGL-3:	$C^3 \times 0.5$ h = 6,084 ppm-h C = 23 ppm C = 23 ppm ÷ 10 = 2.3 ppm
1-h AEGL-3:	$C^3 \times 1$ h = 6,084 ppm-h C = 18 ppm C = 18 ppm ÷ 10 = 1.8 ppm
4-h AEGL-3:	11.5 ppm ÷ 10 = 1.2 ppm
8-h AEGL-3:	$C^1 \times 8$ h = 46 ppm-h C = 5.8 ppm C = 5.8 ppm ÷ 10 = 0.58 ppm

APPENDIX B

ACUTE EXPOSURE GUIDELINE LEVELS FOR tert-OCTYL MERCAPTAN

AEGL-1 VALUES

Data are insufficient to derive AEGL-1 values for tert-octyl mercaptan; therefore, AEGL-1 values are not recommended. Absence of AEGL-1 values does not imply that concentrations below the AEGL-2 are without effect.

AEGL-2 VALUES

10 min	30 min	1 h	4 h	8 h
0.77 ppm (4.6 mg/m^3)	0.77 ppm (4.6 mg/m^3)	0.60 ppm (3.6 mg/m^3)	0.40 ppm (2.4 mg/m^3)	0.19 ppm (1.1 mg/m^3)

Data adequacy: Data inadequate to derive AEGL-2 values. AEGL-3 values were divided by 3 to estimate thresholds for the inability to escape.

AEGL-3 VALUES

10 min	30 min	1 h	4 h	8 h
2.3 ppm (14 mg/m^3)	2.3 ppm (14 mg/m^3)	1.8 ppm (11 mg/m^3)	1.2 ppm (7.2 mg/m^3)	0.58 ppm (3.5 mg/m^3)

Reference: Temple University. 1982. Initial Submission: Final Report on a Study to Establish an LC_{50} Concentration of t-Octyl Mercaptan in Adult Sprague-Dawley Rats of Both Sexes (Final), September 17, 1982. Submitted to EPA by Atochem North America, Inc., King of Prussia, PA with Cover Letter Dated 12/23/91. EPA Document No. 88920000497. Microfiche No. OTS0534950.

Test species/Strain/Sex/Number: Rat, Sprague-Dawley, females, 10/group

Exposure route/Concentrations/Durations: Inhalation; 7, 15, 19, 29, 59, 71, 110 ppm and 12, 14, 17, 18, 19 ppm for 4 h

Effects:

Concentration (ppm)	Mortality
7	0/5
15	1/5
19	5/5
29	5/5
59	5/5
71	5/5
110	5/5
12	1/10
14	3/10

(Continued)

AEGL-3 VALUES Continued

17	5/10
18	10/10
19	10/10

BMCL05 = 11.5 ppm

BMC01 = 14.7 ppm

End point/Concentration/Rationale: Threshold for lethality, $BMCL_{05}$ of 11.5 ppm

Uncertainty factors/Rationale:
Interspecies: 3, data suggest no difference in species sensitivity between rats and mice (4-h LC_{50} is 51 ppm for male rats and 47 ppm male mice [Fairchild and Stokinger 1958]).
Intraspecies: 3, considered sufficient because the point of departure is from the more sensitive female rats. Calculated 4-h LC_{50} values were 59 ppm for male rats and 17 ppm for female rats in one study (Temple University 1982) and 79 ppm for males and 24 ppm for females in another (Amoco 1979). Also, the steep concentration-response curve implies limited intraindividual variability. In studies of male rats exposed to tert-octyl mercaptan for 4 h, mortality was 0% at 38 ppm and 100% at 64 ppm (Fairchild and Stokinger 1958), 0% at 59 ppm and 80% at 71 ppm (Temple University 1982), and 0% at 73 ppm and 100% at 79 ppm (Amoco 1979). In a study of female rats exposed to tert-octyl mercaptan for 4 h, mortality was10% at 12 ppm and 100% at 18 ppm. In mice exposed for 4 h, mortality was 0% at 38 ppm and 100% at 64 ppm (Fairchild and Stokinger 1958).

Modifying factor: Not applicable

Animal-to-human dosimetric adjustment: Not applicable

Time scaling: $C^n \times t = k$; default values of n = 3 when extrapolating to shorter durations and n = 1 when extrapolating to longer durations to derive values protective of human health (NRC 2001). The 30-min AEGL-3 value was adopted as the 10-min value because of the uncertainty in extrapolating a 4-h point of departure to 10-min value.

Data adequacy: Well-conducted studies in rats and mice. Additional studies of females in species other than rats species would be useful.

APPENDIX C

BENCHMARK CALCULATION FOR TERT-OCTYL MERCAPTAN

Temple University (1982): Combined female data for two studies

Probit Model (Version: 2.9; Date: 09/23/2007)
Input Data File: C:\BMDS\UNSAVED1.(d)
Gnuplot Plotting File: C:\BMDS\UNSAVED1.plt
Fri Jun 13 10:37:19 2008

BMDS MODEL RUN

The form of the probability function is:

P[response] = Background
+ (1-Background) * CumNorm(Intercept+Slope*Log(Dose)),

where CumNorm(.) is the cumulative normal distribution function

Dependent variable = COLUMN2
Independent variable = COLUMN1
Slope parameter is restricted as slope >= 1

Total number of observations = 13
Total number of records with missing values = 0
Maximum number of iterations = 250
Relative Function Convergence has been set to: 1e-008
Parameter Convergence has been set to: 1e-008

User has chosen the log transformed model

Default Initial (and Specified) Parameter Values
Background = 0
Intercept = -2.865
Slope = 1.09606

Asymptotic Correlation Matrix of Parameter Estimates

	Background	Intercept
Background	1	-0.19
Intercept	-0.19	1

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

Parameter Estimates

Variable	Estimate	Standard Error	95.0% Wald Confidence Interval	
			Lower Confidence Limit	Upper Confidence Limit
Background	0.13443	0.0579167	0.0209153	0.247945
Intercept	-50.7551	0.346663	-51.4345	-50.0756
Slope	18	NA		

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

Analysis of Deviance Table

Model	Log (likelihood)	No. Parameters	Deviance Test	DF	P-value
Full model	-18.793	13			
Fitted model	-22.802	2	8.01802	11	0.7117
Reduced model	-60.1424	1	82.6988	12	<0.0001

AIC: 49.6039

Goodness of Fit

		Scaled			
Dose	Estimated Probability	Expected	Observed	Size	Residual
0.0000	0.1344	0.672	0	5	-0.881
7.0000	0.1344	0.672	0	5	-0.881
15.0000	0.1537	0.768	1	5	0.287
19.0000	0.9893	4.946	5	5	0.233
29.0000	1.0000	5.000	5	5	0.000
59.0000	1.0000	5.000	5	5	0.000
71.0000	1.0000	5.000	5	5	0.000
110.0000	1.0000	5.000	5	5	0.000
12.0000	0.1344	1.344	1	10	-0.319
14.0000	0.1349	1.349	3	10	1.528
17.0000	0.6502	6.502	5	10	-0.996
18.0000	0.9119	9.119	10	10	0.983
19.0000	0.9893	9.893	10	10	0.329

Chi-square = 6.19; DF = 11; P-value = 0.8602

Benchmark Dose Computation

Specified effect = 0.05
Risk type = Extra risk
Confidence level = 0.95
BMD = 15.3075
BMDL = 11.5133

Probit Model (Version: 2.9; Date: 09/23/2007)
Input Data File: C:\BMDS\UNSAVED1.(d)
Gnuplot Plotting File: C:\BMDS\UNSAVED1.plt
Fri Jun 13 10:40:03 2008

BMDS MODEL RUN

The form of the probability function is:

P[response] = Background
+ (1-Background) * CumNorm(Intercept+Slope*Log(Dose)),

where CumNorm(.) is the cumulative normal distribution function

Dependent variable = COLUMN2
Independent variable = COLUMN1
Slope parameter is restricted as slope >= 1

Total number of observations = 13
Total number of records with missing values = 0
Maximum number of iterations = 250
Relative Function Convergence has been set to: 1e-008
Parameter Convergence has been set to: 1e-008

User has chosen the log transformed model

Default Initial (and Specified) Parameter Values
Background = 0
Intercept = -2.865
Slope = 1.09606

Asymptotic Correlation Matrix of Parameter Estimates

	Background	Intercept
Background	1	-0.19
Intercept	-0.19	1

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

Parameter Estimates

		Standard	95.0% Wald Confidence Interval	
Variable	Estimate	error	Lower confidence limit	Upper confidence limit
Background	0.13443	0.0579167	0.0209153	0.247945
Intercept	-50.7551	0.346663	-51.4345	-50.0756
Slope	18	NA		

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

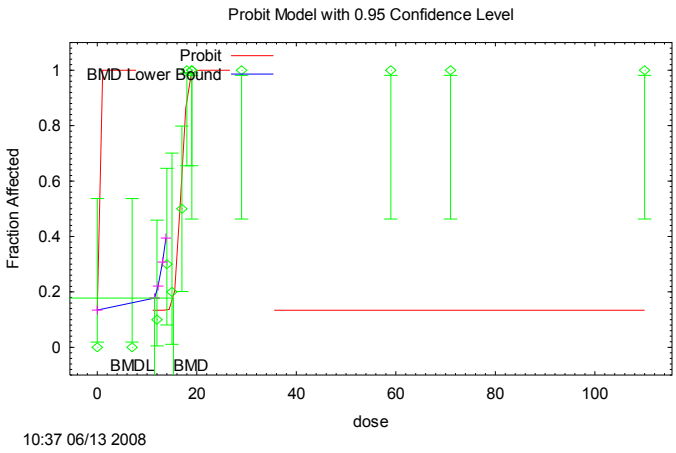

FIGURE C-1 Probit model with 0.95 confidence level.

Analysis of Deviance Table

Model	Log (likelihood)	No. Parameters	Deviance Test	DF	P-value
Full model	-18.793	13			
Fitted model	-22.802	2	8.01802	11	0.7117
Reduced model	-60.1424	1	82.6988	12	<0.0001

AIC: 49.6039

Goodness of Fit

	Scaled				
Dose	Estimated prob-ability	Expected	Observed	Size	Residual
0.0000	0.1344	0.672	0	5	-0.881
7.0000	0.1344	0.672	0	5	-0.881
15.0000	0.1537	0.768	1	5	0.287
19.0000	0.9893	4.946	5	5	0.233
29.0000	1.0000	5.000	5	5	0.000
59.0000	1.0000	5.000	5	5	0.000
71.0000	1.0000	5.000	5	5	0.000
110.0000	1.0000	5.000	5	5	0.000
12.0000	0.1344	1.344	1	10	-0.319
14.0000	0.1349	1.349	3	10	1.528
17.0000	0.6502	6.502	5	10	-0.996
18.0000	0.9119	9.119	10	10	0.983
19.0000	0.9893	9.893	10	10	0.329

Chi-square = 6.19; DF = 11; P-value = 0.8602

Benchmark Dose Computation

Specified effect = 0.01
Risk type = Extra risk
Confidence level = 0.95
BMD = 14.7388
BMDL = 10.2853

APPENDIX D

CATEGORY PLOT FOR tert-OCTYL MERCAPTAN

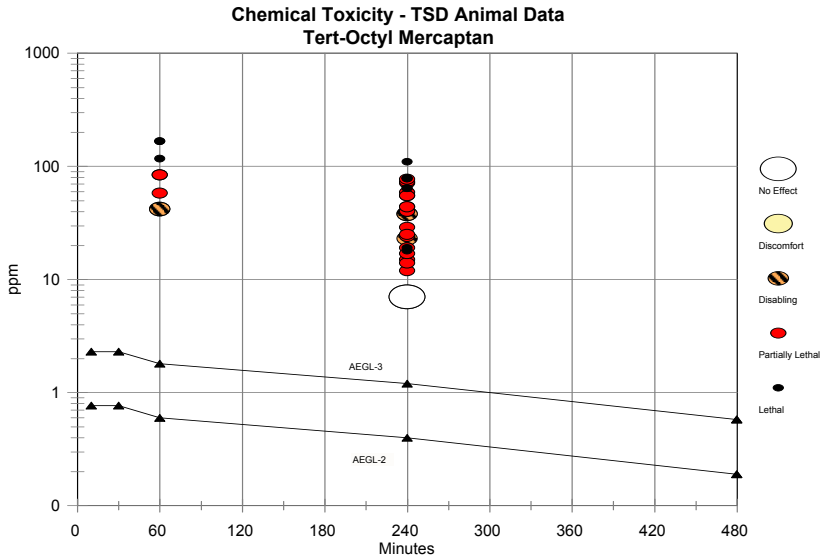

FIGURE D-1 Category plot of toxicity data and AEGL values for tert-octyl mercaptan. The decimal point is lost on this log-scale plot.

TABLE D-1 Data Used in Category Plot for tert-Octyl Mercaptan

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				0.77	10	AEGL	
AEGL-2				0.77	30	AEGL	
AEGL-2				0.60	60	AEGL	
AEGL-2				0.40	240	AEGL	
AEGL-2				0.19	480	AEGL	
AEGL-3				2.3	10	AEGL	
AEGL-3				2.3	30	AEGL	
AEGL-3				1.8	60	AEGL	
AEGL-3				1.2	240	AEGL	
AEGL-3				0.58	480	AEGL	
	Rat	Male	1	38	240	2	Seizures
	Rat	Male	1	40	240	PL	Mortality 1/6; seizures
	Rat	Male	1	44	240	PL	Mortality 1/5; seizures
	Rat	Male	1	55	240	PL	Mortality 3/5; seizures
	Rat	Male	1	64	240	3	Mortality 5/5; seizures
	Rat	Male	1	78	240	3	Mortality 6/6; seizures

(Continued)

TABLE D-1 Continued

Source	Species	Sex	No. Exposures	ppm	Minutes	Category	Effect
	Rat	Male	1	110	240	3	Mortality 6/6; seizures
	Rat	Male/Female	1	7	240	0	No effects
	Rat	Male/Female	1	15	240	PL	Mortality: male 0/5; female 1/5
	Rat	Male/Female	1	19	240	PL	Mortality: male 0/5; female 5/5
	Rat	Male/Female	1	29	240	PL	Mortality: male 0/5; female 5/5
	Rat	Male/Female	1	59	240	PL	Mortality: male 0/5; female 5/5
	Rat	Male/Female	1	71	240	PL	Mortality: male 4/5; female 5/5
	Rat	Female	1	12	240	PL	Mortality 1/10
	Rat	Female	1	14	240	PL	Mortality 3/10
	Rat	Female	1	17	240	PL	Mortality 5/10
	Rat	Female	1	18	240	3	Mortality 10/10
	Rat	Female	1	19	240	3	Mortality 10/10
	Rat	Male/Female	1	23	240	2	Convulsions
	Rat	Male/Female	1	24	240	PL	Mortality: male 0/5; female 1/5
	Rat	Male/Female	1	25	240	PL	Mortality: male 0/5; female 5/5
	Rat	Male/Female	1	73	240	PL	Mortality: male 0/5; female 5/5
	Rat	Male/Female	1	77	240	PL	Mortality: male 4/5; female 5/5
	Rat	Male/Female	1	79	240	3	Mortality: male 5/5; female 5/5
	Mouse	Male	1	38	240	2	Seizures
	Mouse	Male	1	40	240	PL	Mortality 2/10
	Mouse	Male	1	44	240	PL	Mortality 4/10

Mouse	Male	1	55	240	PL	Mortality 9/10
Mouse	Male	1	64	240	3	Mortality 10/10
Mouse	Male	1	78	240	3	Mortality 10/10
Mouse	Male	1	42	60	2	Convulsions
Mouse	Male	1	58	60	PL	Mortality 2/5
Mouse	Male	1	84	60	PL	Mortality 4/5
Mouse	Male	1	117	60	3	Mortality 5/5
Mouse	Male	1	167	60	3	Mortality 5/5

For category: 0 = no effect, 1 = discomfort, 2 = disabling, 3 = lethal; PL = partially lethality.