Acute Exposure Guideline Levels for Selected Airborne Chemicals

VOLUME 14

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 fourteenth volume in that series. AEGL documents for BZ (2-quinuclidinyl benzilate), ethyl

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

phosphorodichloridate, hexane, methanesulfonyl chloride, nitric acid, propargyl alcohol, and vinyl acetate monomer 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 BZ (interim reports 19a, 20a, and 21a), ethyl phosphorodichloridate (interim reports 20a and 21a), hexane (interim reports 17 and 21a), methanesulfonyl chloride (interim reports 20a and 21a), nitric acid (interim reports 15, 18, and 21a), propargyl alcohol (interim reports 16 and 19a), and vinyl acetate monomer (interim reports 18 and 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], Charles Reinhardt (DuPont Haskell Laboratory [retired]), Andrew Salmon (California Environmental Protection Agency), Kenneth Still, Occupational Toxicology Associates, Joyce Tsuji (Exponent, Inc.), and Judith Zelikoff (New York University).

Although the reviewers listed above have provided many constructive comments and suggestions, they were not asked to endorse the conclusions or recommendations, nor did they see the final draft of this volume before its release. The review of interim reports 15-21 was overseen by Robert Goyer (University of Western Ontario [retired]). Appointed by the NRC, he was responsible for making certain that an independent examination of the interim reports was

carried out in accordance with institutional procedures and that all review comments were carefully considered. Responsibility for the final content of this report rests entirely with the authoring committee and the institution.

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

Donald E. Gardner, *Chair*
Committee on Acute Exposure
Guideline Levels

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Acute Exposure Guideline Levels for Selected Airborne Chemicals

VOLUME 14

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

This report is the fourteenth 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 extrap-

olation 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 Syracuse Research Corporation. 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 recommenda-

tions 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 for the accuracy and completeness of the toxicity data cited in the AEGL reports. Thus far, the committee has prepared thirteen 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). This report is the fourteenth volume in that series. AEGL documents for BZ (2-quinuclidinyl benzilate), ethyl phosphorodichloridate, hexane, methanesulfonyl chloride, nitric acid, propargyl alcohol, and vinyl acetate monomer 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

2

Ethyl Phosphorodichloridate[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 Cheryl Bast (Oak Ridge National Laboratory), Lisa Ingerman (SRC, Inc.), Chemical Manager Dieter Heinz (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

Ethyl phosphorodichloridate is a colorless liquid used as an intermediate in the preparation of the pesticide ethoprop. The vapor irritates the eyes, nose, and throat; the liquid burns skin and eyes and causes severe burns of the mouth and stomach if ingested. Ethyl phosphorodichloridate reacts with water to produce hydrogen chloride fumes.

Data were insufficient for derivation of AEGL-1 values. Therefore, AEGL-1 values are not recommended for ethyl phosphorodichloridate.

In the absence of appropriate chemical-specific data, a fractional reduction of the AEGL-3 values was used to derive AEGL-2 values. For chemicals with a steep concentration-response curve, AEGL-3 values may be divided by 3 to estimate AEGL-2 values (NRC 2001). Therefore, the AEGL-2 values for ethyl phosphorodichloridate were obtained by dividing the AEGL-3 values for ethyl phosphorodichloridate by 3.

A 4-h $BMCL_{05}$ (benchmark concentration, 95% lower confidence limit with 5% response) of 38.0 ppm (Bayer 1983) for male and female rats exposed to ethyl phosphorodichloridate was used as the point of departure for calculating AEGL-3 values. The $BMCL_{05}$ is considered a threshold for lethality, and is supported by the fact that no mortality was observed in rats exposed to ethyl phosphorodichloridate at 37 ppm for 4 h. Values were scaled across time using the equation $C^n \times t = k$, where $n = 3$ when extrapolating to shorter durations and

n = 1 when extrapolating to longer durations in order to derive values protective of human health (NRC 2001). Extrapolating a 4-h value to a 10-min AEGL-3 value is justified because no deaths were noted in male rats exposed to ethyl phosphorodichloridate at 20,900 ppm or in female rats exposed at 16,700 ppm for 10 min (Bayer 1983). Uncertainty factors of 10 were applied to account for interspecies differences and intraspecies variability, because of the lack of information available to describe species differences in toxicity and inter-individual variability. Rat studies suggest that vapors are irritating to the eyes and nose, and that pulmonary edema increases with concentration (Bayer 1983; Rhone-Poulenc, Inc. 1990). The liquid was corrosive to the skin and eyes of rabbits (Rhone- Poulenc, Inc. 1990). It also reportedly reacts with water to produce hydrogen chloride, which supports a mechanism of primary irritation.

AEGL values for ethyl phosphorodichloridate are presented in Table 2-1.

1. INTRODUCTION

Ethyl phosphorodichloridate is a colorless liquid used as an intermediate in the preparation of the pesticide ethoprop. The vapor irritates the eyes, nose, and throat; the liquid burns the skin and eyes and causes severe burns of the mouth and stomach if ingested. Ethyl phosphorodichloridate reacts with water to produce hydrogen chloride fumes. When heated to decomposition, toxic fumes of hydrogen chloride and phosphoric acid or phosphorus oxides may be formed (HSDB 2002).

Selected physicochemical properties of ethyl phosphorodichloridate are presented in Table 2-2.

TABLE 2-1 AEGL Values for Ethyl Phosphorodichloridate

Classification	10 min	30 min	1 h	4 h	8 h	End Point (Reference)
AEGL-1 (nondisabling)[a]	NR	NR	NR	NR	NR	Insufficient data
AEGL-2 (disabling)	0.37 ppm (2.4 mg/m^3)	0.25 ppm (1.7 mg/m^3)	0.20 ppm (1.3 mg/m^3)	0.13 ppm (0.86 mg/m^3)	0.063 ppm (0.40 mg/m^3)	One-third the AEGL-3 values.
AEGL-3 (lethal)	1.1 ppm (7.3 mg/m^3)	0.76 ppm (5.0 mg/m^3)	0.60 ppm (4.0 mg/m^3)	0.38 ppm (2.5 mg/m^3)	0.19 ppm (1.3 mg/m^3)	4-h threshold for lethality ($BMCL_{05}$) of 38 ppm in rats (Bayer 1983).

Abbreviations: $BMCL_{05}$, benchmark concentration, 95% lower confidence limit with 5% response; NR, not recommended.

[a]Absence of an AEGL-1 value does not imply that concentrations below the AEGL-2 are without effect.

TABLE 2-2 Chemical and Physical Data for Ethyl Phosphorodichloridate

Parameter	Value	Reference
Synonyms	Ethyl diphosphorodichloridate; ethylesterdichloride; dichloroethoxyphosphine oxide; dichlorophosphoric acid, ethyl ester	Bayer 1983; HSDB 2002
CAS registry no.	1498-51-7	HSDB 2002
Chemical formula	$C_2H_5Cl_2O_2P$	HSDB 2002
Molecular weight	162.94	HSDB 2002
Physical state	Colorless liquid	HSDB 2002
Boiling point	167°C	HSDB 2002
Specific gravity	1.35 at 19°C	HSDB 2002
Solubility in water	1.4388 g/100 mL at 20°C;	Lide 1999
Surface tension	32.8 dynes/cm at 20°C	HSDB 2002
Heat of combustion	-2,600 cal/g	HSDB 2002
Conversion factors in air	1 ppm = 6.6 mg/m^3 1 mg/m^3 = 0.15 ppm	

2. HUMAN TOXICITY DATA

2.1. Acute Lethality

Human lethality data were not found.

2.2. Nonlethal Toxicity

Human nonlethal toxicity data were not found.

2.3. Case Reports

Ocular irritation was reported in a worker exposed to ethyl phosphorodichloridate at a plant in Mount Pleasant, Tennessee (Rhone-Poulenc, Inc. 1990). No other information was available.

2.4. Developmental and Reproductive Effects

Data on the developmental and reproductive toxicity of ethyl phosphorodichloridate in humans were not available.

2.5. Genotoxicity

No information regarding the genotoxicity of ethyl phosphorodichloridate in humans was available.

2.6. Carcinogenicity

No information regarding the carcinogenicity of ethyl phosphorodichloridate in humans was available.

2.7. Summary

Ocular irritation was reported in a worker exposed to ethyl phosphorodichloridate; however, no other information regarding this case was available. No other human data were located.

3. ANIMAL TOXICITY DATA

3.1. Acute Lethality

3.1.1. Rats

One-Hour Exposure

In a range-finding study, groups of five male and five female Sprague-Dawley rats were exposed to ethyl phosphorodichloridate (97.5% active ingredient) at 6.16, 66, or 134 ppm (analytic concentrations) for 1 h, followed by a 14-day observation period (Rhone-Poulenc, Inc. 1990). Because the test material is sensitive to oxygen and moisture, the test atmosphere was generated using a dry nitrogen-oxygen mixture. Ethyl phosphorodichloridate was delivered to the breathing zone of the animals, and exposure concentrations were determined by gas chromatographic analysis of impinger samples. Exposures were conducted in a 100-L plexiglass chamber with a glass front. Physical observations for clinical signs were recorded at 15-min intervals during exposure, and all animals received detailed physical examinations immediately prior to exposure, hourly for 2 h post-exposure, and daily thereafter. Animals were weighed just prior to exposure on day 1, on day 8, and just prior to sacrifice on day 15. All surviving animals were killed on day 15 and complete gross necropsies were performed on all rats. During exposures, labored breathing, gasping, and decreased activity were noted in all treatment groups; the time of onset was not reported. Clinical signs observed in all treatment groups during the 2 h immediately following exposure included labored breathing, gasping, decreased activity, anogenital staining, and moist rales

(anogenital staining and moist rales developed after exposure). During the 14-day observation period, surviving rats in the 66- and 134-ppm groups continued to exhibit labored breathing and rales throughout the observation period without full recovery. Rats in the 6.16-ppm group exhibited labored breathing, rales, fine tremors, and nasal discharge for a "few days" after exposure; however, the animals fully recovered during the second week post-exposure prior to sacrifice. "Significant" weight loss was noted one week following exposure in the 66- and 134-ppm groups; however, surviving rats showed some recovery prior to sacrifice. Animals in the 6.16 ppm-group gained weight during the 2 week observation period. Mortality was seen in the 66- and 134-ppm groups (see Table 2-3). All deaths occurred between days 2 and 9, with "most" being within 48-h post-exposure. There appeared to be a dose-related increase in lung weights in animals sacrificed 2-weeks post-exposure; the investigators suggest this increase may be the result of edema. No other treatment-related effects were noted at necropsy. The investigators calculated LC_{50} (lethal concentration, 50% lethality) values of 43.4 ppm for both sexes, 64.6 ppm for males, and 48.1 ppm for females.

A group of 10 male rats was exposed to ethyl phosphorodichloridate at approximately 350 ppm (nominal concentration) for 1 h, followed by a 14-day observation period (Rhone-Poulenc, Inc. 1990). The test material was metered, using a syringe infusion pump, into a stainless steel pneumatic spraying system driven by houseline air. The resulting aerosol was passed into a 40-L exposure chamber. A nominal concentration was calculated on basis of the amount of test material used and total air volume. During exposure, mild hyperemia, decreased locomotor activity, salivation, and lacrimation were noted; severe respiratory difficulty was observed during the final 15 min of exposure. Post-exposure, weight gain was reportedly slow. Seven of 10 rats died; deaths occurred on post-exposure days 2, 5, 6, 8, 10, 12, and 14.

Four-Hour Exposure

Groups of 10 male and 10 female rats (strain not specified) were exposed to ethyl phosphorodichloridate (98-99% active ingredient) at 37, 61, 75, 90, 143, or 355 ppm (analytic concentrations) for 4 h, followed by a 14-day observation period (Bayer 1983). Exposures were conducted in a 10-L glass chamber, and "minimized dermal contact". Test atmosphere concentrations were determined by absorption spectrometry. Animals were weighed before exposure and once weekly during the observation period. Gross necropsies were performed on all test animals. Clinical signs during and after exposure included disturbed behavioral patterns associated with severe respiratory problems. Ocular and nasal irritation was also noted. Clinical signs were assumed to be noted in all dose groups; however, specific signs associated with different exposure concentrations were not reported. No significant treatment-related effects on body weight were found. Necropsy findings in rats that died during the study

included severely bloated edematous lungs, spots in the lungs, brownish colored liver, pale kidneys, red renal pelvis, stomach ulcers, red intestinal wall, and dark red gastrointestinal tract contents of slimy consistency. The investigators suggested that the gastrointestinal effects were the result of ingestion. Rats killed after the 14-day observation period exhibited slightly bloated lungs at the higher concentrations. Specific necropsy findings associated with the different concentrations were not reported. The investigators calculated LC_{50} values of 91.6 ppm for both sexes, 85 ppm for males, and 99.8 ppm for females. The time of deaths was not reported. Mortality data and $BMCL_{05}$ (see Appendix B) and BMC_{01} (benchmark concentration with 1% response) values are presented in Table 2-4.

TABLE 2-3 Mortality in Rats Exposed by Inhalation to Ethyl Phosphorodichloridate for 1 Hour

	Mortality Incidence		
Concentration (ppm)	Male	Female	Total
6.16	0/5	0/5	0/10
66	5/5	3/5	8/10
134	3/5	4/5	7/10
Estimated LC_{50} (ppm)	64.6	48.1	43.4

Source: Rhone-Poulenc, Inc. 1990.

TABLE 2-4 Mortality in Rats Exposed by Inhalation to Ethyl Phosphorodichloridate for 4 Hours

	Mortality Incidence		
Concentration (ppm)	Male	Female	Total
37	0/10	0/10	0/20
61	2/10	NR	2/10
75	1/10	3/10	4/20
90	7/10	5/10	12/20
143	10/10	7/10	17/20
355	10/10	10/10	20/20
LC_{50} (ppm)	85	99.8	91.6
$BMCL_{05}$ (ppm)[a]	43.7	25.8	38.0
BMC_{01} (ppm)[a]	48.1	32.1	38.2

Abbreviations: NR, not reported; no explanation provided.
[a]Values calculated for this technical support document.
Source: Bayer 1983.

In another experiment, Bayer (1983) exposed groups of five male or five female rats to 'saturated' atmospheres of ethyl phosphorodichloridate for 10 min, 30 min, or 1 h, followed by a 14-day observation period. Exposure and analytic methods were similar to those described in the 4-h study (Bayer 1983). Clinical signs and gross necropsy results were similar to those described in the 4-h study (see Table 2-5).

Oral Exposure

An oral LD_{50} of 220 ± 41 mg/kg in rats was reported for ethyl phosphorodichloridate (Rhone- Poulenc, Inc. 1990).

3.1.2. Rabbits

A dermal LD_{50} of 2,350 ± 997 mg/kg in rabbits was reported for ethyl phosphorodichloridate (Rhone-Poulenc, Inc. 1990).

3.1.3. Summary of Animal Lethality Data

Animal lethality data on ethyl phosphorodichloridate are limited to rats. One-hour LC_{50} values of 43.4 ppm for rats of both sexes, 64.6 ppm for males, and 48.1 ppm for females were calculated (Rhone-Poulenc, Inc. 1990). In another 1-h study, seven of 10 male rats died after exposure to ethyl phosphorodichloridate at approximately 350 ppm (Rhone-Poulenc, Inc. 1990). Four-hour LC_{50} values of 85 ppm for male and 99.8 ppm for female rats were calculated (Bayer 1983). No lethality was reported in rats exposed to ethyl phosphorodichloridate at 16,700-20,900 ppm for 10 min; whereas, 90% mortality was noted in rats exposed at 10,700-14,400 ppm for 30 min and 100% mortality was noted in rats exposed at 12,000-13,700 ppm for 1 h (Bayer 1983). In all studies, clinical signs were consistent with irritation, and deaths were likely due to pulmonary edema.

3.2. Nonlethal Toxicity

3.2.1. Rabbits

A primary dermal irritation index for ethyl phosphorodichloridate of 7.16 was reported for rabbits. Ocular irritation scores of 92 at 1 h, and 100 at 1, 2, 3, 4, 7, 8, 9, 10, and 14 days were also reported (Rhone-Poulenc, Inc. 1990). These scores classify ethyl phosphorodichloridate as corrosive.

TABLE 2-5 Mortality and Clinical Findings in Rats Exposed by Inhalation to Saturated Concentrations of Ethyl Phosphorodichloridate

Concentration (ppm)	Duration	Sex	Mortality Incidence	Time of Death	Clinical Signs, Comments
20,900	10 min	Male	0/5	–	No weight gain during week 1 post-exposure; significant weight gain during week 2 post-exposure.
16,700	10 min	Female	0/5	–	
14,400	30 min	Male	5/5	Day 1	Significant weight loss throughout 14-day follow-up period in single surviving female.
10,700	30 min	Female	4/5	Days 3-4	
13,700	1 h	Male	5/5	Day 1	During exposure: audible oral noises; cramped walking; ocular and nasal irritation.
12,000	1 h	Female	5/5	Days 1-3	

Source: Bayer 1983.

3.2.2. Guinea Pigs

Ethyl phosphorodichloridate was negative in a guinea pig sensitization (Buehler) test (Rhone- Poulenc, Inc. 1990).

3.2.3. Summary of Nonlethal Toxicity in Animals

Ethyl phosphorodichloridate was corrosive to the skin and eyes of rabbits and was negative in a guinea pig sensitization test (Rhone-Poulenc, Inc. 1990).

3.3. Developmental and Reproductive Effects

No developmental or reproductive data were found.

3.4. Genotoxicity

No genotoxicity data were found.

3.5. Carcinogenicity

No carcinogenicity data were found.

4. SPECIAL CONSIDERATIONS

4.1. Metabolism and Disposition

Metabolism and disposition data for ethyl phosphorodichloridate in humans or animals were not available.

4.2. Mechanism of Toxicity

On the basis of clinical signs of toxicity and the physico-chemical properties of ethyl phosphorodichloridate, its mechanism of toxicity appears to be that of primary irritation. Rat lethality studies reported that vapors of ethyl phosphorodichloridate are irritating to the eyes and nose, and that the incidence of pulmonary edema increases with concentration (Bayer 1983; Rhone-Poulenc, Inc. 1990). Liquid ethyl phosphorodichloridate was corrosive to the skin and eyes of rabbits (Rhone-Poulenc, Inc. 1990).

Little information on the reactivity of ethyl phosphorodichloridate was found in the literature. It reportedly reacts with water to produce hydrogen chloride fumes, and may also produce fumes of phosphoric acid when heated (HSDB 2002). Because those products are irritating and corrosive, they may contribute to or be responsible for the irritation observed after exposure to ethyl phosphorodichloridate; however, the rate of decomposition and relative contribution of these decomposition products to the toxicity of the parent compound is unknown. Under conditions that promote aerosolization of ethyl phosphorodichloridate, transport to the deeper airways may occur, leading to greater lung injury and possibly delayed clinically manifested effects.

4.3. Structure-Activity Relationships

No structure-activity information on ethyl phosphorodichloridate was available.

4.4. Species Variability

Data are insufficient to determine species variability for ethyl phosphorodichloridate; however, because the clinical signs and physico-chemical properties suggest that its mechanism of toxicity may be primary irritation, little species variability is expected (NRC 2001).

4.5. 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 ranges from 0.8 to 3.5 (ten Berge et al. 1986). In the absence of data to allow empirical derivation of the exponent n, temporal scaling was performed using n = 3 when extrapolating to shorter durations and n = 1 when extrapolating to longer durations (NRC 2001).

5. DATA ANALYSIS FOR AEGL-1

5.1. Human Data Relevant to AEGL-1

No human data relevant to derivation of AEGL-1 values for ethyl phosphorodichloridate were available.

5.2. Animal Data Relevant to AEGL-1

No animal data relevant to derivation of AEGL-1 values for ethyl phosphorodichloridate were available.

5.3. Derivation of AEGL-1 Values

No human or animal data were available for derivation of AEGL-1 values for ethyl phosphorodichloridate. Therefore, AEGL-1 values are not recommended.

6. DATA ANALYSIS FOR AEGL-2

6.1. Human Data Relevant to AEGL-2

No human data relevant to derivation of AEGL-2 values for ethyl phosphorodichloridate were available.

6.2. Animal Data Relevant to AEGL-2

No animal data relevant to derivation of AEGL-2 values for ethyl phosphorodichloridate were available.

6.3. Derivation of AEGL-2 Values

In the absence of appropriate chemical-specific data, a fractional reduction of the AEGL-3 values may be used to derive AEGL-2 values (NRC 2001). For chemicals with a steep concentration-response curve, AEGL-3 values may be divided by 3 to estimate AEGL-2 values (NRC 2001). Therefore, AEGL-2 values will be estimated by dividing AEGL-3 values by 3. AEGL-2 values are presented in Table 2-6, and calculations are presented in Appendix A.

7. DATA ANALYSIS FOR AEGL-3

7.1. Human Data Relevant to AEGL-3

No human data relevant to derivation of AEGL-3 values for ethyl phosphorodichloridate were located.

TABLE 2-6 AEGL-2 Values for Ethyl Phosphorodichloridate

10 min	30 min	1 h	4 h	8 h
0.37 ppm (2.4 mg/m^3)	0.25 ppm (1.7 mg/m^3)	0.20 ppm (1.3 mg/m^3)	0.13 ppm (0.86 mg/m^3)	0.063 ppm (0.40 mg/m^3)

7.2. Animal Data Relevant to AEGL-3

Animal lethality data are available for rats. On the basis of a 1-h study, LC_{50} values of 64.6 ppm for male rats, 48.1 ppm for female rats, and 43.4 ppm for the sexes combined were calculated (Rhone-Poulenc, Inc. 1990). On the basis of a 4-h study, LC_{50} values of 85 ppm for males, 99.8 ppm for females, and 91.6 ppm for the sexes combined were calculated. $BMCL_{05}$ values were 43.7 ppm for males, 25.8 ppm for females, and 38.0 ppm for the sexes combined, and BMC_{01} values were 48.1 ppm, 32.1 ppm, 38.2 ppm, respectively (Bayer 1983). No deaths were noted in male rats exposed to ethyl phosphorodichloridate at 20,900 ppm or in female rats exposed at 16,700 ppm for 10 min (Bayer 1983).

7.3. Derivation of AEGL-3 Values

The 4-h $BMCL_{05}$ of 38.0 ppm for male and female rats (Bayer 1983) was used as the point of departure for AEGL-3 values. That value is considered a threshold for lethality, and is supported by the fact that no mortality was observed in rats exposed to ethyl phosphorodichloridate at 37 ppm for 4 h. The 4-h study was chosen over the 1-h study because it included more animals per exposure group and more exposure concentrations, and yielded a better concentration-response relationship. Due to the concentrations of ethyl phosphorodichloridate used in the 1-h study, the concentration-response relationship resembles a step function (1-h mortality data were 0/10 at 6.16 ppm, 8/10 at 66 ppm, 7/10 at 134 ppm, and 7/10 at 350 ppm [Rhone-Poulenc, Inc. 1990]); whereas, the 4-h study used narrower exposure intervals and yielded more variable responses (4-h mortality data were 0/20 at 37 ppm, 2/10 at 61 ppm, 4/20 at 75 ppm, 12/20 at 90 ppm, 17/20 at 143 ppm, and 20/20 at 355 ppm [Bayer 1983]). Furthermore, the goodness of fit for benchmark calculations was better for the 4-h data (p-value = 0.7465) than for the 1-h data (p-value = 0.21). Values were be scaled across time using the equation $C^n \times t = k$, where n = 3 when extrapolating to shorter durations and n = 1 when extrapolating to longer durations to derive values protective of human health (NRC 2001). Extrapolating from a 4-h study duration to the 10-min AEGL-3 value is justified because no deaths were noted in male rats exposed to ethyl phosphorodichloridate at 20,900 ppm or in female rats exposed at 16,700 ppm for 10 min (Bayer 1983). A factor of 10 was used to account for interspecies differences and another factor of 10 was used for intraspecieis variability because of the lack information available to describe species differences in toxicity and interindividual variability. Ani-

mals exposed to ethyl phosphorodichloridate experienced labored breathing, rales, nasal discharge, salivation, lacrimation, and ocular irritation following exposure for 1 or 4 h (Bayer 1983; Rhone-Poulenc, Inc. 1990), which are signs of irritation. Liquid ethyl phosphorodichloridate was corrosive to the skin and eyes of rabbits (Rhone-Poulenc, Inc. 1990), and may also produce fumes of hydrogen chloride and phosphoric acid (HSDB 2002). Because those fumes are irritating and corrosive, they may contribute to or be responsible for the irritation observed after exposure to ethyl phosphorodichloridate; however, the relative contribution of these decomposition products to the toxicity of the parent compound is unknown, as is the rate of decomposition.

AEGL-3 values for ethyl phosphorodichloridate are presented in Table 2-7 and their derivation is summarized in Appendix A.

8. SUMMARY OF AEGLs

8.1. AEGL Values and Toxicity End Points

AEGL values for ethyl phosphorodichloridate are presented in Table 2-8. AEGL-1 values were not recommended because insufficient data. AEGL-2 values were derived by dividing the AEGL-3 values by 3, and the AEGL-3 values are based on a threshold for lethality in rats (4-h $BMCL_{05}$).

8.2. Comparisons with Other Standards and Guidelines

No other standards or guidelines for ethyl phosphorodichloridate were found for ethyl phosphorodichloridate.

TABLE 2-7 AEGL-3 Values for Ethyl Phosphorodichloridate

10 min	30 min	1 h	4 h	8 h
1.1 ppm ($7.3\ mg/m^3$)	0.76 ppm ($5.0\ mg/m^3$)	0.60 ppm ($4.0\ mg/m^3$)	0.38 ppm ($2.5\ mg/m^3$)	0.19 ppm ($1.3\ mg/m^3$)

TABLE 2-8 AEGL Values for Ethyl Phosphorodichloridate

Classification	10 min	30 min	1 h	4 h	8 h
AEGL-1 (nondisabling)[a]	NR	NR	NR	NR	NR
AEGL-2 (disabling)	0.37 ppm ($2.4\ mg/m^3$)	0.25 ppm ($1.7\ mg/m^3$)	0.20 ppm ($1.3\ mg/m^3$)	0.13 ppm ($0.86\ mg/m^3$)	0.063 ppm ($0.40\ mg/m^3$)
AEGL-3 (lethal)	1.1 ppm ($7.3\ mg/m^3$)	0.76 ppm ($5.0\ mg/m^3$)	0.60 ppm ($4.0\ mg/m^3$)	0.38 ppm ($2.5\ mg/m^3$)	0.19 ppm ($1.3\ mg/m^3$)

Abbreviations: NR, not recommended.

[a]Absence of an AEGL-1 value does not imply that concentrations below the AEGL-2 are without effect.

8.3. Data Adequacy and Research Needs

No human or animal data on ethyl phosphorodichloridate relevant to AEGL-1 or AEGL-2 end points were available. Toxicity data on this compound were limited to unpublished studies, including 1-h and 4-h lethality studies in rats exposed by inhalation (Bayer 1983; Rhone-Poulenc, Inc. 1990), LD50 estimates in rats (oral) and rabbits (dermal), dermal and ocular irritation data in rabbits, and a guinea pig sensitization study (Rhone-Poulenc, Inc. 1990). No data were available on the metabolism and disposition of ethyl phosphorodichloridate in humans or animals. Anecdotal information provided by HSDB (2002) suggests that hydrogen chloride and phosphoric acid may represent decomposition products of ethyl phosphorodichloridate, but the rate of decomposition and relative contribution of these decomposition products to the toxicity of the parent compound is unknown. Additional research on the acute inhalation toxicity of ethyl phosphorodichloridate in other species, the metabolism and disposition of ethyl phosphorodichloridate in the respiratory tract, and identification of the ultimate chemical compound(s) responsible for toxicity of this compound would enhance confidence in the AEGL values.

9. REFERENCES

Bayer AG. 1983. Ethylesterdichloride [in German]. Report No. 11439 and 11715. Bayer AG, Wuppertal-Elberfeld. Attachment in letter from Mobay Corporation, Pittsburg, PA, to U.S. EPA Submitting Toxicology Study on Ethylesterdichloride, Dated 12/31/90. EPA Document No. 86910000570, Microfiche No. OTS0530306; and EPA Document No. 86910000571, Microfiche No. OTS0530307.

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APPENDIX A

DERIVATION OF AEGL VALUES FOR ETHYL PHOSPHORODICHLORIDATE

Derivation of AEGL-1 Values

The available data were insufficient to derive AEGL-1 values for ethyl phosphorodichloridate. Therefore, AEGL-1 values were not recommended.

Derivation of AEGL-2 Values

In the absence of appropriate chemical-specific data, a fractional reduction of the AEGL-3 values may be used to derive AEGL-2 values. For chemicals with a steep concentration-response curve, AEGL-3 values may be divided by 3 to estimate AEGL-2 values (NRC 2001).

10-min AEGL-2: 1.1 ppm ÷ 3 = 0.37 ppm

30-min AEGL-2: 0.76 ppm ÷ 3 = 0.25 ppm

1-h AEGL-2: 0.60 ppm ÷ 3 = 0.20 ppm

4-h AEGL-2: 0.38 ppm ÷ 3 = 0.13 ppm

8-h AEGL-2: 0.19 ppm ÷ 3 = 0.06 ppm

Derivation of AEGL-3 Values

Key study: Bayer AG. 1983. Ethylesterdichloride [in German]. Report No. 11439 and 11715. Bayer AG, Wuppertal-Elberfeld. Attachment in Letter from Mobay Corporation, Pittsburg, PA, to U.S. EPA Submitting Toxicology Study on Ethylesterdichloride, Dated 12/31/90. EPA Document No. 86910000570, Microfiche No. OTS0530306; and EPA Document No. 86910000571, Microfiche No. OTS0530307.

Toxicity end point: 4-h threshold for lethality in rats ($BMCL_{05}$ = 38 ppm).

Time scaling:	Values scaled across time using the equation $C^n \times t = k$, where n = 3 when extrapolating to shorter durations and n = 1 when extrapolating to longer durations to derive values protective of human health (NRC 2001). Extrapolating from the 4-h point of departure to the 10-min AEGL-3 value is justified because no deaths were noted in male rats exposed to ethyl phosphorodichloridate at 20,900 ppm or in female rats exposed at 16,700 ppm for 10 min (Bayer 1983). $(38 \text{ ppm})^3 \times 4 \text{ h} = 219{,}488 \text{ ppm-h}$ $(38 \text{ ppm})^1 \times 4 \text{ h} = 152 \text{ ppm-h}$
Uncertainty factors:	10 for interspecies differences 10 for intraspecies variability
Modifying factor:	None
10-min AEGL-3:	$C^3 \times 0.167 \text{ h} = 219{,}488 \text{ ppm-h}$ $C^3 = 1{,}314{,}299 \text{ ppm}$ $C = 109 \text{ ppm}$ $109 \text{ ppm} \div 100 = 1.1 \text{ ppm}$
30-min AEGL-3:	$C^3 \times 0.5 \text{ h} = 219{,}488 \text{ ppm-h}$ $C^3 = 438{,}976 \text{ ppm}$ $C = 76 \text{ ppm}$ $76 \text{ ppm} \div 100 = 0.76 \text{ ppm}$
1-h AEGL-3:	$C^3 \times 1 \text{ hr} = 219{,}488 \text{ ppm-h}$ $C^3 = 219{,}488 \text{ ppm}$ $C = 60 \text{ ppm}$ $60 \text{ ppm} \div 100 = 0.60 \text{ ppm}$
4-h AEGL-3:	$C = 38 \text{ ppm}$ $38 \text{ ppm} \div 100 = 0.38 \text{ ppm}$
8-h AEGL-3:	$C^1 \times 8 \text{ h} = 152 \text{ ppm-h}$ $C = 19 \text{ ppm}$ $19 \text{ ppm} \div 100 = 0.19 \text{ ppm}$

APPENDIX B

BENCHMARK CALCULATION FOR ETHYL PHOSPHORODICHLORIDATE

Probit Model $Revision: 2.1 $ $Date: 2000/02/26 03:38:53 $
Input Data File: C:\BMDS\
Mon Jan 28 09:33:17 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 = COLUMN3
Independent variable = COLUMN1
Slope parameter is not restricted

Total number of observations = 7
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 = -8.25812
Slope = 1.795

Asymptotic Correlation Matrix of Parameter Estimates

	Intercept	Slope
Intercept	1	-1
Slope	-1	1

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

Parameter Estimates

Variable	Estimate	Standard error
Intercept	-12.0173	2.35981
Slope	2.6604	0.526262

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)	Deviance Test	DF	P-value
Full model	-36.9265			
Fitted model	-38.3731	2.89329	5	0.7164
Reduced model	-88.5645	103.276	6	<0.0001

AIC: 80.7463.

Goodness of Fit

		Scaled			
Dose	Estimated probability	Expected	Observed	Size	Residual
0.0000	0.0000	0.000	0	20	0
37.0000	0.0080	0.159	0	20	-0.4006
61.0000	0.1399	1.399	2	10	0.5477
75.0000	0.2977	5.954	4	20	-0.9556
90.0000	0.4817	9.633	12	20	1.059
143.0000	0.8822	17.643	17	20	-0.4462
355.0000	0.9998	19.997	20	20	0.05588

Chi-square = 2.70; DF = 5; P-value = 0.7465.

Benchmark Dose Computation
Specified effect = 0.05

Risk Type = Extra risk
Confidence level = 0.95
BMD = 49.3439
BMDL = 37.9523

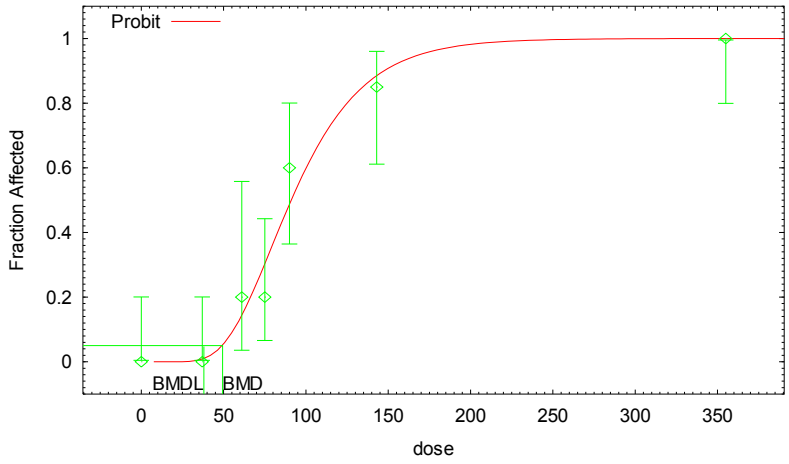

FIGURE B-1 Probit model with 0.95 confidence level.

APPENDIX C

ACUTE EXPOSURE GUIDELINE LEVELS FOR ETHYL PHOSPHORODICHLORIDATE

Derivation Summary

AEGL-1 VALUES

The available data were insufficient to derive AEGL-1 values for ethyl phosphorodichloridate. Therefore, AEGL-1 values were not recommended.

AEGL-2 VALUES

10 min	30 min	1 h	4 h	8 h
0.37 ppm (2.4 mg/m^3)	0.25 ppm (1.7 mg/m^3)	0.20 ppm (1.3 mg/m^3)	0.13 ppm (0.86 mg/m^3)	0.063 ppm (0.40 mg/m^3)

Data adequacy: The available data were insufficient to derive AEGL-2 values for ethyl phosphorodichloridate. A fractional reduction of the AEGL-3 values may be used to derive AEGL-2 values. For chemicals with a steep concentration-response curve, AEGL-3 values may be divided by 3 to estimate AEGL-2 values (NRC 2001).

AEGL -3 VALUES

10 min	30 min	1 h	4 h	8 h
1.1 ppm (7.3 mg/m^3)	0.76 ppm (5.0 mg/m^3)	0.60 ppm (4.0 mg/m^3)	0.38 ppm (2.5 mg/m^3)	0.19 ppm (1.3 mg/m^3)

Reference: Bayer AG. 1983. Ethylesterdichloride [in German]. Report No. 11439 and 11715. Bayer AG, Wuppertal-Elberfeld. Attachment in Letter from Mobay Corporation to U.S. EPA Submitting Toxicology Study on Ethylesterdichloride, Dated 12/31/90.EPA Document No. 86910000570, Microfiche No.OTS05030306; and EPA Document No. 86910000571, Microfiche No. OTS05030307.

Test Species/Strain/Sex/Number: Rat, strain not specified , 10 males and 10 females per group

Exposure route/Concentrations/Durations: Inhalation; 37, 61, 75, 90, 143, or 355 ppm for 4 h

Effects: Lethality

Concentration	Mortality		
(ppm)	Male	Female	Total
37	0/10	0/10	0/20
61	0/10	Not reported	0/10
75	1/10	3/10	4/20

75	1/10	3/10	4/20
90	7/10	5/10	12/20
143	10/10	7/10	17/20
355	10/10	10/10	20/20
LC_{50}	85 ppm	99.8 ppm	91.6 ppm
$BMCL_{05}$	43.7 ppm	25.8 ppm	38.0 ppm
BMC_{01}	48.1 ppm	32.1 ppm	38.2 ppm

End point/Concentration/Rationale: 4-h $BMCL_{05}$ in rats of 38 ppm; threshold for lethality

Uncertainty factors/Rationale:
Interspecies: 10, no interspecies or mechanistic data.
Intraspecies: 10, no data on interindividual variability.

Modifying factor: None

Animal-to-human dosimetric adjustment: Not applicable

Time scaling: $C^n \times t = k$, where n = 3 when extrapolating to shorter durations and n = 1 when extrapolating to longer durations to derive values protective of human health (NRC 2001). Extrapolating from a 4-h point of departure to a 10-min AEGL-3 value is justified because no deaths were noted in male rats exposed to ethyl phosphorodichloridate at 20,900 ppm or in female rats exposed at 16,700 ppm for 10 min (Bayer 1983).

Data adequacy: Sparse data set.

APPENDIX D

CATEGORY PLOT FOR ETHYL PHOSPHORODICHLORIDATE

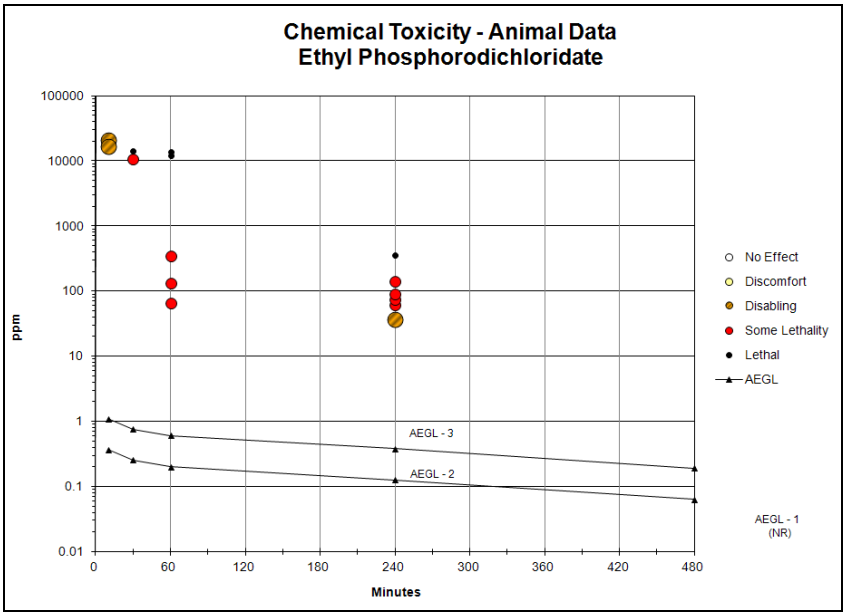

TABLE D-1 Category plot of animal toxicity data on ethyl phosphorodichloridate compared with AEGL values.

TABLE D-1 Data Used in Category Plot of AEGL Values for Ethyl Phosphorodichloridate

Source	Species	Sex	No. Exposures	ppm	Minutes	Category	Reference
NAC/AEGL-1				NR	10	AEGL	
NAC/AEGL-1				NR	30	AEGL	
NAC/AEGL-1				NR	60	AEGL	
NAC/AEGL-1				NR	240	AEGL	
NAC/AEGL-1				NR	480	AEGL	
NAC/AEGL-2				0.37	10	AEGL	
NAC/AEGL-2				0.25	30	AEGL	
NAC/AEGL-2				0.20	60	AEGL	
NAC/AEGL-2				0.13	240	AEGL	
NAC/AEGL-2				0.063	480	AEGL	
NAC/AEGL-3				1.1	10	AEGL	
NAC/AEGL-3				0.76	30	AEGL	
NAC/AEGL-3				0.60	60	AEGL	
NAC/AEGL-3				0.38	240	AEGL	
NAC/AEGL-3				0.19	480	AEGL	
	Rat		1	6.16	60	2	Labored breathing, gasping, decreased activity, rales, tremors (Rhone-Poulenc, Inc. 1990).
	Rat		1	66	60	SL	Labored breathing, gasping, decreased activity, rales, tremors, weight loss, mortality 8/10 (Rhone-Poulenc, Inc. 1990).

(Continued)

TABLE D-1 Continued

Source	Species	Sex	No. Exposures	ppm	Minutes	Category	Reference
	Rat		1	134	60	SL	Labored breathing, gasping, decreased activity, rales, tremors, weight loss, mortality 7/10 (Rhone-Poulenc, Inc. 1990).
	Rat		1	37	240	2	Severe ocular and nasal irritation, disturbed behavior, severe respiratory signs (Bayer 1983).
	Rat		1	61	240	SL	Severe ocular and nasal irritation, disturbed behavior, severe respiratory signs, mortality 2/10 (Bayer 1983).
	Rat		1	75	240	SL	Severe ocular and nasal irritation, disturbed behavior, severe respiratory signs, mortality 4/20 (Bayer 1983).
	Rat		1	90	240	SL	Severe ocular and nasal irritation, disturbed behavior, severe respiratory signs, mortality 12/20 (Bayer 1983).
	Rat		1	143	240	SL	Severe ocular and nasal irritation, disturbed behavior, severe respiratory signs, mortality 17/20 (Bayer 1983).
	Rat		1	355	240	3	Severe ocular and nasal irritation, disturbed behavior, severe respiratory signs, mortality 2/10 (Bayer 1983).
	Rat		1	350	60	SL	Hyperemia, decreased activity, salivation, lacrimation, mortality 20/20 (Rhone-Poulenc, Inc. 1990).

Rat	1	20,900	10	2	Severe ocular and nasal irritation, disturbed behavior, severe respiratory signs, no weight gain (Bayer 1983).
Rat	1	16,700	10	2	Severe ocular and nasal irritation, disturbed behavior, severe respiratory signs, no weight gain (Bayer 1983).
Rat	1	14,400	30	3	Severe ocular and nasal irritation, disturbed behavior, severe respiratory signs, weight loss, mortality 5/5 (Bayer 1983).
Rat	1	10,700	30	SL	Severe ocular and nasal irritation, disturbed behavior, severe respiratory signs, weight loss, mortality 4/5 (Bayer 1983).
Rat	1	13,700	60	3	Severe ocular and nasal irritation, oral noises, cramped walking, mortality 5/5 (Bayer 1983).
Rat	1	12,000	60	3	Severe ocular and nasal irritation, oral noises, cramped walking, mortality 5/5 (Bayer 1983).

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