2. *100–EUP–112*. Issuance. Syngenta Crop Protection, 410 Swing Road, Greensboro, NC 27419–8300. This EUP allows the use of 74 pounds active ingredient of the insecticide Lufenuron around 125 structures to be used as an outdoor in-ground termite bait. The program is authorized in the States of Alabama, Arizona, Arkansas, California, Florida, Georgia, Hawaii, Indiana, Kansas, Kentucky, Louisiana, Maryland, Mississippi, Missouri, Nebraska, Nevada, North Carolina, Ohio, Oklahoma, Pennsylvania, South Carolina, Texas, and Virginia. The EUP is effective from April 3, 2003 to April 3, 2006.

3. *100–EUP–113*. Issuance. Syngenta Crop Protection, 410 Swing Road, Greensboro, NC 27419–8300. This EUP allows the use of 1 pound active ingredient of the insecticide Lufenuron around 25 structures to be used as an above ground termite bait. The program is authorized only in the States of Arizona, California, Florida, Georgia, Hawaii, Louisiana, Ohio, South Carolina, and Texas. The EUP is effective from May 7, 2003 to May 7, 2006.

4. *352–EUP–167*. Issuance. E. I. Dupont de Nemours and Company, P.O. Box 30, Newark, DE 19714. This EUP allows the use of 450 pounds of the insecticide Dupont Avaunt, containing 135 pounds of the active ingredient indoxacarb on 300 acres of peaches to evaluate the control of the Oriental fruit moth and plum curculio. The program is authorized only in the States of Georgia, Michigan, New Jersey, Pennsylvania, South Carolina, and West Virginia. The EUP is effective from May 2, 2003 to May 2, 2005.

5. *70341–EUP–2*. Issuance. IPM Technologies, Inc., 4134 North Vancouver Avenue #105, Portland, OR 97217. This EUP allows the use of 300 pounds of the insecticide Last Call PLR, containing 18 pounds of the active ingredient permethrin and 4.8 pounds of a pheromone blend on 68 acres of apples to evaluate the control of Pandemis leafroller moth. The program is authorized only in the State of Washington. The EUP is effective from May 15, 2003 to May 14, 2004.

6. *70341–EUP–3*. Issuance. IPM Technologies, Inc., 4134 North Vancouver Avenue #105, Portland, OR 97217. This EUP allows the use of 300 pounds of the insecticide Last Call OBLR, containing 18 pounds of the active ingredient permethrin and 4.8 pounds of a pheromone blend on 68 acres of apples to evaluate the control of Oblique banded leafroller moth. The program is authorized only in the State of Washington. The EUP is effective from May 15, 2003 to May 14, 2004.

7. *71715–EUP–2*. Issuance. Tonnie L. C. Casey, Kamehameha Schools, 78–6831 Alii Drive, Suite 232, Kailua-Kona, HI 96740. This EUP allows the use of 16,000 pounds of the rodenticide Eaton's Bait Pellet Rodenticide with Fish Flavorizer, containing 80 pounds of the active ingredient diphacinone on 800 acres of forested ranchland to evaluate the control of invasive rodents and mongooses. The program is authorized only in the State of Hawaii. The EUP is effective from May 6, 2003 to May 6, 2004.

Authority: 7 U.S.C. 136c.

List of Subjects

Environmental protection, Experimental use permits.

Dated: July 1, 2003.

Debra Edwards

Director, Registration Division, Office of Pesticide Programs.

[FR Doc. 03–18318 Filed 7–17–03; 8:45 am]

BILLING CODE 6560–50–S

ENVIRONMENTAL PROTECTION AGENCY

[OPPT–2002–0027; FRL–7189–8]

National Advisory Committee for Acute Exposure Guideline Levels (AEGLs) for Hazardous Substances; Proposed AEGL Values

AGENCY: Environmental Protection Agency (EPA).

ACTION: Notice.

SUMMARY: The National Advisory Committee for Acute Exposure Guideline Levels for Hazardous Substances (NAC/AEGL Committee) is developing AEGLs on an ongoing basis to provide Federal, State, and local agencies with information on short-term exposures to hazardous chemicals. This notice provides AEGL values and executive summaries for 10 chemicals for public review and comment. Comments are welcome on both the AEGL values in this notice and the technical support documents placed in the public version of the official docket for these 10 chemicals.

DATES: Comments, identified by docket ID number OPPT–2002–0027, must be received on or before August 18, 2003.

ADDRESSES: Comments may be submitted electronically, by mail, or through hand delivery/courier. Follow the detailed instructions as provided in Unit I. of the **SUPPLEMENTARY INFORMATION**.

FOR FURTHER INFORMATION CONTACT: *For general information contact*: Barbara Cunningham, Acting Director, Environmental Assistance Division (7408M), Office of Pollution Prevention and Toxics, Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460; telephone number: (202) 554–1404; e-mail address: *TSCA-Hotline@epa.gov*.

For technical information contact: Paul S. Tobin, Designated Federal Officer (DFO), Office of Pollution Prevention and Toxics (7406M), Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460; telephone number: (202) 564–8557; e-mail address: *tobin.paul@epa.gov*.

SUPPLEMENTARY INFORMATION:

I. General Information

A. Does this Action Apply to Me?

This action is directed to the general public to provide an opportunity for review and comment on ''Proposed'' AEGL values and their supporting scientific rationale. This action may be of particular interest to anyone who may be affected if the AEGL values are adopted by government agencies for emergency planning, prevention, or response programs, such as EPA's Risk Management Program under the Clean Air Act and Amendments Section 112r. It is possible that other Federal agencies besides EPA, as well as State and local agencies and private organizations, may adopt the AEGL values for their programs. As such, the Agency has not attempted to describe all the specific entities that may be affected by this action. If you have any questions regarding the applicability of this action to a particular entity, consult the DFO listed under **FOR FURTHER INFORMATION CONTACT**.

B. How Can I Get Copies of this Document and Other Related Information?

1. *Docket*. EPA has established an official public docket for this action under docket identification (ID) number OPPT–2002–0027. The official public docket consists of the documents specifically referenced in this action, any public comments received, and other information related to this action. Although a part of the official docket, the public docket does not include Confidential Business Information (CBI) or other information whose disclosure is restricted by statute. The official public docket is the collection of materials that is available for public viewing at the EPA Docket Center, Rm. B102-Reading Room, EPA West, 1301 Constitution

Ave., NW., Washington, DC. The EPA Docket Center is open from 8:30 a.m. to 4:30 p.m., Monday through Friday, excluding legal holidays. The EPA Docket Center Reading Room telephone number is (202) 566–1744 and the telephone number for the OPPT Docket, which is located in EPA Docket Center, is (202) 566–0280.

2. *Electronic access*. You may access this **Federal Register** document electronically through the EPA Internet under the ''**Federal Register**'' listings at *http://www.epa.gov/fedrgstr/*.

An electronic version of the public docket is available through EPA's electronic public docket and comment system, EPA Dockets. You may use EPA Dockets at *http://www.epa.gov/edocket/* to submit or view public comments, access the index listing of the contents of the official public docket, and to access those documents in the public docket that are available electronically. Although not all docket materials may be available electronically, you may still access any of the publicly available docket materials through the docket facility identified in Unit I.B.1. Once in the system, select ''search,'' then key in the appropriate docket ID number.

Certain types of information will not be placed in the EPA Dockets. Information claimed as CBI and other information whose disclosure is restricted by statute, which is not included in the official public docket, will not be available for public viewing in EPA's electronic public docket. EPA's policy is that copyrighted material will not be placed in EPA's electronic public docket but will be available only in printed, paper form in the official public docket. To the extent feasible, publicly available docket materials will be made available in EPA's electronic public docket. When a document is selected from the index list in EPA Dockets, the system will identify whether the document is available for viewing in EPA's electronic public docket. Although not all docket materials may be available electronically, you may still access any of the publicly available docket materials through the docket facility identified in Unit I.B.1. EPA intends to work towards providing electronic access to all of the publicly available docket materials through EPA's electronic public docket.

For public commenters, it is important to note that EPA's policy is that public comments, whether submitted electronically or in paper, will be made available for public viewing in EPA's electronic public docket as EPA receives them and without change, unless the comment contains copyrighted material, CBI, or other information whose disclosure is restricted by statute. When EPA identifies a comment containing copyrighted material, EPA will provide a reference to that material in the version of the comment that is placed in EPA's electronic public docket. The entire printed comment, including the copyrighted material, will be available in the public docket.

Public comments submitted on computer disks that are mailed or delivered to the docket will be transferred to EPA's electronic public docket. Public comments that are mailed or delivered to the docket will be scanned and placed in EPA's electronic public docket. Where practical, physical objects will be photographed, and the photograph will be placed in EPA's electronic public docket along with a brief description written by the docket staff.

C. How and To Whom Do I Submit Comments?

You may submit comments electronically, by mail, or through hand delivery/courier. To ensure proper receipt by EPA, identify the appropriate docket ID number in the subject line on the first page of your comment. Please ensure that your comments are submitted within the specified comment period. Comments received after the close of the comment period will be marked ''late.'' EPA is not required to consider these late comments. If you wish to submit CBI or information that is otherwise protected by statute, please follow the instructions in Unit I.D. Do not use EPA Dockets or e-mail to submit CBI or information protected by statute.

1. *Electronically*. If you submit an electronic comment as prescribed in this unit, EPA recommends that you include your name, mailing address, and an e-mail address or other contact information in the body of your comment. Also include this contact information on the outside of any disk or CD ROM you submit, and in any cover letter accompanying the disk or CD ROM. This ensures that you can be identified as the submitter of the comment and allows EPA to contact you in case EPA cannot read your comment due to technical difficulties or needs further information on the substance of your comment. EPA's policy is that EPA will not edit your comment, and any identifying or contact information provided in the body of a comment will be included as part of the comment that is placed in the official public docket, and made available in EPA's electronic public docket. If EPA cannot read your comment due to technical difficulties and cannot contact you for clarification, EPA may not be able to consider your comment.

i. *EPA Dockets*. Your use of EPA's electronic public docket to submit comments to EPA electronically is EPA's preferred method for receiving comments. Go directly to EPA Dockets at *http://www.epa.gov/edocket/*, and follow the online instructions for submitting comments. Once in the system, select ''search,'' and then key in docket ID number OPPT–2002–0027. The system is an ''anonymous access'' system, which means EPA will not know your identity, e-mail address, or other contact information unless you provide it in the body of your comment.

ii. *E-mail*. Comments may be sent by e-mail to *oppt.ncic@epa.gov*, Attention: Docket ID Number OPPT–2002–0027. In contrast to EPA's electronic public docket, EPA's e-mail system is not an ''anonymous access'' system. If you send an e-mail comment directly to the docket without going through EPA's electronic public docket, EPA's e-mail system automatically captures your e-mail address. E-mail addresses that are automatically captured by EPA's e-mail system are included as part of the comment that is placed in the official public docket, and made available in EPA's electronic public docket.

iii. *Disk or CD ROM*. You may submit comments on a disk or CD ROM that you mail to the mailing address identified in Unit I.C.2. These electronic submissions will be accepted in WordPerfect or ASCII file format. Avoid the use of special characters and any form of encryption.

2. *By mail*. Send your comments to: Document Control Office (7407M), Office of Pollution Prevention and Toxics (OPPT), Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460–0001.

3. *By hand delivery or courier*. Deliver your comments to: OPPT Document Control Office (DCO) in EPA East Building Rm. 6428, 1201 Constitution Ave., NW., Washington, DC. Attention: Docket ID Number OPPT–2002–0027. The DCO is open from 8 a.m. to 4 p.m., Monday through Friday, excluding legal holidays. The telephone number for the DCO is (202) 564–8930.

D. How Should I Submit CBI to the Agency?

Do not submit information that you consider to be CBI electronically through EPA's electronic public docket or by e-mail. You may claim information that you submit to EPA as CBI by marking any part or all of that information as CBI (if you submit CBI on disk or CD ROM, mark the outside

of the disk or CD ROM as CBI and then identify electronically within the disk or CD ROM the specific information that is CBI). Information so marked will not be disclosed except in accordance with procedures set forth in 40 CFR part 2.

In addition to one complete version of the comment that includes any information claimed as CBI, a copy of the comment that does not contain the information claimed as CBI must be submitted for inclusion in the public docket and EPA's electronic public docket. If you submit the copy that does not contain CBI on disk or CD ROM, mark the outside of the disk or CD ROM clearly that it does not contain CBI. Information not marked as CBI will be included in the public docket and EPA's electronic public docket without prior notice. If you have any questions about CBI or the procedures for claiming CBI, please consult the technical person listed under **FOR FURTHER INFORMATION CONTACT**.

E. What Should I Consider as I Prepare My Comments for EPA?

You may find the following suggestions helpful for preparing your comments:

1. Explain your views as clearly as possible.
2. Describe any assumptions that you used.
3. Provide copies of any technical information and/or data you used that support your views.
4. If you estimate potential burden or costs, explain how you arrived at the estimate that you provide.
5. Provide specific examples to illustrate your concerns.
6. Offer alternative ways to improve the notice or collection activity.
7. Make sure to submit your comments by the deadline in this document.
8. To ensure proper receipt by EPA, be sure to identify the docket ID number assigned to this action in the subject line on the first page of your response. You may also provide the name, date, and **Federal Register** citation.

II. Background

A. What Action is the Agency Taking?

EPA's Office of Prevention, Pesticides and Toxic Substances (OPPTS) provided notice in the **Federal Register** of October 31, 1995 (60 FR 55376) (FRL–4987–3) of the establishment of the NAC/AEGL Committee with the stated charter objective as ''the efficient and effective development of AEGLs and the preparation of supplementary qualitative information on the hazardous substances for federal, state, and local agencies and organizations in the private sector concerned with [chemical] emergency planning, prevention, and response.'' The NAC/AEGL Committee is a discretionary Federal advisory committee formed with the intent to develop AEGLs for chemicals through the combined efforts of stakeholder members from both the public and private sectors in a cost-effective approach that avoids duplication of efforts and provides uniform values, while employing the most scientifically sound methods available. An initial priority list of 85 chemicals for AEGL development was published in the **Federal Register** of May 21, 1997 (62 FR 27734) (FRL–5718–9). This list is intended for expansion and modification as priorities of the stakeholder member organizations are further developed. While the development of AEGLs for chemicals are currently not statutorily based, at lease one rulemaking references their planned adoption. The Clean Air Act and Amendments Section 112(r) Risk Management Program states, ''EPA recognizes potential limitations associated with the Emergency Response Planning Guidelines and Level of Concern and is working with other agencies to develop AEGLs. When these values have been developed and peer-reviewed, EPA intends to adopt them, through rulemaking, as the toxic endpoint for substances under this rule (see 61 FR 31685).'' It is believed that other Federal and State agencies and private organizations will also adopt AEGLs for chemical emergency programs in the future.

B. Characterization of the AEGLs

The AEGLs represent threshold exposure limits for the general public and are applicable to emergency exposure periods ranging from 10 minutes to 8 hours. AEGL-2 and AEGL-3 levels, and AEGL-1 levels as appropriate, will be developed for each of five exposure periods (10 and 30 minutes, 1 hour, 4 hours, and 8 hours) and will be distinguished by varying degrees of severity of toxic effects. It is believed that the recommended exposure levels are applicable to the general population including infants and children, and other individuals who may be sensitive and susceptible. The AEGLs have been defined as follows:

AEGL-1 is the airborne concentration (expressed as parts per million (ppm) or milligram/meter cubed (mg/m3) of a substance above which it is predicted that the general population, including susceptible individuals, could experience notable discomfort, irritation, or certain asymptomatic, non-sensory 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/m3) 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/m3) 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 levels that could produce mild and progressively increasing odor, taste, and sensory irritation, or certain non-symptomatic, non-sensory effects. With increasing airborne concentrations above each AEGL level, there is a progressive increase in the likelihood of occurrence and the severity of effects described for each corresponding AEGL level. Although the AEGL values represent threshold levels for the general public, including sensitive subpopulations, it is recognized that certain individuals, subject to unique or idiosyncratic responses, could experience the effects described at concentrations below the corresponding AEGL level.

C. Development of the AEGLs

The NAC/AEGL Committee develops the AEGL values on a chemical-by-chemical basis. Relevant data and information are gathered from all known sources including published scientific literature, State and Federal agency publications, private industry, public data bases, and individual experts in both the public and private sectors. All key data and information are summarized for the NAC/AEGL Committee in draft form by Oak Ridge National Laboratories together with ''draft'' AEGL values prepared in conjunction with NAC/AEGL Committee members. Both the ''draft'' AEGLs and ''draft'' technical support documents are reviewed and revised as necessary by the NAC/AEGL Committee members prior to formal NAC/AEGL Committee meetings. Following deliberations on the AEGL values and the relevant data and information for each chemical, the NAC/AEGL Committee attempts to reach a consensus. Once the NAC/AEGL Committee reaches a consensus, the values are considered ''Proposed'' AEGLs. The Proposed AEGL values and the accompanying scientific rationale

for their development are the subject of this notice.

The NAC/AEGL Committee publishes proposed AEGL values and the accompanying scientific rationale for their development for 10 hazardous substances. These values represent the sixth set of exposure levels proposed and published by the NAC/AEGL Committee EPA published the first ''Proposed'' AEGLs for 12 chemicals from the initial priority list in the **Federal Register** of October 30, 1997 (62 FR 58840–58851) (FRL–5737–3); for 10 chemicals in the **Federal Register** of March 15, 2000 (65 FR 14186–14196) (FRL–6492–4); for 14 chemicals in the **Federal Register** of June 23, 2000 (65 FR 39263–39277) (FRL–659–2); for 7 chemicals in the **Federal Register** of December 13, 2000 (65 FR 77866–77874) (FRL–6752–5) for 18 chemicals in the **Federal Register** of May 2, 2001 (66 FR 21940–21964) (FRL–6776–3); and for 8 chemicals in the **Federal Register** of February 15, 2002 (67 FR 7164–7176) (FRL–6815–8) in order to provide an opportunity for public review and comment. In developing the proposed AEGL values, the Committee has followed the methodology guidance Guidelines for Developing Community Emergency Exposure Levels for Hazardous Substances, published by the National Research Council of the National Academy of Sciences (NAS) in 1993. The term Community Emergency Exposure Levels (CEELS) is synonymous with AEGLs in every way. The NAC/AEGL Committee has adopted the term Acute Exposure Guideline Levels to better connote the broad application of the values to the population defined by the NAS and addressed by the NAC/AEGL Committee. The NAC/AEGL Committee invites public comment on the proposed AEGL values and the scientific rationale used as the basis for their development.

Following public review and comment, the NAC/AEGL Committee will reconvene to consider relevant comments, data, and information that may have an impact on the NAC/AEGL Committee's position and will again seek consensus for the establishment of Interim AEGL values. Although the Interim AEGL values will be available to Federal, State, and local agencies and to organizations in the private sector as biological reference values, it is intended to have them reviewed by a subcommittee of the NAS. The NAS subcommittee will serve as a peer review of the Interim AEGLs and as the final arbiter in the resolution of issues regarding the AEGL values, and the data and basic methodology used for setting AEGLs. Following concurrence, ''Final'' AEGL values will be published under the auspices of the NAS.

D. Use of Human Data

The NAC/AEGL Program is working to ensure that emergency responders and risk managers in this country and abroad are armed with vital information they need to protect the public and themselves from harm in the event of chemical accidents or homeland security emergencies. Because of the serious nature of chemical emergency situations, it is essential that involved personnel have access to the most comprehensive and realistic assessments of human health hazards posed by released chemicals. Under estimation of human health hazard would not be protective, while over estimation might suggest a larger than necessary response zone. The Department of Army and Federal Emergency Management Agency Chemical Stockpile Emergency Preparedness Program (CSEPP), for example, has adopted, as outlined in CSEPP Policy Paper Number 20, AEGLs for sulfur mustard and nerve agents for use in CSEPP community emergency planning and response activities ''to prevent or minimize exposures above AEGL-2, above which some temporary but potentially escape-impairing effects could occur.'' Thus, with the application of the procedures discussed in this unit, the AEGL Program recognizes the importance of considering all available domestic and international test data, both animal and human, to determine threshold levels of harm for a range of exposure scenarios critical to those at the front line in defending public health.

The process for development of AEGL values incorporates essential scientific and ethical considerations posed by the possible use of research with human subjects. All human studies that were used as key or supporting evidence to derive AEGL values were judged acceptable for use according to ethical considerations detailed in the Standing Operating Procedures for Developing Acute Exposure Guideline Levels for Hazardous Substances, Subcommittee on Acute Exposure Guideline Levels, National Research Council, *National Academy Press*, 2001, p. 53. The SOP states ''The NAC/AEGL Committee is dependent upon existing clinical, epidemiologic, and case report studies published in the literature for data on humans. Many of these studies do not necessarily follow current guidelines on ethical standards that require effective, documented, informed consent from participating human subjects. Further, recent studies that followed such guidelines may not include that fact in the publication. Although human data may be important in deriving AEGL values that protect the general public, utmost care must be exercised to ensure first of all that such data have been developed in accordance with ethical standards. No data on humans known to be obtained through force, coercion, misrepresentation, or any other such means will be used in the development of AEGLs. The NAC/AEGL Committee will use its best judgment to determine whether the human studies were ethically conducted and whether the human subjects were likely to have provided their informed consent. Additionally, human data from epidemiologic studies and chemical accidents may be used. However, in all instances described here, only human data, documents, and records will be used from sources that are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified directly or indirectly. These restrictions on the use of human data are consistent with the 'Common Rule' published in the Code of Federal Regulations (Protection of Human Subjects, 40 CFR 26, 2000).'' Additionally, EPA has recently asked the NAC/AEGL Committee to add an explicit documentation step early in the AEGL development process that the studies proposed for consideration have been consistent with the Program's Standing Operating Procedures (SOPs).

III. List of Chemicals

On behalf of the NAC/AEGL Committee, EPA is providing an opportunity for public comment on the AEGLs for the 10 chemicals identified in Table 1 of this unit.

A. Proposed AEGL Chemical Table

TABLE 1.—10 CHEMICALS FOR PROPOSED AEGLS

CAS No.	Chemical name
75–86–5	Acetone cyanohydrin
7664–41–7	Ammonia
7726–95–6	Bromine
79–11–8	Chloroacetic acid
7782–41–4	Fluorine
70892–10–3	Jet Fuel 8
78–93–3	Methyl ethyl ketone
10025–87–3	Phosphorus oxychloride
7719–12–2	Phosphorus trichloride

TABLE 1.—10 CHEMICALS FOR PROPOSED AEGLS—Continued

CAS No.	Chemical name
1330–20–7	Xylenes

B. Executive Summaries

The following are executive summaries from the chemical specific technical support documents (which may be obtained as described in Unit I.B. and III.) that support the NAC/AEGL Committee's development of AEGL values for each chemical substance. This information provides the following information: A general description of each chemical, including its properties and principle uses; a summary of the rationale supporting the AEGL-1, 2, and 3 concentration levels; a summary table of the AEGL values; and a listing of key references that were used to develop the AEGL values. More extensive toxicological information and additional references for each chemical may be found in the complete technical support documents. Risk managers may be interested to review the complete technical support document for a chemical when deciding issues related to use of the AEGL values within various programs.

1. *Acetone cyanohydrin*—i. *Description.* Acetone cyanohydrin is a colorless to yellowish liquid with a characteristic bitter almond odor due to the presence of free HCN. The major use of acetone cyanohydrin is in the production of α-methacrylic acid and its esters; the latter are used for the production of plexiglass. Further uses of acetone cyanohydrin are in the production of acrylic esters, polyacrylic plastics, and synthetic resins as well as in the manufacture of insecticides, pharmaceuticals, fragances, and perfumes. Acetone cyanohydrin decomposes spontaneously to acetone and hydrogen cyanide; this process is catalyzed by heat and contact with water (especially under alkaline conditions).

Fatal cases and life-threatening poisonings in workers have been described after accidental inhalation, skin contact, and oral uptake. Initial symptoms following mild exposure to acetone cyanohydrin are predominantly cardiac palpitation, headache, weakness, dizziness, nausea, vomiting, and nose, eye, throat, and skin irritation. The systemic toxicity of acetone cyanohydrin is caused by free cyanide ions and is primarily due to complex formation with the iron moiety in the tissue enzyme ferri cytochrome c oxidase or cytochrome a_3. The blockage of the electron transport system of mitochondria results in inhibition of oxygen utilization and causes tissue hypoxia and cellular and tissue destruction.

Four studies exposed rats repeatedly to acetone cyanohydrin concentrations of about 10, 30, and 60 ppm for 6 hours/day, 5 days/week for a total of 4 weeks (Monsanto Co., 1986a; using groups of 10 male and 10 female rats), 10 weeks (Monsanto Co., 1982b; using groups of 15 male rats) and 14 weeks (Monsanto Co., 1986b; using groups of 15 male and 15 female rats) or for 6 hours/day for 21 days (Monsanto Co., 1982c; using groups of 15 female rats). Death was observed at 60 ppm after the first exposure in 3 animals of the Monsanto Co. (1986a) study, but not in subsequent exposures or in the other studies at a similar exposure concentration. Preceding death, respiratory distress, prostration, convulsions, and tremors were observed. In all studies, exposure to 60 and 30 ppm caused signs of irritation (red nasal discharge, clear nasal discharge, perioral wetness, encrustations) during the first and subsequent weeks of exposure. At 10 ppm, red nasal discharge was not observed in one study (Monsanto Co., 1986a); its incidence was not increased compared to control group in two studies (Monsanto Co., 1982b; 1982c) and increased compared to the control group in the fourth study (Monsanto Co., 1986b). No other effects were reported in these four studies.

The AEGL-1 was based on a repeated exposure study in rats in which a concentration of 9.2 ppm for 6 hours/day, 5 days/week for 4 weeks did not result in red nasal discharge (Monsanto Co., 1986a). An uncertainty factor of 3 was applied for interspecies variability because the lowest-observed-effect-level (LOEL) for irritation in humans exposed to cyanide at the workplace is about 6–10 ppm cyanide (El Ghawabi et al., 1975), which is a factor of about 3 below the irritation threshold of acetone cyanohydrin in rats (about 30 ppm) and because a multiple exposure study was used for the derivation of AEGL values. An uncertainty factor of 3 was applied for intraspecies variability because decomposition of acetone cyanohydrin does not involve enzyme-catalyzed steps and the binding to evolutionary conservative iron-containing proteins/enzymes, i.e., the target protein cytochrome c oxidase, is unlikely to differ substantially between individuals. A modifying factor of 2 was applied due to the lack of more adequate and supporting data for the derivation of AEGL-1 values. The exposure duration-specific values were derived by time scaling according to the dose-response regression equation $C^n \times t = k$, using the default of n = 3 for shorter exposure periods and n = 1 for longer exposure periods, due to the lack of suitable experimental data for deriving the concentration exponent. For the 10-minute AEGL-1 the 30-minute value was applied because the derivation of AEGL values was based on a long experimental exposure period and no supporting studies using short-exposure periods were available for characterizing the concentration-time-response relationship.

The AEGL-2 was based on a repeated exposure study in rats in which a concentration of 29.9 ppm for 6 hours/day, 5 days/week for 4 weeks did not result in respiratory distress (red nasal discharge as a sign of irritation was observed during the first and subsequent weeks of exposure) (Monsanto Co., 1986a). An uncertainty factor of 3 was applied for interspecies variability because repeated exposure of humans at the workplace to cyanide concentrations only about 3-fold lower than the lethality threshold of about 60 ppm acetone cyanohydrin in rats did not lead to life-threatening or irreversible health effects and because a multiple exposure study was used for the derivation of AEGL values. An uncertainty factor of 3 was applied for intraspecies variability because decomposition of acetone cyanohydrin does not involve enzyme-catalyzed steps and the binding to evolutionary conservative iron-containing proteins/enzymes, i.e., the target protein cytochrome c oxidase, is unlikely to differ substantially between individuals. The exposure duration-specific values were derived by time scaling according to the dose-response regression equation $C^n \times t = k$, using the default of n = 3 for shorter exposure periods and n = 1 for longer exposure periods, due to the lack of suitable experimental data for deriving the concentration exponent. For the 10-minute AEGL-2 the 30-minute value was applied because the derivation of AEGL values was based on a long experimental exposure period and no supporting studies using short-exposure periods were available for characterizing the concentration-time-response relationship.

For the derivation of AEGL-3 values, it was taken into account that:

a. Acetone cyanohydrin decomposes spontaneously into hydrogen cyanide and acetone,

b. The decomposition of acetone cyanohydrin is accelerated by heat and water,

c. The systemic toxic effects of acetone cyanohydrin are caused by free cyanide ions, and

d. Hydrogen cyanide has a far higher vapor pressure than acetone cyanohydrin.

From these facts it was concluded that with every exposure to acetone cyanohydrin a concomitant exposure to hydrogen cyanide will occur. It therefore seemed reasonable to apply the AEGL-3 values (on a ppm basis) derived for hydrogen cyanide to acetone cyanohydrin. This procedure is supported by a close similarity of acetone cyanohydrin and hydrogen cyanide regarding lethal effects in rats exposed for 6 hours.

The proposed AEGL values are listed in Table 2 of this unit.

TABLE 2.—SUMMARY TABLE OF PROPOSED AEGL VALUES FOR ACETONE CYANOHYDRIN[A]

Classification	10-minutes	30-minutes	1-hour	4-hours	8-hours	Endpoint (Reference)
AEGL-1 (Nondisabling)	1.1 ppm (3.9 mg/m^3)	1.1 ppm (3.9 mg/m^3)	0.84 ppm (2.9 mg/m^3)	0.53 ppm (1.9 mg/m^3)	0.35 ppm (1.2 mg/m^3)	No red nasal discharge in rats (Monsanto Co., 1986a)
AEGL-2 (Disabling)	6.8 ppm (24 mg/m^3)	6.8 ppm (24 mg/m^3)	5.4 ppm (19 mg/m^3)	3.4 ppm (12 mg/m^3)	2.2 ppm (7.7 mg/m^3)	No respiratory distress in rats (Monsanto Co., 1986a)
AEGL-3 (Lethal)	27 ppm (95 mg/m^3)	21 ppm (74 mg/m^3)	15 ppm (53 mg/m^3)	8.6 ppm (30 mg/m^3)	6.6 ppm (23 mg/m^3)	Application of AEGL-3 values for hydrogen cyanide

[a] Cutaneous absorption may occur; direct skin contact with the liquid should be avoided; fatal intoxications have been reported upon skin contact.

ii. *References.* a. El Ghawabi A.; M. Gaafar; A. El Saharta; S.H. Ahmed; K.K. Malash; and R. Fares. 1975. Chronic cyanide exposure: a clinical radioisotope and laboratory study. *British Journal of Industrial Medicine*. 32:215–219.

b. Monsanto Co. 1982b. Male fertility study of Sprague-Dawley rats exposed by inhalation route to acetone cyanohydrin. Monsanto Co. Report No. ML-82-144. Monsanto Co., St. Louis, MO, USA.

c. Monsanto Co. 1982c. Female fertility study of Sprague-Dawley rats exposed by inhalation route to acetone cyanohydrin. Monsanto Co. Report No. ML-82-125. Monsanto Co., St. Louis, MO, USA.

d. Monsanto Co. 1986a. One-month inhalation toxicity of acetone cyanohydrin in male and female Sprague-Dawley rats with cover letter dated 04-25-86. Report No. BN-81-178. Monsanto Co., St. Louis, MO, USA.

e. Monsanto Co. 1986b. Three-month inhalation toxicity of acetone cyanohydrin in male and female Sprague-Dawley rats with cover letter dated 04-25-86. Report No. ML-82-143. Monsanto Co., St. Louis, MO, USA.

2. *Ammonia*—i. *Description.* Ammonia is a colorless, corrosive, alkaline gas that has a very pungent odor. The odor detection level ranges from 5–53 ppm. Ammonia is used as a compressed gas and in aqueous solutions. It also is used as a household cleaning product, in fertilizers, and as a refrigerant. Exposures to ammonia occur as a result of accidents during highway and railway transportation, by releases at manufacturing facilities, and from farming accidents.

Ammonia is very soluble in water. Because of its exothermic properties, ammonia forms ammonium hydroxide and produces heat when it contacts moist surfaces, such as mucous membranes. The corrosive and exothermic properties of ammonia can result in immediate damage (severe irritation and burns) to eyes, skin, and mucous membranes of the oral cavity and respiratory tract. In addition, ammonia is effectively scrubbed in the nasopharyngeal region of the respiratory tract because of its high solubility in water.

The data for deriving AEGL values were obtained primarily from case studies of accident victims, experimental studies in humans, and experimental studies on lethality and irritation in animals. The case studies were of limited use for quantitative evaluation, but the experimental studies in humans and animals contained quantitative data that would be used for deriving AEGL values.

No reliable quantitative lethality data were available for humans dying as a result of exposure to ammonia. One case study reported the death of an individual exposed to a high but unknown concentrations of ammonia. Other case studies also contained no exposure estimates, but showed that high concentrations of ammonia cause severe damage to the respiratory tract, particularly in the tracheobronchial and pulmonary regions. Death, however, is most likely to occur when damage causes pulmonary edema. Non-lethal, irreversible, or long-term effects occur when damage progresses to the tracheobronchial region, manifested by reduced performance on pulmonary function tests, bronchitis, bronchiolitis, emphysema, and bronchiectasis. Nondisabling, reversible effects are manifested by irritation to the eyes, throat, and nasopharyngeal region of the respiratory tract. The odor of ammonia is detected by humans at concentrations >5 ppm; the odor is highly penetrating at 50 ppm (10 minutes). Experimental studies on human volunteers, showed that slight irritation may occur at 30 ppm (10 minutes), moderate irritation to the eyes, nose, throat, and chest occurs at 50 ppm (10 minutes to 2 hours), moderate to highly intense irritation occurs at 80 ppm (30 minutes to 2 hours), highly intense irritation occurs at 110 ppm (30 minutes to 2 hours), unbearable irritation occurs at 140 ppm (30 minutes to 2 hours), and excessive lacrimation and irritation at 500 ppm. In addition, some subjects were able to breathe 140 ppm for up to 2 hours or 500 ppm for 30 minutes without suffering long-lasting effects. Reflex glottis closure, a response to irritant vapors, occurred at 570 ppm for 21- to 30-year-old subjects, 1,000 ppm for 60-year-old subjects, and 1,790 ppm for 86- to 90-year-old subjects.

Acute lethality studies in animals showed that the LC_{50} values for rats ranged from 40,300 ppm for a 10-minute exposure to 7,338 and 16,600 ppm for 60-minute exposures. For the mouse, LC_{50} values were 21,430 ppm for a 30-minute exposure (almost all animals died in less than 13 minutes), 10,096 ppm for a 10-minute exposure, and 4,230 and 4,837 ppm for 60-minute

exposures. Comparative data for the same exposure duration show that mice are more sensitive than rats to the acute toxic effects of ammonia (10 minute LC_{50} values for mice and rats, are 10,096 ppm and 40,300 ppm, respectively). The lowest lethal concentrations reported was 1,000 ppm for the cat. However, cats were exposed via an endotracheal tube, which probably exacerbated the effects in the tracheobronchial region by bypassing the scrubbing action of the nasopharyngeal region. Rats exposed by inhalation to lethal concentrations of ammonia, showed signs of dyspnea, irritation to the eyes and nose, and hemorrhage in the lungs. Mice exposed to lethal concentrations of ammonia showed signs of irritation to the eyes and nose, along with tremors, ataxia, convulsions, seizures, and pathologic lesions in the alveoli. Cats exposed to the lowest lethal concentration showed evidence of severe airway damage, bronchopneumonia, bronchitis, bronchiolitis, and emphysema. Toxic effects at non-lethal concentrations in mice and rats consisted of mild effects on respiratory epithelium of the nasal cavity (mice and rats), reduction in the respiratory rate (mice), and evidence of eye irritation (rat). The RD_{50} (concentration causing a 50% reduction in respiratory rate) for the mouse was 300 ppm for a 30-minute exposure.

The AEGL values for the three toxicity levels (nondisabling, disabling, and lethal) were derived from both human and animal data. The odor of ammonia is detected by humans at concentrations ranging from 5 to 53 ppm and data showed that it is irritating to the upper respiratory tract of humans at 30 ppm. The AEGL-1 value of 25 ppm is based the concentration slightly below the lowest concentration showing irritation in humans. An intraspecies uncertainty factor of 1 was applied, because 25 ppm is below the concentration causing irritation; however, if irritation did occur, it would be mild or only slightly noticeable, confined to the nasal cavity and eyes (ammonia is efficiently scrubbed), and would not be expected to affect asthmatic or other sensitive individuals to a greater degree than nonasthmatic individuals. Atopic and nonatopic subjects did not respond differently to a nasal exposure to ammonia. The AEGL-1 values are based on human data; therefore, an interspecies uncertainty factor is not applicable. Because upper respiratory tract irritation at low ammonia concentrations is not expected to change or become more severe with duration of exposure, except for adaptation, the same value of 25 ppm is applied to all AEGL-1 exposure durations.

The AEGL-2 values were based on a study of nonexpert human subjects who had no previous exposure to ammonia and were not familiar with effects of ammonia. At least one of eight subjects reported nuisance or offensive irritation to the eyes and throat during exposure to 110 ppm of ammonia for 1 hour (Verberk, 1977). The effects reported were less serious than those described in the AEGL-2 definition, no residual effects were reported after termination of exposure, and pulmonary function was not affected by exposure. At the next highest concentration, some of the subjects reported the effects to be unbearable and left the chamber between 30 minutes and 1 hour. Their responses suggest that this concentration would impair escape. An intraspecies uncertainty factor of 1 was used for deriving the AEGL 2 values because the responses of the non-expert group ranged from just perceptible to offensive, but the AEGL-2 value was based on the response of the most sensitive individuals. The reported effects from this group involved primarily the upper respiratory tract and eyes and is unlikely to affect asthmatics differently from the most sensitive non-expert individuals. In addition, atopic subjects responded similarly to non-atopic subjects to a brief nasal exposure to ammonia, and exercising subjects showed only a small equivocal decrease in pulmonary function. The equation $C^n H t = k$, where n = 2, was used to extrapolate to 5-, 10-, and 30-minute exposure durations. This equation was based on mouse and rat lethality data. The same AEGL-2 values were established for 1-, 4-, and 8-hour exposures, because the responses of the subjects exposed to 110 ppm of ammonia were similar after 1- and 2-hour exposures.

The AEGL-3 values were based on LC_{01} values of 3,317 and 3,374 ppm derived by probit analysis of mouse lethality data reported by Kapeghian et al. (1982) and MacEwen and Vernot (1972), respectively. An uncertainty factor of 3 was applied to account for intraspecies variability because at high concentrations of ammonia, severe irritation is elicited immediately upon contact with the eyes and mucous membranes of the respiratory tract and the severity of effects such as pulmonary edema and damage to the tracheobronchial region would be similar in asthmatics and non-asthmatics. There is no reason to apply a larger uncertainty factor to protect individuals with asthma because the severe damage to the respiratory tract would have a greater and longer-lasting consequence than that of asthma. Another reason for not applying a larger intraspecies uncertainty factor to protect children is the evidence from one study showing that a child recovered from an accidental exposure to ammonia, whereas the mother carrying the child suffered severe permanent damage to the lungs. An interspecies uncertainty factor or 1 was applied to the mouse data, because the mouse was the most sensitive species among mammals. In addition, applying a larger uncertainty factor would result in a 30-minute AEGL-3 value less than the 500 ppm that human can tolerate for 30 minutes without lethal or long-term consequences. The equation, $C^n H t = k$ (where n = 2) based on mouse lethality data, was used to extrapolate to different exposure durations

The proposed AEGL values are listed in Table 3 of this unit.

TABLE 3.—SUMMARY OF PROPOSED AEGL VALUES FOR AMMONIA [PPM (MG/M^3)]

Classification	Exposure duration						Endpoint (Reference)
	5-minutes	10-minutes	30-minutes	1-hour	4-hours	8-hours	
AEGL-1 (Nondisabling)	25 (17)	25 (17)	25 (17)	25 (17)	25 (17)	25 (17)	No-observed-adverse-effect-level (NOAEL) for irritation (MacEwen et al., 1970); Verberk, 1977
AEGL-2 (Disabling)	380 (266)	270 (189)	160 (112)	110 (77)	110 (77)	110 (77)	Irritation: Eyes and throat; urge to cough (Verberk, 1977)

TABLE 3.—SUMMARY OF PROPOSED AEGL VALUES FOR AMMONIA [PPM (MG/M^3)]—Continued

Classification	Exposure duration						Endpoint (Reference)
	5-minutes	10-minutes	30-minutes	1-hour	4-hours	8-hours	
AEGL-3 (Lethal)	3,800 (2,657)	2,700 (1,890)	1,600 (1,119)	1,100 (769)	550 (385)	390 (273)	Lethality (Kapeghian et al., 1982; MacEwen and Vernot, 1972)

ii. *References*. a. Kapeghian, J.C.; Mincer, H.H.; and Hones, A.B., et al. 1982. Acute inhalation toxicity of ammonia in mice. *Bulletin of Environmental Contamination and Toxicology*. 29:371–378.

b. MacEwen, J.D.; Theodore, J; and Vernot, E.H. 1970. Human exposure to EEL concentrations of monomethylhydrazine, AMRL-TR-70-102, Paper No 23. *Proceedings of the 1st Annual Conference on Environmental Toxicology*. September 9–11, 1970. Wright-Patterson AFB, OH. pp. 355–363.

c. MacEwen, J.D. and Vernot, E.H. 1972. Toxic Hazards Research Unit Annual Technical Report: 1972. SysteMed Report No. W-72003, AMRL-TR-72-62. Sponsor: Aerospace Medical Research Laboratory, Wright-Patterson AFB, OH. AD-755-358.

d. Verberk, M.M. 1977. Effects of ammonia on volunteers. *International Archives of Occupational and Environmental Health*. 39:73–81.

3. *Bromine*—i. *Description*. The halogen bromine (Br_2) is a dark reddish-brown volatile liquid at room temperature. Its oxidizing potential lies between that of chlorine and iodine. Bromine is used as a water disinfectant, for bleaching fibers and silk, and in the manufacture of medicinal bromine compounds, dyestuffs, flame retardants, agricultural chemicals, inorganic bromide drilling fluids, and gasoline additives.

Bromine is a skin, eye, and respiratory tract irritant. Inhalation causes respiratory tract irritation and pulmonary edema. Although accidental human exposures have occurred, concentrations were either not reported or were judged unreliable. Aside from old and anecdotal information, the data base is limited to one study with human subjects and two lethality studies with the mouse as the test species. One of the lethality studies (Bitron and Aharonson 1978) provided data sufficient for derivation of the relationship between concentrations that result in lethality (LC_{50} values) and exposure duration: $C^{2.2} \times t = k$.

The AEGL-1 was based on exposures of 20 healthy human volunteers to concentrations of 0.1 to 1.0 ppm for at least 30 minutes (Rupp and Henschler 1967). Eye irritation, but not nose or throat irritation, occurred during a 30-minute exposure to 0.1 ppm. At concentrations $0.5 ppm, there was a stinging and burning sensation of the conjunctiva. The 30-minute 0.1 ppm was chosen as the basis for the AEGL-1. The 0.1 ppm concentration was divided by an intraspecies uncertainty factor of 3 to protect susceptible individuals. An intraspecies uncertainty factor of 3 was considered sufficient because workers have been occupationally exposed to 1 ppm with no symptoms other than ''excess irritation'' (Elkins 1959). Furthermore, effects at this low concentration appear to be limited to the eyes and upper respiratory tract; there was no penetration to the lower respiratory tract. The resulting 30-minute AEGL-1 value of 0.03 ppm was time-scaled to the other AEGL exposure durations using the $C^{2.2} \times t = k$ relationship derived from the mouse lethality study.

The AEGL-2 was based on the concentration of 1 ppm for 30 minutes which the volunteers in the above study (Rupp and Henschler 1967) found irritating (stinging and burning sensation of the conjunctiva; nose and throat irritation). The 30-minute 1 ppm value was divided by an intraspecies uncertainty factor of 3 to protect susceptible individuals and time scaled to the other AEGL-2 exposure durations using the concentration-exposure duration relationship from the mouse lethality study of $C^{2.2} \times t = k$. An intraspecies uncertainty factor of 3 was considered sufficient as the symptoms may be below those defining an AEGL-2. However, no reliable studies with exposures to higher concentrations were located.

Both lethality studies with the mouse described the inhalation toxicity of chlorine and bromine. However, both studies reported lower LC_{50} values for chlorine than those reported in more recent well-conducted studies. Nevertheless, the study that reported the lower lethal concentrations for chlorine was used for derivation of the AEGL-3 values for bromine (Schlagbauer and Henschler 1967). The data in this study showed a clear concentration-response relationship; the exposure duration was 30 minutes. Using probit analysis, a 30-minute LC_{50} value of 204 ppm and a 30-minute LC_{01} of 116 ppm were calculated. The 30-minute LC_{01} of 116 ppm was used as the basis for calculation of AEGL-3 values. The 116 ppm LC_{01} was divided by a combined uncertainty factor of 10 (3 for interspecies differences [the mouse was the most sensitive species for lethal effects in tests with other halogens] and 3 for intraspecies differences [at high concentrations bromine is corrosive to the mucous membranes of the respiratory system; effects are not expected to differ greatly among individuals]) and scaled across time using the relationship $C^{2.2} \times t = k$, derived from the same study.

The proposed AEGL values are listed in Table 4 of this unit.

TABLE 4.—SUMMARY OF PROPOSED AEGL VALUES FOR BROMINE [PPM (MG/M^3)]

Classification	10-minutes	30-minutes	1-hour	4-hours	8-hours	Endpoint (Reference)
AEGL-1 (Nondisabling)	0.055 (0.36)	0.033 (0.22)	0.024 (0.16)	0.013 (0.09)	0.0095 (0.06)	Rupp and Henschler 1967
AEGL-2 (Disabling)	0.55 (3.6)	0.33 (2.1)	0.24 (1.6)	0.13 (0.85)	0.095 (0.62)	Rupp and Henschler 1967

TABLE 4.—SUMMARY OF PROPOSED AEGL VALUES FOR BROMINE [PPM (MG/M^3)]—Continued

Classification	10-minutes	30-minutes	1-hour	4-hours	8-hours	Endpoint (Reference)
AEGL-3 (Lethal)	19 (124)	12 (78)	8.5 (55)	4.5 (29)	3.2 (21)	Schlagbauer and Henschler 1967

ii. *References*. a. Bitron, M.D. and E.F. Aharonson. 1978. Delayed mortality of mice following inhalation of acute doses of CH_2, SO_2, Cl_2, and Br_2. *American Industrial Hygiene Association Journal*. 39:129–138.

b. Elkins, H.B. 1959. Inorganic compounds: Bromine. *Chemistry of Industrial Toxicology*. John Wiley & Sons, New York. p. 89.

c. Rupp, H. and D. Henschler. 1967. Effects of low chlorine and bromine concentrations in man. *Internationales Archiv fuer Gewerbepathologie und Gewerbehygiene*. 23:79–90.

d. Schlagbauer, M. and D. Henschler. 1967. Inhalation toxicity of chlorine and bromine with single and repeated exposures. *Internationales Archiv fuer Gewerbepathologie und Gewerbehygiene*. 23:91–98.

4. *Chloroacetic acid*—i. *Description*. Monochloroacetic acid (MCAA) is a colorless crystalline material, which is highly soluble in water and soluble in organic solvents. Its vapor pressure at room temperature is moderate with reported values between 0.2 hPa (crystalline substance) and 10 hPa (solution in water). MCAA has a pungent odor.

MCAA is produced by chlorination of acetic acid or hydrolysis of trichloroethene using sulfuric acid. The world production capacity was estimated at 362,500 tons/year in 1987. MCAA or its sodium salt, sodium monochloroacetate, are used primarily in the industrial production of carboxymethylcellulose, herbicides, thioglycolic acid as well as in the production plastics, pharmaceuticals, flavors, cosmetics, and other organic chemicals.

MCAA is an acid (pK_a 2.85) and therefore can cause eye and skin irritation upon contact with a diluted MCAA solution and skin corrosion and conjunctival burns upon contact with more concentrated solutions. The systemic toxicity of MCAA is caused by inhibition of enzymes of the glycolytic pathway and the tricarboxylic acid cycle. This metabolic blockage damages organs with a high energy-demand, such as heart, central nervous system (CNS), and muscles, and leads to metabolic acidosis due to the accumulation of lactic acid and citric acid in the body.

No studies are available reporting severe toxic effects in humans after inhalation exposure to MCAA. Mortality was reported in a child after oral uptake of 5–6 ml of an 80% MCAA solution (Rogers, 1995). Several lethal accidents have been reported, in which workers were dermally exposed to hot, liquid MCAA. An inadequately described study reported an irritation threshold of 1.48 ppm (Maksimov and Dubinina, 1974); no respiratory tract irritation, effects on lung function parameters or irritation of skin and mucous membranes were reported for >33 workers potentially exposed to MCAA concentrations between <0.13 ppm for 3 hours and 0.31 ppm for 7 hours (Clariant GmbH, 2000).

The only animal study reporting lethal effects after inhalation exposure was an inadequately described study in which a LC_{50} of 46.8 ppm for 4 hours was reported for rats (Maksimov and Dubinina, 1974). Several studies report lethal effects after oral exposure with LD_{50} values mostly between 50–200 mg/kilogram (kg) for rats, mice and guinea pigs. In a single inhalation experiment on rats, eye squint and slight lethargy were observed during exposure to an analytical concentration of 66 ppm for 1 hour (Dow Chemical Co., 1987). In an inadequately reported study, an irritation threshold in rats of 6.16 ppm and a no-observed-effect-level (NOEL) for histological changes in the respiratory tract in rats and guinea pigs of 1.5 ppm after 4 months have been reported (Maksimov and Dubinina, 1974).

No relevant studies of adequate quality were available for the derivation of the AEGL-1. Therefore, due to insufficient data, AEGL-1 values were not derived.

The AEGL-2 was based on a single inhalation study in rats (Dow Chemical Co., 1987) in which eye squint and lethargy were observed in rats exposure to 66 ppm for 1 hour. A total uncertainty factor of 10 was used. A factor of 3 was applied for interspecies variability because the effect level was considered below that of an AEGL-2 and because the available data do not point at a large interspecies variability for more severe (lethal) effects. A factor of 3 was applied for intraspecies variability because a higher factor was not considered adequate on the basis of a comparison with human data for oral exposure. The other exposure duration-specific values were derived by time scaling according to the dose-response regression equation $C^n \times t = k$, using the default of n = 3 for shorter exposure periods and n=1 for longer exposure periods, due to the lack of suitable experimental data for deriving the concentration exponent.

No relevant studies of adequate quality were available for the derivation of the AEGL-3 value. Therefore, due to insufficient data and the uncertainties of a route-to-route extrapolation, AEGL-3 values were not derived.

The proposed AEGL values are listed in Table 5 of this unit.

TABLE 5.—SUMMARY OF PROPOSED AEGL VALUES FOR MONOCHLOROACETIC ACID [A]

Classification	10-minutes	30-minutes	1-hour	4-hours	8-hours	Endpoint (Reference)
AEGL-1 (Nondisabling)	Insufficient data (I.D.)	I.D.	I.D.	I.D.	I.D.	I.D.
AEGL-2 (Disabling)	12 ppm (47 mg/m^3)	8.3 ppm (33 mg/m^3)	6.6 ppm (26 mg/m^3)	1.7 ppm (6.7 mg/m^3)	0.83 ppm (3.3 mg/m^3)	Eye squint and lethargy in rats (Dow Chemical Co., 1987)
AEGL-3 (Lethal)	I.D.	I.D.	I.D.	I.D.	I.D.	I.D.

[a] Skin contact with molten MCAA or MCAA solutions should be avoided; dermal penetration is rapid and fatal intoxications have been observed when 10% or more of the body surface was involved.

ii. *References.* a. Clariant GmbH, 2000. Unpublished. Letter of Dr. Kreiling dated 23.08.2000. Dow Chemical Co., 1987. Monochloroacetic acid: an acute vapor inhalation limit study with Fischer 344 rats. Unpublished Report, Dow Chemical Company, Midland, USA.

b. Maksimov, G.G. and O.N. Dubinina, 1974. Materials of experimental substantiation of maximally permissible concentration of monochloroacetic acid in the air of production area. *Gigiena Truda i Professional nye Zabolevarija.* 9:32–35.

c. Rogers D.R. 1995. Accidental fatal monochloroacetic acid poisoning. *American Journal of Forensic Medicine and Pathology.* 16:115–116.

5. *Fluorine*—i. *Description.* Fluorine is a reactive, highly irritating and corrosive gas used in the nuclear energy industry, as an oxidizer of liquid rocket fuels, and in the manufacture of various fluorides and fluorocarbons. Fluorine is a severe irritant to the eyes, mucous membranes, lungs, and skin; the eyes and the respiratory tract are the target organ/tissues of an acute inhalation exposure. Death is due to pulmonary edema. Data on irritant effects in humans and lethal and sublethal effects in five species of mammals (dog, rat, mouse, guinea pig, and rabbit) were available for development of AEGL values.

Regression analyses of the concentration-exposure durations (for the fixed endpoint of mortality) for all of the animal species reported in the key study (Keplinger and Suissa 1968) determined that the relationship between concentration and time is $C^n \times t = k$, where n = approximately 2 (actual value of n for the most sensitive species in irritation and lethality studies, the mouse, is 1.77). This concentration exposure duration relationship was applied both the AEGL-2 and AEGL-3 levels because the irritant and corrosive action of fluorine on the respiratory tissues differs by only a matter of degree for these AEGL levels:

a. Respiratory irritation with edema resulting in mild, reversible lung congestion, and

b. Severe respiratory irritation resulting in severe lung congestion. Although the data base for fluorine is small, the data from the key study, augmented with data from several other studies, were considered adequate for derivation of the three AEGL classifications for four time periods.

The AEGL-1 was based on the observation that human volunteers could tolerate exposure to 10 ppm for 15 minutes without irritant effects (Keplinger and Suissa 1968). Although this value is below the definition of an AEGL-1 (notable discomfort), it provides the longest exposure duration for which no irritation in humans was reported. An intraspecies uncertainty factor of 3 was applied because fluorine is highly corrosive to the tissues of the respiratory tract and effects are not expected to vary greatly among individuals, including susceptible individuals. Although no data on asthmatics were found, the uncertainty factor of 3 was considered adequate to protect this sensitive subpopulation because the value was a NOAEL and because shorter-term, repeated exposures produced no substantially greater effects in healthy individuals. The value is supported by a second study in which volunteers ''tolerated'' exposure to 10 ppm for an undefined period of time. Furthermore, occupational exposure concentrations for healthy adults have ranged up to 17 ppm, albeit for short, undefined periods of time (Lyon 1962). A modifying factor of 2 was applied based on a limited data base. The resulting value of 1.7 ppm was used across all AEGL-1 exposure durations because at mildly irritating concentrations there is accommodation to irritating gases. As noted, this value is supported by limited workplace monitoring data: Workers exposed to fluorine at average yearly concentrations up to 1.2 ppm (range, 0.0–17 ppm) over a 4-year period reported fewer incidences of respiratory complaints or diseases than a similar group of nonexposed workers (Lyon 1962). The workers are assumed to encompass a small range of sensitivity; the additional intraspecies uncertainty factor of 3 was considered sufficient to protect sensitive individuals.

Mild lung congestion was selected as the threshold for irreversible, long-lasting effects as defined by the AEGL-2. The AEGL-2 was based on an animal study in which mild lung congestion was observed in mice at 67 ppm for 30 minutes and 30 ppm for 60 minutes (Keplinger and Suissa 1968). Effects were slightly less serious in three other species. Although concentrations causing irritant effects or lethality for three other species for the same time periods suggested similar species sensitivity, the mouse data, because of slightly lower values, were chosen as the basis for developing the AEGL-2 and AEGL-3. Because similar sensitivity was observed among five species in the key study, no uncertainty factor for interspecies variability was applied. Fluorine is a highly corrosive gas that reacts directly with the tissues of the respiratory tract, with no pharmacokinetic component involved in the toxicity; therefore, there is likely to be little difference among individuals in response to fluorine at concentrations that define the AEGL-2. The 30- and 60-minute values for the mouse were divided by an intraspecies uncertainty factor of 3 to protect sensitive individuals, since effects are not likely to differ greatly among individuals, and by a modifying factor of 2, based on a limited data base. The 30-minute value was used for the 10- and 30-minute AEGL-2 and the 60-minute value was used for the 60-minute AEGL-2. The 4-hour AEGL-2 value was scaled from the 60-minute value based on the $C^{1.77} \times t = k$ relationship. The value of n was derived from regression analysis of the mouse lethality data in the key study. The 8-hour-AEGL-2 value was set equal to the 4-hour value because at low concentrations the hygroscopic fluorine would react with and/or be scrubbed by the nasal passages and because at low concentrations there is accommodation to irritant gases. The 10- and 3-minute AEGL-2 values are supported by studies in which human volunteers found short-term exposures to 15–25 ppm irritating to the eyes, nose, and throat (Rickey 1959; Keplinger and Suissa 1968).

The AEGL-3 values were derived from the highest exposures that resulted in no deaths in five species over four exposure durations (13 tests) for up to 45 days post exposure, but did produce severe lung congestion in the mouse (Keplinger and Suissa 1968). Severe lung congestion in the sensitive mouse was considered the threshold for lethality as defined by the AEGL-3. For the mouse, the 60-minute value was 75 ppm. Because of the similar species sensitivity in the key study, based on both irritant effects and lethality, no uncertainty factor for interspecies variability was applied. The values were divided by an uncertainty factor of 3 to protect sensitive individuals (fluorine is a highly reactive, corrosive gas whose effect on respiratory tract tissues is not expected to differ greatly among individuals) and by a modifying factor of 2, based on a limited data base. Using the 60-minute value of 75 ppm, AEGL-3 values for the other exposure times were calculated based on the $C^{1.77} \times t = k$ relationship. The value of n was derived from regression analysis of the mouse lethality data in the key study. The 8-hour value was set equal to the 4-hour value because fluorine would react with or be scrubbed by the nasal passages at fairly low concentrations. The safety of setting the 8-hour value equal to the 4-hour value is supported by another study in which a 7-hour experimental exposure concentrations

resulting in an overall 60% mortality for four species (Eriksen 1945; Stokinger 1949) is higher than the extrapolated 7-hour values for the mouse and rat based on the Keplinger and Suissa study.

The proposed AEGL values are listed in Table 6 of this unit.

TABLE 6.—SUMMARY OF PROPOSED AEGL VALUES FOR FLUORINE [PPM (MG/M^3)]

Classification	10-minutes	30-minutes	1-hour	4-hours	8-hours	Endpoint (Reference)
AEGL-1[a, b] (Nondisabling)	1.7 (2.6)	1.7 (2.6)	1.7 (2.6)	1.7 (2.6)	1.7 (2.6)	No irritant effects—humans (Keplinger and Suissa 1968)
AEGL-2 (Disabling)	20 (31)	11 (17)	5.0 (7.8)	2.3 (3.6)	2.3 (3.6)	Mild lung congestion—mice (Keplinger and Suissa 1968)
AEGL-3[c] (Lethal)	36 (56)	19 (29)	13 (20)	5.7 (8.8)	5.7 (8.8)	Severe lung congestion—mice (Keplinger and Suissa 1968)

[a]The characteristic, pungent odor of fluorine will be noticeable at this concentration.
[b]The same value was used across all time periods because at low concentrations there is accommodation to irritant gases.
[c]30-Minute and 1-hour values are based on separate data points.

ii. *References.* a. Eriksen, N. 1945. A Study of the Lethal Effect of the Inhalation of Gaseous Fluorine (F_2) at Concentrations from 100 ppm to 10,000 ppm. DOE/EV/03490-T3, United States Atomic Energy Commission. Pharmacology Report 435. University of Rochester, Rochester, NY.

b. Keplinger, M.L. and L.W. Suissa. 1968. Toxicity of fluorine short-term inhalation.*American Industrial Hygiene Association Journal.* 29:10–18.

c. Lyon, J.S. 1962. Observations on personnel working with fluorine at a gaseous diffusion plant. *Journal of Occupational Medicine.* 4:199–201.

d. Rickey, R.P. 1959. *Decontamination of Large Liquid Fluorine Spills.* AFFTC-TR-59-31, U.S. Air Force, Air Research and Development Command, Air Force Flight Test Center, Edwards Air Force Base, CA; AD-228–033, Defense Technical Information Center, Ft. Belvoir, VA.

e. Stokinger, H.E. 1949. Toxicity following inhalation of fluorine and hydrogen fluoride, Chapter 17. *Pharmacology and Toxicology of Uranium Compounds.* C. Voegtlin and H.C. Hodge, eds. McGraw-Hill Book Company, New York.

6. *Jet Fuel 8*—i. *Description.* Jet propellant (JP) fuels, used in military and civilian aircraft, are complex mixtures of aliphatic and aromatic hydrocarbons made by blending various distillate stocks of petroleum. The primary military fuel for land-based military aircraft is JP-8; JP-5 was developed by the U.S. Navy for shipboard service. The composition of these two fuels is basically that of kerosene (with additives) and they have similar chemical and physical characteristics. Worldwide, approximately 60 billion gallons of military JP-8 and the equivalent commercial Jet A and Jet A-1 are consumed on an annual basis. The military jet fuels contain additives that are not contained in commercial jet fuels. Civilian and military personnel may be exposed to jet fuels during fuel production, aircraft fueling operations, aircraft maintenance operations, and accidental spills or pipeline leaks.

Although several jet fuels are discussed in this document (JP-4, JP-5, JP-7, and JP-8), the discussion focuses on the toxicity of JP-8 with some attention to the chemically similar JP-5. These two fuels have a similar composition and appear to have similar toxicities. Monitoring data indicate that exposures to JP-4 which has a higher vapor pressure than JP-8 and JP-5 were higher than to the presently used JP-8 and JP-5. Data were located on acute sensory and systemic effects of JP-8 and JP-5 to mice and rats; subchronic studies addressed systemic effects, particularly effects on the lungs. For all fuels, tests of eye irritation were generally negative, whereas mild skin irritation occurred for some fuels. Several short-term and repeated exposure studies addressed the particular issue of the toxicity of aerosols. Exposure to aerosols of jet fuels induces more toxic effects than exposure to vapors, with the lungs and immune system identified as the target organs. Animal studies also addressed neurotoxicity, developmental/reproductive effects, and carcinogenicity. These fuels are generally not considered genotoxic or carcinogenic and, in a preliminary study, JP-8 failed to cause spermatotoxic effects in humans. A nephropathy and resulting carcinogenic effect, unique to male rats exposed to hydrocarbons, is not relevant to humans. No information relevant to time scaling was available.

The AEGL-1 is based on the sensory irritation study of Whitman et al. (2001), specifically the RD_{50} (the concentration that reduces the respiratory rate by 50%) for JP-8 of 2,876 mg/m^3 vapor plus aerosol. The RD_{50} test is a standard test for estimating sensory irritancy of airborne chemicals (ASTM E981–84). In the key study, male Swiss-Webster mice were exposed for 30 minutes to 681; 1,090; 1,837; or 3,565 mg/m^3. JP-8 is not a primary irritant and reductions in the respiratory rate did not occur within 10 minutes at the lower concentrations. However, reductions in the respiratory rate within the 30-minute exposure durations were concentration-dependent and allowed calculation of an RD_{50}. Based on the correlation between RD_{50} data and sensory irritancy levels for numerous chemicals, a 0.1-fold reduction of the RD_{50} results in a concentration that elicits some sensory irritation in humans but that can be tolerated for hours to days (Alarie 1981). Using this reasoning, the resulting concentration of 290 mg/m^3 can be tolerated over all AEGL-1 exposure durations. The 290 mg/m^3 value is supported by the lack of adverse health effects in animal studies with repeated exposures to 1,000 mg/m^3 of JP-8 vapor (continuous exposures up to 90 days) (Mattie et al. 1991; Briggs 2001; Rossi et al. 2001). Dividing the 1,000 mg/m^3 value by an interspecies uncertainty factor of 1 (no species differences were observed in multiple studies with rats and mice and the exposures were repeated) and an intraspecies uncertainty factor of 3 (to account for potential differences in human susceptibilities to sensory irritation) results in 330 mg/m^3, a value similar to that derived from the RD_{50} study. The repeated nature of the support studies also supports the use of a single value for all exposure durations.

The AEGL-2 is based on several studies with rodents (rats and mice) that indicate that exposure to 1,100 mg/m^3 of JP-8 would not elicit adverse health effects but may be the threshold for such effects. The shorter-term studies (30

minutes to 4 hours) with exposures to 3,430–5,000 mg/m^3 of JP-8 or JP-5 in the vapor/aerosol form (MacEwen and Vernot 1985; Wolfe et al. 1996; Whitman et al. 2001) with support from the studies using repeated exposures to 1,000 mg/m^3 (Mattie et al. 1991; Briggs 2001; Rossi et al. 2001) were used as the basis for the AEGL-2. No uncertainty factors were applied to the 1,000 mg/m^3 concentration because there were no adverse effects and the exposures were repeated for up to 90 days. The higher concentrations of JP-8, 3430 and 4,440 mg/m^3, and of JP-5, 5,000 mg/m^3, were divided by an interspecies factor of 1 (there were no species differences) and by an intraspecies uncertainty factor of 3 to protect potentially sensitive individuals. An intraspecies uncertainty factor of 3 is considered adequate because the thresholds for both sensory irritation and central nervous system depression to solvents do not generally differ by more than 3-fold. The resulting value is 1,100 mg/m^3 (1,100–1,700 mg/m^3), approximately the same concentration as in the no-adverse-effect repeated exposure studies. No information was available for time scaling. Central nervous system depression is a concentration-related effect. Therefore, the 1,100 mg/m^3 value was used for the 4-hour and shorter time period. But, because the exposures to 1,000 mg/m^3 were repeated for up to 90 days, the 1,100 mg/m^3 value can also be used for the longest AEGL exposure duration of 8 hours. The fact that the exposures in most of these studies, especially at the higher concentrations, were to both the vapor and the more toxic aerosol supports the appropriateness of the derived value.

It should be noted that, because of its relatively low vapor pressure, JP-8 might not attain a sustained vapor concentration high enough to cause death. In a laboratory study reported by Wolfe et al. (1996), the highest vapor concentration of JP-8 that could be attained was 3,430 mg/m^3. The highest vapor/aerosol concentration that could be attained was 4,440 mg/m^3. The highest vapor/aerosol attainable under ambient concentrations has been estimated at 700 mg/m^3. However, higher concentrations might be attained in closed spaces at high temperatures. A concentration of 500 mg/m^3 is assumed to be the upper bound for a stable cloud of inhalable dust (and aerosols). Based on the likelihood that lethal concentrations of JP-8 cannot be sustained under ambient conditions, an AEGL-3 was not determined.

The proposed AEGL values are listed in Table 7 of this unit.

TABLE 7.—SUMMARY OF PROPOSED AEGL VALUES FOR JP-8 (MG/M^3)[A, B]

Classification	10-minutes	30-minutes	1-hour	4-hours	8-hours	Endpoint (Reference)
AEGL-1 (Nondisabling)	290	290	290	290	290	Slight sensory irritation in humans (mouse RD_{50} test) (Whitman et al. 2001)
AEGL-2 (Disabling)	1,100	1,100	1,100	1,100	1,100	No clinical signs during repeated exposures to 1,000 mg/m^3— rats and mice (Mattie et al. 1991; Briggs 2001; Rossi et al. 2001); sensory irritation at >3,430 mg/m^3— rats and mice (Wolfe et al. 1996; Whitman et al. 2001)
AEGL-3 (Lethal)	Not determined	Not determined	Not determined	Not determined	Not determined	[c]No data

[a] The values apply to JP-8 vapor or vapor/aerosol and not to the pure aerosol.
[b] The values apply to JP-8 vapor and not to JP-8+100.
[c] A lethal concentration was not attained in the available toxicity studies; the low vapor pressure of JP-8 may preclude attainment of a lethal concentration.

ii. *References*. a. Alarie, Y. 1981. Dose-response analysis in animal studies: prediction of human responses. *Environmental Health Perspectives*. 42:9–13.

b. Briggs, G.B. 2001. Evaluation of military fuel potential to produce male reproductive toxicity. Presented at the International Conference on the Environmental Health and Safety of Jet Fuel held in San Antonio, TX, August 8–11, 2001.

c. MacEwen, J.D. and E.H. Vernot. 1985. Investigation of the 1-hour emergency exposure limit of JP-5. In Toxic Hazards Research Unit Annual Report, Report No. AAMRL-TR-85-058; Aerospace Medical Research Laboratory, Wright-Patterson Air Force Base, OH. pp. 137–144. Available from Defense Technical information Center, Doc. No. AD-A161558.

d. Mattie, D.R.; C.L. Alden; T.K. Newell; C.L. Gaworski; and C.D. Flemming. 1991. A 90-day continuous vapor inhalation toxicity study of JP-8 jet fuel followed by 20 or 21 months of recovery in Fischer 344 rats and C57BL/6 mice. *Toxicologic Pathology*. 19:77–87.

e. Rossi, J., III; A.F. Nordholm; R.L Carpenter; G.D. Ritchie; and W. Malcomb. 2001. Effects of repeated exposure of rats to JP-5 or JP-8 jet fuel vapor on neurobehavioral capacity and neurotransmitter levels. *Journal of Toxicology and Environmental Health*. Part A 63:397–428.

f. Whitman, F.T.; J.J. Freeman; G.W. Trimmer; J.L. Martin; E.J. Febbo; W.J. Bover; and R.L. Harris. 2001. Sensory Irritation Study in Mice. Final Report, Project No. 162951, ExxonMobil Biomedical Sciences, Inc., Annandale, NJ.

g. Wolfe, R.E.; E.R. Kinkead; M.L. Feldmann; H.F. Leahy; W.W. Jederberg; K.R. Still; and D.R. Mattie. 1996. Acute toxicity evaluation of JP-8 jet fuel containing additives. AL/OE-TR-1996-0136, NMRI-94-114, Armstrong Laboratory, Occupational and Environmental Health Directorate, Toxicology Division, Wright-Patterson AFB, OH.

7. *Methyl ethyl ketone*—i. *Description*. Methyl ethyl ketone (MEK) is a volatile solvent with a sweet/sharp acetone-like odor. MEK is widely used as a solvent in common household products such as inks, paints, cleaning fluids, varnishes, and glues. In most industrial applications it is used as a component of a mixture of organic solvents. It has also been detected in a wide variety of

natural products and may be a minor product of normal mammalian metabolism. In 1999, U.S. production capacity was 675 million pounds.

The inhalation toxicity of MEK is low. Low concentrations are only mildly irritating. At high concentrations MEK causes a narcotic effect on the central nervous system as evidenced by neurobehavioral effects in animals. MEK is not teratogenic, but at high concentrations is mildly fetotoxic to rats and mice. Data on human exposures were available from clinical studies and workplace monitoring. Animal studies with a variety of species (baboon, rat, mouse, and guinea pig) addressed irritation, neurotoxicity, developmental toxicity, chronic toxicity/carcinogenicity, and lethality. Exposure durations ranged from acute to chronic. Genotoxicity was also addressed.

Two studies with human volunteers exposed to 100, 200, or 350 ppm were evaluated for the AEGL-1; the exposure times were 5 minutes (Nelson et al. 1943) and 4 hours (Dick et al. 1992). Although a concentration of 200 ppm was judged unobjectionable in both studies, slight nose and throat irritation were noted at 100 ppm in the Nelson et al. (1943) study. Therefore, 100 ppm was selected as the threshold for sensory irritation. The safety of this value is supported by numerous clinical studies in which volunteers were routinely exposed to 200–400 ppm for up to 4 hours without reports of irritation or changes in neurobehavioral parameters. Because this is a threshold value and slight irritation should not increase in intensity with time, an intraspecies uncertainty factor of 1 was applied. Because accommodation to slight irritation occurs, the 100 ppm concentration was used across all AEGL-1 exposure durations. Furthermore, MEK is rapidly metabolized and will not accumulate in the blood or in the body which further supports using the same value for all the time intervals.

The AEGL-2 was based on the chronic study of Cavender et al. (1983) in which rats were exposed to 5,000 ppm for 5 days/week for 90 days. No lesions were reported in this study, but the concentration is close to the threshold for neurotoxicity as evidenced by somnolence in another repeated exposure study in which rats were exposed to 6,000 ppm for several weeks (Altenkirch et al. 1978). Because this was a no-effect repeated-exposure study, no interspecies uncertainty factor was applied. Because the threshold for narcosis differs by no more than 2- to 3-fold among the general population, an intraspecies uncertainty factor of 3 was applied to protect sensitive individuals. Because the threshold for narcosis is concentration dependent, the resulting 1,700 ppm concentration was applied across all AEGL-2 exposure durations.

The AEGL-3 values were based on two different studies. The 10- and 30-minute values were based on a study with mice in which a 30-minute exposure to 31,426 ppm was projected to reduce the respiratory rate by 50%; there were no deaths at the highest tested concentration of 26,416 ppm (Hansen et al. 1992). Because a 30-minute exposure of rats to 3 times this concentration (92,239 ppm) also resulted in no deaths (Klimisch 1988), the 31,426 ppm value was adjusted by an interspecies uncertainty factor of 1. Because the threshold for narcosis differs by no more than 2- to 3-fold among the general population, an intraspecies uncertainty factor of 3 was applied to protect sensitive individuals. The resulting value of 10,000 ppm was used for the 10-minute and 30-minute AEGL-3 exposure durations. The longer-term values were based on an MLE_{01} of 7,500 ppm calculated by Fowles et al. (1999) from a 4-hour study with rats exposed to several concentrations for 4 hours (La Belle and Brieger 1955). In this study the 4-hour LC_{50} was 11,700 ppm and the highest concentration resulting in no deaths was 7,850 ppm for 4 hours. The 7,500 ppm concentration was divided by an intraspecies uncertainty factor of 3. The resulting value of 2,500 ppm was used for both the 4-hour and 8-hour AEGL-3 values because MEK would reach equilibrium in the body prior to this time period. The 4-hour 2,500 ppm value was time scaled to the 1 hour time using the default n value of 3 for scaling to shorter time intervals.

The proposed AEGL values are listed in Table 8 of this unit.

TABLE 8.—SUMMARY OF PROPOSED AEGL VALUES FOR METHYL ETHYL KETONE [PPM (MG/M^3)]

Classification	10-minutes	30-minutes	1-hour	4-hours	8-hours	Endpoint (Reference)
AEGL-1 (Nondisabling)	100 (293)	100 (293)	100 (293)	100 (293)	100 (293)	Threshold for sensory irritation in humans (Nelson et al. 1943)
AEGL-2 (Disabling)	1,700 (4,980)	1,700 (4,980)	1,700 (4,980)	1,700 (4,980)	1,700 (4,980)	Threshold for narcosis— rats (Cavender et al. 1983)
AEGL-3(Lethal)	10,000[a,b] (29,300)	10,000 (29,300)	4,000[c] (11,720)	2,500 (7,325)	2,500 (7,325)	Threshold for lethality— mouse (Hansen et al. 1992; La Belle and Brieger 1955)

[a]Based on Hansen et al. (1992).
[b]This value is more than one-half of the lower explosive limit of 18,000 ppm.
[c]Based on La Belle and Brieger (1955).

ii.*References*. a. Altenkirch, H.; G. Stoltenburg; and H.M. Wagner. 1978. Experimental studies on hydrocarbon neuropathies induced by methyl-ethyl-ketone (MEK). *Journal of Neurology*. 219:159–170.

b. Cavender, F.L; H.W. Casey; H. Salem; J.A. Swenberg; and E.J. Gralla. 1983. A 90-day vapor inhalation toxicity study of methyl ethyl ketone. *Fundamental and Applied Toxicology*. 3:264–270.

c. Dick, R.B.; E.F. Krieg, Jr.; J. Setzer; and B. Taylor. 1992. Neurobehavioral effects from acute exposures to methyl isobutyl ketone and methyl ethyl ketone. *Fundamental and Applied Toxicology*. 19:453–473.

d. Fowles, J.R.; G.V. Alexeeff; and D. Dodge. 1999. The use of the benchmark dose methodology with acute inhalation lethality data. *Regulatory Toxicology and Pharmacology*. 29:262–278.

e. Hansen, L.F.; A. Knudsen; and G.D. Nielsen. 1992. Sensory irritation effects of methyl ethyl ketone and its receptor activation mechanism. *Pharmacology & Toxicology*. 71:201–208.

f. Klimisch, H. 1988. The inhalation hazard test; principle and method. *Archives of Toxicology*. 61:411–416.

g. La Belle, C. and H. Brieger. 1955. The vapor toxicity of a composite solvent and its principal components.

Archives of Industrial Health. 12:623–627.

h. Nelson, K.W.; J.F. Ege, Jr.; M. Ross; L.E. Woodman; and L. Silverman. 1943. Sensory response to certain industrial solvent vapors. *Journal of Industrial Hygiene and Toxicology*. 25:282–285.

8. *Phosphorus oxychloride*—i. *Description*. Phosphorus oxychloride (CAS No. 10025–87–3), a colorless fuming liquid with a pungent odor, is stable to above 300° C but is highly reactive with water yielding phosphoric acid and hydrogen chloride. It is used in the manufacture of plasticizers, hydraulic fluids, gasoline additives, fire retarding agents, and in the manufacture of alkyl and aryl orthophosphate triesters.

Information regarding exposure of humans to phosphorus oxychloride are limited to qualitative reports that indicate notable dermal, ocular, pharyngeal and pulmonary irritation following acute and subchronic (intermittent) exposures. Most reports lacked exposure terms although one report of occupational exposures indicated that air concentrations of phosphorus oxychloride ranged from 1.6 to 11.2 ppm. The effects often persisted after cessation of exposure, especially in those individuals experiencing more severe effects. Neither odor detection data nor lethality data are available for humans.

Quantitative data in animals are limited to reports of lethality. These data include a 4-hour LC_{50} for rata (44.4 ppm) and guinea pigs (52.5 ppm), and an unverified 4-hour LC_{50} of 32 ppm for rats. A 5–15 minute exposure of rats and guinea pigs to 0.96 ppm phosphorus oxychloride was noted as a ''threshold response'' in a Russian report. A brief report from industry indicated immediate adverse responses (at 2 minutes) and death (18 minutes) following exposure to a very high concentration (25,462 ppm). The available studies affirm the extreme irritation properties of phosphorus oxychloride, although the exposures described also resulted in lethality. No information was available regarding reproductive/developmental toxicity, genotoxicity, or carcinogenicity.

There are no definitive data regarding the metabolism or precise mechanism of action of phosphorus oxychloride toxicity. Based upon the limited human and animal toxicity data, and the chemical properties of phosphorus oxychloride, it may be assumed that the primary effect involves damage to epithelial tissue and, for respiratory effects, subsequent pulmonary edema. The lethal potency of phosphorus oxychloride, however, does not appear to be explained simply by the activity of its degradation products (phosphoric acid and hydrogen chloride).

In the absence of odor detection data and quantitative data pertaining to effects consistent with AEGL-1 definition, AEGL-1 values were not developed.

Exposure-response data pertaining to AEGL-2 level effects were unavailable and, therefore no AEGL-2 values were developed. Because of the lack of exposure-response data for any effects, estimating AEGL-2 values by a reduction in AEGL-3 values was considered tenuous and difficult to justify.

AEGL-3 values were developed using an estimate of the lethality threshold based upon the 4-hour LC_{50} of 48.4 ppm in rats that was reported by Weeks et al. (1964). Although exposure-response data were unavailable, the lethality threshold was estimated a one third of the 4-hour LC_{50} (i.e., 48.4 ppm/3 = 16.1 ppm). Due to uncertainties regarding species variability in the lethal response to phosphorus oxychloride and the lack of lethality data in humans, an order-of-magnitude uncertainty adjustment was applied for interspecies variability. Contact irritation resulting in damage to epithelial tissue appears to be involved in the toxic response to phosphorus oxychloride. It is likely that this response is a function of the extreme reactivity of phosphorus oxychloride with tissues (e.g., pulmonary epithelium) and not likely to vary greatly among individuals. The uncertainty adjustment for intraspecies variability, therefore, was limited to 3. The concentration exposure time relationship for many irritant and systemically acting vapors and gases may be described by $C^n \times t = k$, where the exponent, n, ranges from 0.8 to 3.5. In the absence of an empirically derived exponent (n), and to obtain conservative and protective AEGL values, temporal scaling was performed using n = 3 when extrapolating to shorter time points and n = 1 when extrapolating to longer time points using the $C^n \times t = k$ equation.

The range of interspecies variability remains uncertain due to limited animal data and the absence of quantitative exposure-response data for humans. The absence of exposure-response data for non-lethal effects in animals or humans is a significant data deficiency.

The proposed AEGL values are listed in Table 9 of this unit.

TABLE 9.—SUMMARY OF PROPOSED AEGL VALUES FOR PHOSPHORUS OXYCHLORIDE

Classification	10-minutes	30-minutes	1-hour	4-hours	8-hours	Endpoint (Reference)
AEGL-1 (Nondisabling)	NR	NR	NR	NR	NR	Data unavailable for development
AEGL-2 (Disabling)	NR	NR	NR	NR	NR	Data unavailable for development
AEGL-3 (Lethal)	1.1 ppm (6.9 mg/m^3)	1.1 ppm (6.9 mg/m^3)	0.85 ppm (5.3 mg/m^3)	0.54 ppm (3.4 mg/m^3)	0.27 ppm (1.7 mg/m^3)	Weeks et al., (1964). Estimate of lethality threshold in rats (16.1 ppm) based upon 3-fold reduction in 4-hour LC_{50} of 48.4 ppm.

NR: Not recommended. Numeric values for AEGL-1and AEGL-2 are not recommended due to the lack of available data Absence of AEGL-1 and AEGL-2 values does not imply that exposure below the AEGL-3 is without effect.

ii. *References*. Weeks, M.H.; Mussleman, N.P.; Yevich, P.P.; Jacobson, K.H.; and Oberst, F.W. 1964. Acute vapor toxicity of phosphorus oxychloride, phosphorus trichloride and methyl phosphonic dichloride. *Industrial Hygiene Journal*. 25:470–475.

9. *Phosphorus trichloride*—i. *Description*. Phosphorus trichloride (CAS No. 007719–12–2) is a colorless, clear fuming liquid with a pungent, irritating odor. In the presence of water, the chemical decomposes rapidly in a highly exothermic reaction to phosphonic acid, hydrogen chloride, and pyrophosphonic acids.

No acute lethality data are available in humans. Qualitative data regarding human exposures indicate signs and symptoms of exposure consistent with a highly irritating chemical; ocular and dermal irritation, respiratory tract irritation, shortness of breath, and nausea.

Lethality data in animals are available for rats, cats, and guinea pigs. Cursory studies conducted nearly 100 years ago in Germany provided preliminary data on lethal and nonlethal effects in cats and guinea pigs following various treatment regimens with inhaled phosphorus trichloride. Although results of the studies indicated the respiratory tract to a be a critical target, the methods and results of these studies were not verifiable. Weeks et al. (1964) reported 4-hour LC_{50} values of 104.5 ppm and 50.1 ppm for rats and guinea pigs, respectively. An unpublished study by Hazleton Laboratories (1983) identified a NOAEL of 3.4 ppm and a LOAEL (histopathologic changes in the respiratory tract) of 11 ppm following repeated exposure (6 hours/day, 5 days/week for 4 weeks) of rats. There are no data regarding reproductive/developmental toxicity, genotoxicity, or carcinogenicity of phosphorus trichloride. Definitive data regarding the mechanism of action of phosphorus trichloride are unavailable. Decomposition products (hydrogen chloride, phosphonic acid, and pyrophosphonic acids) are responsible, at least in part, for the contact irritation reported by humans, and the irritation and tissue damage observed in animal species.

The concentration-time relationship for may irritant and systemically acting vapors and gases may be described by $C^n \times t = k$, where the exponent n ranges from 0.8 to 3.5. Due to the limited toxicity data for this chemical, an empirical derivation of n was not possible. In the absence of an empirically derived exponent (n), and to obtain conservative and protective AEGL values, temporal scaling was performed using n = 3 when extrapolating to shorter time points and n = 1 when extrapolating to longer time points using the $C^n \times t = k$ equation. For 10-minute AEGL-3 values were set at equivalence to the 30-minute values due to uncertainties in extrapolating from the experimental exposure durations of 4 hours and greater.

Quantitative data consistent with AEGL-1 effects were unavailable. Occupational exposures of humans to 1.8–3.6 ppm for 2–6 hours and exposure of rats to 3.4 ppm for 6 hours/day, 5 days/week for 4 weeks were without notable effect. These data can be considered a NOAEL for AEGL-1 effects. Because they were derived from controlled experiments, the AEGL-1 values were based upon the Hazleton Laboratories (1983) report. These data as well as the AEGL-1 values are supported by the human experience data reported by Sassi (1952). The interspecies uncertainty factor was limited to 3 because of the concordance of the animal data with the human experience and because the most sensitive species tested (guinea pig) was only about 2-fold more sensitive. The intraspecies uncertainty factor was limited to 3 because primary effects of phosphorus trichloride (irritation and subsequent tissue damage) appear to be due, in part, to hydrogen chloride and phosphonic acid resulting from chemical dissociation. Additional reduction of the AEGL-1 values would be inconsistent with available human and animal data .

Information consistent with AEGL-2 effects were limited to an occupational exposure report and a multiple exposure study with rats. For occupational exposures, there was notable irritation following 2–6 hours of exposure to approximately 14–27 ppm phosphorus trichloride and more severe but reversible irritation following exposures of 1–8 weeks. Reports providing qualitative information but no exposure terms affirmed the potential for respiratory tract irritation following acute exposures to phosphorus trichloride. Data for rats showed upper respiratory tract involvement following multiple exposures over 4 weeks to 11 ppm but not to 3.4 ppm (Hazleton Laboratories, 1983). For development of AEGL-2 values, the 11 ppm exposure in rats was considered a NOAEL for AEGL-2 effects. Uncertainty factor application was the same as for the AEGL-1 tier.

AEGL-3 values were developed based upon a 3-fold reduction of the 4-hour LC_{50} (Weeks et al., 1964) as an estimate of the lethality threshold (50.1 ppm/3 = 16.7 ppm). A total uncertainty factor adjustment of 10 was used to develop the AEGL-3 values. Animal data indicated some variability in the toxic response to phosphorus trichloride with guinea pigs being the more sensitive among the species tested. Therefore, uncertainty adjustment regarding interspecies variability was limited to 3. To account for intraspecies variability, a factor of 3 was applied. The uncertainty of intraspecies variability was limited to 3 because primary effects of phosphorus trichloride (irritation and subsequent tissue damage) appear to be due, in part, to hydrogen chloride and phosphonic acid resulting from chemical dissociation. The total uncertainty factor of 10 may be justified by human exposure data showing that repeated 2 to 6-hour exposures of up to 27 ppm were without life-threatening consequences. Furthermore, the results of the Hazleton Laboratories (1983) study showed no fatalities in rats following multiple 6-hour exposures to 11 ppm.

The proposed AEGL values are listed in Table 10 of this unit.

TABLE 10.—SUMMARY OF PROPOSED AEGL VALUES FOR PHOSPHORUS TRICHLORIDE

Classification	10-minutes	30-minutes	1-hour	4-hours	8-hours	Endpoint (Reference)
AEGL-1 (Nondisabling)	0.78 ppm	0.78 ppm	0.62 ppm	0.39 ppm	0.26 ppm	NOAEL of 3.4 ppm in rats exposed 6 hours/day, 5 days/week for 4 weeks (Hazleton Laboratories, 1983)
AEGL-2 (Disabling)	2.5 ppm	2.5 ppm	2.0 ppm	1.3 ppm	0.83 ppm	NOAEL for AEGL-2 tier effects; based upon respiratory tract histopathology in rats exposed 6 hours/day, 5 days/week for 4 weeks (Hazleton Laboratories, 1983)

TABLE 10.—SUMMARY OF PROPOSED AEGL VALUES FOR PHOSPHORUS TRICHLORIDE—Continued

Classification	10-minutes	30-minutes	1-hour	4-hours	8-hours	Endpoint (Reference)
AEGL-3 (Lethal)	7.0 ppm	7.0 ppm	5.6 ppm	3.5 ppm	1.8 ppm	Estimated lethality threshold based upon 3-fold reduction of guinea pig 4-hour LC_{50} (50.1 ppm/3 = 16.7 ppm) (Weeks et al., 1964)[a]

[a]Based upon animal data, lethality may be delayed.

ii. *References.* a. Hazleton Laboratories. 1983. Subacute inhalation toxicity study in rats— phosphorus trichloride. Final Report. Project No. 241–141. Hazleton Laboratories America, Inc. Unpublished.

b. Weeks, M.H.; Mussleman, N.P.; Yevich, P.P.; Jacobson, K.H.; and Oberst, F.W. 1964. Acute vapor toxicity of phosphorus oxychloride, phosphorus trichloride and methyl phosphonic dichloride. *American Industrial Hygiene Journal.* 25:470–475.

10. *Xylenes*—i. *Description.* Xylene is found in a number of consumer products, including solvents, paints, or coatings, and as a blend in gasoline. Mixed xylenes are comprised of 3 isomers: M-xylene, o-xylene, and p-xylene, with the m-isomer predominating. Ethyl benzene is also present in the technical product formulation. Absorbed xylene is rapidly metabolized and is excreted almost exclusively in the urine as methylhippuric acid isomers in humans and as methylhippuric acid isomers and toluic acid glucuronides in animals. In both humans and animals, xylene causes irritation and effects the central nervous system following acute inhalation exposure. No consistent developmental or reproductive effects were observed in the studies found in the available literature. Commercial xylene and all 3 isomers have generally tested negative for genotoxicity. Xylenes are currently not classifiable as to its carcinogenicity by the International Agency on Research for Cancer (IARC) or the EPA because of inadequate evidence.

The AEGL-1 is based upon slight eye irritation noted during a 30-minute exposure to 400 ppm mixed xylenes (Hastings et al., 1986). An interspecies uncertainty factor was not applied because the key study used human data. An intraspecies uncertainty factor of 3 was applied because the toxic effect (slight irritation) was less severe than that defined for the AEGL-1 tier (notable discomfort). The resulting value of 130 ppm is supported by several other studies, including: A 150 ppm p-xylene exposure resulting in eye irritation in a contact lens wearer (Hake et al., 1981); a 15-minute exposure to 230 ppm mixed xylenes resulting in mild eye irritation and dizziness in one individual; and a 3-hour exposure to 200 ppm m- or p-xylene (Ogata et al., 1970), a 4-hour exposure to 200 ppm m-xylene (Savolainen et al., 1981), and a 5.5 hour exposure to 200 ppm m-xylene (Laine et al., 1993) all representing no-effect levels.

The AEGL-2 is based upon poor coordination resulting when rats were exposed to 1,300 ppm mixed xylenes for 4 hours (Carpenter et al., 1975). This concentration represents the threshold for reversible equilibrium disturbances. This concentration and endpoint are consistent with the preponderance of available data for 4-hour exposures in rats: The EC_{50} for decreased rotarod performance was 1982 ppm (Korsak et al., 1993); the minimum narcotic concentrations for m-, o-, and p-xylene ranged from 1,940–2,180 ppm (Molnár et al., 1986); and exposure to 1,600 ppm p-xylene resulted in hyperactivity, fine tremor, and unsteadiness (Bushnell, 1989), induced flavor aversion (Bushnell and Peele, 1988), and caused changes in the flash evoked potential suggestive of increased arousal (Dyer et al., 1988). In dogs, exposure to 1,200 ppm for 4 hours represented a threshold for eye irritation (Carpenter et al., 1975). An interspecies uncertainty factor of 1 was applied because rats receive a greater systemic dose of inhaled xylene as compared to humans. An intraspecies uncertainty factor of 3 was applied because the minimum alveolar concentration (MAC) for volatile anesthetics should not vary by more than a factor of 2–3-fold among humans. A 3-fold factor is also adequate to account for moderate physical activity during exposure, which would result in greater uptake of the chemical.

The AEGL-3 derivation is based upon prostration occurring in all 10 rats exposed for 4 hours to 2,800 ppm mixed xylenes, with recovery occurring within 1 hour of exposure (Carpenter et al., 1975). Although coordination initially remained poor, it returned to normal the following day. This concentration also represents a no-effect level for lethality. An interspecies uncertainty factor of 1 was applied because rats receive a greater systemic dose of inhaled xylene as compared to humans. An intraspecies uncertainty factor of 3 was applied because the MAC for volatile anesthetics should not vary by more than a factor of 2–3-fold among humans. A 3-fold factor is also adequate to account for moderate physical activity during exposure, which would result in greater uptake of the chemical.

The two primary effects of concern for xylene are those of irritation and central nervous system effects. Irritation is considered a threshold effect and therefore should not vary over time. The AEGL-1 value based on irritation is therefore not scaled across time, but rather the threshold value is applied to all times.

Data indicate that once steady state is reached, concentration, not duration, is the prime determinant in xylene-induced central nervous system toxicity. Pharmacokinetic modeling in both humans and rats indicate that venous blood concentrations rapidly increase during the first 15 minutes of exposure, followed by minimal increases in blood concentrations with continuing exposure (i.e., increases follow a hyperbolic curve). Likewise, available human data indicate that once the initial increase in blood xylene concentration is reached, blood concentrations level off with increasing exposure duration. Conversely, available human and animal data demonstrate that increasing exposure concentrations correlate with increases in venous blood xylene concentrations. Therefore, the AEGL 2- and -3 values are set equal across time once steady state is approached (starting at approximately 1 hour), while pharmacokinetic modeling was used to extrapolate to exposure durations of 10- and 30-minutes.

The AEGL values should be protective of human health. The AEGL-1 values are consistent with other human studies, and represent a value consistent with exposure concentrations that might result in mild eye irritation. The AEGL-2 levels are protective, especially when considering numerous human studies investigating the effects of exposure to

200 ppm xylene with 20-minute peak exposures to 400 ppm, in some cases additionally combining peak exposures with physical exercise resulting in greater uptake of the chemical, and finding only minimal central nervous system effects. The difficultly in defining an AEGL-2 level for xylene comes from its ''all-or-nothing'' continuum of toxicity: Toxicity ranges from mild irritation to narcosis, with little happening in between. The AEGL-3 levels represent the threshold for narcosis, and are protective as supported by human data demonstrating that exposure to 690 ppm for 15 minutes resulted in lightheadedness/dizziness and a 30 minute exposure to 700 ppm resulted in nausea, vomiting, dizziness, or vertigo.

The proposed AEGL values are listed in Table 11 of this unit.

TABLE 11.—SUMMARY OF PROPOSED AEGL VALUES FOR XYLENES [PPM (MG/M^3)]

Classification	10-minutes	30-minutes	1-hour	4-hours	8-hours	Endpoint (Reference)
AEGL-1 (Nondisabling)	130 (560)	130 (560)	130 (560)	130 (560)	130 (560)	Eye irritation in human volunteers exposed to 400 ppm mixed xylenes for 30 minutes (Hastings et al., 1986)
AEGL-2 (Disabling)	990 (4,300)	480 (2,100)	430 (1,900)	430 (1,900)	430 (1,900)	Rats exposed to 1,300 ppm mixed xylenes for 4 hours exhibited poor coordination (Carpenter et al., 1975)
AEGL-3 (Lethal)	2,100 (9,100)	1,000 (4,300)	930 (4,000)	930 (4,000)	930 (4,000)	Rats exposed to 2,800 ppm for 4 hours exhibited prostration followed by a full recovery (Carpenter et al., 1975)

ii. *References.* a. Bushnell, P.J. 1989. Behavioral effects of acute p-xylene inhalation in rats: Autoshaping, motor activity, and reversal learning. *Neurotoxicology and Teratology*. 10:569–577.

b. Bushnell, P.J. and Peele, D.B. 1988. Conditioned flavor aversion induced by inhaled p-xylene in rats. *Neurotoxicology and Teratology*. 10:273–277.

c. Carpenter, C.P.; Kinkead, E.R.; Geary, D.L. Jr.; Sullivan, L.J.; and King, J.M. 1975b. Petroleum hydrocarbon toxicity studies. V. Animal and human response to vapors of mixed xylene. *Toxicology and Applied Pharmacology*. 33:543–58.

d. Dyer, R.S.; Bercegeay, M.S.; and Mayo, L.M. 1988. Acute exposures to p-xylene and toluene alter visual information processing. *Neurotoxicology and Teratology*. 10:147–153.

e. Hake, C.R.L.; Stewart, R.D.; and Wu, A., et al. 1981. p-Xylene: Development of a biological standard for the industrial worker. Report to the National Institute for Occupational Safety and Health, Cincinnati, OH, by the Medical College of Wisconsin, Inc., Milwaukee, WI. PB82-152844.

f. Hastings, L.; Cooper, G.P.; and Burg, W. 1986. Human sensory response to selected petroleum hydrocarbons. In: MacFarland, H.N. ed. Advances in Modern Environmental Toxicology. Vol. VI. Applied Toxicology of Petroleum Hydrocarbons. Princeton, NJ: Princeton Scientific Publishers. pp. 255–270.

g. Korsak, Z.; Swiercz, R.; and Jedrychowski, R. 1993. Effects of acute combined exposure to—n-butyl alcohol and m-xylene. *Polish Journal of Occupational Medicine and Environmental Health*. 6:35–41.

h. Laine, A.; Savolainen, K.; and Riihimäki, V., et al. 1993. Acute effects of m-xylene inhalation onbody sway, reaction times, and sleep in man. *International Archives of Occupational and Environmental Health*. 65:179–188.

i. Molnár, J.; Paksy, K.Á.;and Náray, M. 1986. Changes in the rat's motor behavior during 4-hour inhalation exposure to prenarcotic concentrations of benzene and its derivatives. *Acta Physiologica Hungarica*. 67:349–354.

j. Ogata, M.; Tomokuni, K.; and Takatsuka, Y. 1970. Urinary excretion of hippuric acid and m- or p-methylhippuric acid in the urine of persons exposed to vapours of toluene and m- or p-xylene as a test of exposure. *British Journal of Industrial Medicine*. 27:43–50.

k. Savolainen, K.; Riihimäki, V.; Laine, A.; and Kekoni, J. 1981. Short-term exposure of human subjects to m-xylene and 1,1,1-trichloroethane. *International Archives of Occupational Environmental Health*. 49:89–98.

IV. Next Steps

The NAC/AEGL Committee plans to publish ''Proposed'' AEGL values for five-exposure periods for other chemicals on the priority list of 85 in groups of approximately 10 to 20 chemicals in future **Federal Register** notices during the calendar year 2003.

The NAC/AEGL Committee will review and consider all public comments received on this notice, with revisions to the ''Proposed'' AEGL values as appropriate. The resulting AEGL values will be established as ''Interim'' AEGLs and will be forwarded to the National Research Council, National Academy of Sciences (NRC/NAS), for review and comment. The ''Final'' AEGLs will be published under the auspices of the NRC/NAS following concurrence on the values and the scientific rationale used in their development.

List of Subjects

Environmental protection, Hazardous chemicals, Worker protection.

Dated: July 7, 2003.

Susan B. Hazen,

Acting Assistant Administrator for Prevention, Pesticides and Toxic Substances.

[FR Doc. 03–18306 Filed 7–17–03; 8:45 am]

BILLING CODE 6560–50–S