National Advisory Committee (NAC)
for Acute Exposure Guideline Levels (AEGLs) for Hazardous Substances
Final Meeting 16 Highlights
U.S. Department of Transportation
DOT Headquarters Building, Rooms 6200-6204
400 7th Street, S.W., Washington, D.C.
December 6-8, 1999

INTRODUCTION

The highlights of the meeting are noted below, and the meeting agenda (Attachment 1) and attendee lists (Attachment 2) are attached. Highlights of the NAC Meeting 15 (September 14-15, 1999) were reviewed and approved with minor corrections (Appendix A).

GENERAL INTEREST ITEMS

Roger Garrett, AEGL Program Director, welcomed the international collaborators: Annick Pichard from France, Ursula Stephan from Germany, and Marc Ruijten and Marcel Van Raaij from the Netherlands.

Roger Garrett reported on the progress of the NAS/COT–NAS/AEGL subcommittee review process for the Standing Operating Procedures (SOP) and the Technical Support Documents (TSDs). The subcommittee has tentatively reached consensuses on the SOP as well as TSDs and respective AEGL values for five priority chemicals (aniline, arsine, hydrazine, methyl hydrazine, and two isomers of dimethyl hydrazine). Following the changes recommended by the NAS/AEGL, these documents are still subject to internal and external NAS review prior to the final publication. The AEGLs for chlorine and fluorine are undergoing minor revisions and will not be published along with the TSDs listed above. July 2000 was indicated as a tentative publication date. He also announced that the committee will begin the development of 10-minute AEGL values (also desired by certain U.S. organizations in the private sector and OECD member countries); In addition, he also summarized some of the SOP issues that must be resolved before the first publication by the NAS. These included: (1) the inclusion of the discussion of Multiple Chemical Sensitivity in the SOP; (2) a more robust and scholarly discussion of the uncertainty factors; and (3) the development of AEGL-1 values in cases where other than irritation and other sensory effects are known to occur below the AEGL-2 effect levels. Following a discussion, the NAC/AEGL approved a modification of the AEGL-1 definition to include circumstances where individuals may experience asymptomatic and nonsensory effects when exposed at low concentrations (Appendix B). The issue of the sensitivity of adult versus pediatric asthmatics will be addressed in the future.

John Morawetz circulated a memorandum (Attachment 3) regarding a request to finalize issues regarding ceiling levels, their relationship to AEGLs, and their discussion in the SOPs. Discussion focused on the need to emphasize that emergency responders should not develop AEGL values of increasing concentrations for less-than-30-minute periods by simple extrapolation. John proposed the following statement: "A ceiling level not to be exceeded is the AEGL value with the shortest (least) time be incorporated into SOP. For most chemicals, this will be the 30-minute value, unless a shorter period is determined (for example 10 minutes)." AEGL values are not intended to apply to infrequent exposures. It was approved by NAC/AEGL (Appendix C). AEGL values are not intended to apply to infrequent exposures. A request was made for NAS/AEGL members to submit thoughts/comments to Ernie Falke and John Morawetz for possible inclusion in the SOP document.

AEGL PRIORITY CHEMICALS

Ethylene Oxide, CAS Reg. No. 75-21-8

Chemical Manager: Kyle Blackman, FEMA
Author: Kowetha Davidson, ORNL

Kowetha Davidson reviewed the status of the ethylene oxide AEGLs and initiated the discussion regarding an issue revolving around the AEGL-2 assessment (Attachment 4). Specifically, attention was focused on replacing the use of a dominant lethal endpoint with genetic effects on germ cells and potential growth retardation. Kyle Blackman and Kowetha Davidson provided an overview of the new approach noting that it addressed the comments submitted in response to the Federal Register publication. Discussion ensued regarding the appropriateness of the revised AEGL-2 endpoints. William Snellings (Union Carbide) stated that the study and endpoint (neurotoxicity) originally selected in the first TSD draft (prepared in December 1996) was the most appropriate choice. Kyle expressed concern that the AEGL-2 should be protective of the unborn, thereby favoring the growth retardation endpoint. Following extensive discussion of different proposals involving various potential endpoints (all of which provided similar AEGL-2 values), a no-effect level for delayed ossification was selected as the key endpoint for AEGL-2 development. A motion was made by George Rodgers and seconded by John Hinz to accept the values of 80, 45, 14, and 7.9 ppm (for the 30-min, 1-, 4-, and 8-hr AEGLs) based up on fetal growth retardation without a statistical increase in delayed ossification in rats exposed to 100 ppm ethylene oxide for 6 hours in a developmental toxicity study. The n-value was 1.2 and the uncertainty adjustment was 10 (3 each for inter- and intraspecies variability). The motion passed (YES: 14; NO: 4; ABSTAIN:1) (Appendix D).

Methyl Isocyanate, CAS Reg. No. 624-83-9

Chemical Manager: Loren Koller, Oregon State University
Author: Carol Forsyth, ORNL

Carol Forsyth reviewed the relevant data and major effects of methyl isocyanate (Attachment 5) noting that AEGL-3 values had been adopted in March 1999. Following a brief discussion, it was moved by Loren Koller and seconded by Mark McClanahan to accept the AEGL-2 values as presented (0.13, 0.07, 0.017, 0.008 ppm for 30 minute, 1-, 4-, and 8-hr, respectively) based upon decreased fetal body weight. George Rodgers stated that cardiac arrhythmia data should also be incorporated into the justification of the AEGL-2 values. The motion was approved by NAC/AEGL (YES: 17; NO: 1; ABSTAIN: 0) (Appendix E). A motion made by Ernie Falke and seconded by Mark McClanahan not to adopt AEGL-1 values was passed unanimously (Appendix E).

Otto Fuel II, CAS Reg. No. 6423-43-4

Chemical Manager: Bill Bress, ASTHO
Author: Sylvia Talmage, ORNL

Note: The values of AEGL-1 and -2 were approved at the NAC/AEGL-15 meeting.

Bill Bress reviewed the data pertinent to development of AEGL-3 values for Otto Fuel (Attachment 6). The proposed values were based on a study with squirrel monkeys in which exposure to 70-100 ppm for 6 hours caused severe effects on the central nervous system but no deaths. An interspecies uncertainty factor of 3 was applied because the monkey and humans showed similar effects on the central nervous system at low concentrations. In addition, the threshold for central nervous system effects does not vary widely among mammalian species, and the monkey is an appropriate model for extrapolation to humans. An intraspecies uncertainty factor of 3 was chosen because the threshold for central nervous system depression does not vary widely among individuals. Because no data were available for time-scaling for the endpoint of central nervous system depression, the values of $n = 3$ for scaling from 6 hours to the shorter time periods and $n=1$ for scaling to the 8-hour period were used. Bob Benson addressed the concern that methemoglobin formation may be a problem in infants exposed to Otto Fuel. Using the U.S. EPA's reference dose for nitrate-nitrogen which is based on a no-affect level in infants, Bob showed that the intake of nitrate-nitrogen from exposure to an 8-hour AEGL-3 is less than the U.S. EPA reference dose. John Morawetz noted that the TSD needed to be modified to indicate that sampling data for worker exposure was the result of instantaneous readings and not continuous monitoring data. Ten-minute values were also calculated for Otto Fuel. The AEGL-2 and AEGL-3 10-minute values were time-scaled from the existing data. The 10-minute AEGL-1 value was flatlined from the 30-minute value. A motion to accept the AEGL-3 values was made by Ernie Falke and seconded by Mark McClanahan. The motion passed [YES: 17; NO: 0; ABSTAIN: 0] (Appendix F).

SUMMARY OF PROPOSED AEGL VALUES FOR OTTO FUEL (ppm[mg/m^3])

Classification	10-minute	30-minute	1-hour	4-hour	8-hour	Endpoint (Reference)
AEGL-1	0.33 (2.3)	0.33 (2.3)	0.17 (1.1)	0.05 (0.34)	0.03 (0.17)	Mild headaches in humans (Stewart et al., 1974)
AEGL-2	6.0 (43)	2.0 (14)	1.0 (6.8)	0.25 (1.7)	0.13 (0.8)	Severe headaches and slight imbalance in humans (Stewart et al., 1974)
AEGL-3	23 (165)	16 (114)	13 (93)	8.0 (57)	5.3 (38)	Convulsions in monkeys (Jones et al., 1972)

Sulfur Mustard (Agent HD), CAS Reg. No. 505-60-2

Chemical Manager: Kenneth R. Still, U.S. Navy
Author: Robert Young and Annetta Watson, ORNL

An overview (binder distributed to NAC members at meeting [Attachment 7]) of the U.S. Army Chemical Warfare Agent Program was provided by Veronique Hauschild (Environmental Risk Assessment and Risk Communication Program, U.S. Army Center for Health Promotion and Preventive Medicine, Aberdeen Proving Ground, MD). Components of the program were described and the need for scientifically sound health-based exposure criteria for sulfur mustard and nerve agents (GA,GB, GD, and VX) were emphasized. Ms. Hauschild also indicated that it would be helpful if the NAS/AEGL provided more guidance regarding the use of AEGLs. Annetta presented information on the physicochemical properties and toxicology of the warfare agents (Attachment 8), and also showed a video that provided general information on these agents as well as descriptions of their toxic effects. Immediately prior to deliberations on the sulfur mustard draft, Loren Koller gave an overview of a previous evaluation by the National Research Council Committee on Toxicology (for which he served as Chairperson) on human acute toxicity estimates for nerve and vesicant warfare agents (Attachment 9).

Robert Young presented an overview of available data and the draft AEGLs for sulfur mustard (Attachment 10). An emphasis was placed on the availability of human exposure data for nonlethal responses and the fact that the ocular response appears to be a sensitive indicator of exposure. The NAS/AEGL agreed that the human data on ocular responses serve as drivers for the AEGL-1 and AEGL-2 values. Minor alterations in the selection of the key exposure terms and uncertainty factor application resulted in AEGL values differing only slightly from the draft values. The AEGL-1 values were based upon a threshold (12 mg-min/m^3) for ocular irritation in human subjects and adjusted by an uncertainty factor of 3 for protection of sensitive individuals. The AEGL-2 was based the lowest concentration-time product (60 mg-min/m^3) for which ocular effects could be characterized as military casualties (i.e., moderate irritation that might require medical attention and that might result in performance decrement). An uncertainty factor of 3 was again applied for concerns regarding sensitive individuals and a modifying factor of 3 was also applied to account for uncertainties regarding potential long-term ocular effects or the possibility of respiratory tract involvement. The AEGL-3 values were based on an estimated lethality threshold in mice and downwardly adjusted by a total uncertainty factor adjustment of 10 (3 each for intra- and interspecies variability). An n of 1 for time scaling was empirically derived. Ten-minute AEGL value were also developed in response to a needs requested by the U.S. Army and by the European community. For AEGL-1 and AEGL-2 10-min values, linear time scaling (n =1) was applied but for AEGL-3 exponential scaling (n=3) was applied because of the absence of very short-term lethality data. A motion to accept the revised AEGL-1 values was made by Loren Koller and seconded by Glenn Leach. The motion passed [YES: 20; NO: 1; ABSTAIN: 0] (Appendix G). A motion to accept the revised AEGL-2 values was made by Bob Snyder and seconded by Bill Pepelko. The motion passed [YES: 17; NO: 4; ABSTAIN: 0](Appendix G). A motion to accept the AEGL-3 values was made by Bob Benson and seconded by Bill Pepelko. The motion passed [YES: 20; NO: 1; ABSTAIN: 0] (Appendix G).

SUMMARY OF PROPOSED AEGL VALUES FOR SULFUR MUSTARD (AGENT HD)						
Classification	**10-min**	**30-min**	**1-hour**	**4-hour**	**8-hour**	**Endpoint (Reference)**

AEGL-1	0.060 ppm 0.40 mg/m^3	0.020 ppm 0.13 mg/m^3	0.010 ppm 0.067 mg/m^3	0.0026 ppm 0.017 mg/m^3	0.0012 ppm 0.008 mg/m^3	Conjunctival injection and minor discomfort with no functional decrement in human volunteers (Anderson, 1942)
AEGL-2	0.090 ppm 0.60 mg/m^3	0.030 ppm 0.20 mg/m^3	0.015 ppm 0.10 mg/m^3	0.0038 ppm 0.025 mg/m^3	0.0020 ppm 0.013 mg/m^3	Well marked, generalized conjunctivitis, edema, photophobia, and eye irritation in human volunteers (Anderson, 1942)
AEGL-3	0.91 ppm 6.1 mg/m^3	0.63 ppm 4.2 mg/m^3	0.32 ppm 2.1 mg/m^3	0.080 ppm 0.53 mg/m^3	0.041 ppm 0.27 mg/m^3	Lethality estimate in mice (Kumar and Vijayaraghavan, 1998)

1,1,1-Trichloroethane, CAS Reg. No. 71-55-6

Chemical Manager: Mark McClanahan, CDC/NCEH
Author: Tessa Long, ORNL

An overview of the draft AEGLs was provided by Tessa Long (Attachment 11). A motion to accept the draft AEGL-1 values of 150 ppm for all time points based on what appeared to be a time-independent response of six human subjects was made by Zarena Post and seconded by George Rodgers. The motion did not pass [YES: 11; NO: 8; ABSTAIN: 0] (Appendix H). An alternate motion for use of 230 ppm for all time points (UF=2) did pass. The approach was justified by consistency of the effect across studies. For AEGL-2, Ernest Falke suggested that the time scaling calculations utilize the EC_{50} data rather than the LC_{50} data. A motion was made by George Rodgers (seconded by Doan Hansen) to accept 670, 600, 380, and 310 ppm for the 30-min, 1-, 4-, and 8-hr AEGL-2 values. These were based upon an EC_{50} for ataxia in rats and a total uncertainty adjustment of 10 (3 each for inter- and intraspecies variability). The motion passed (YES: 12; NO: 6; ABSTAIN: 0) (Appendix H). A motion was made by Mark McClanahan (seconded by Doan Hansen to accept 4800, 3800, 2400, and 1900 ppm for the 30-min, 1-, 4-, and 8-hr AEGL-3 values An uncertainty factor of 10 was applied. An intraspecies factor of 3 was used to account for sensitive individuals and an interspecies factor of 3 was used. The resulting concentrations were multiplied by a modifying factor of 3 in order to achieve a reasonable concentration at which humans might experience life-threatening toxic effects. The motion passed [YES: 14; NO: 2; ABSTAIN: 0] (Appendix H). The 10-min value for AEGL-1 was designated as the same for all other time points for this level, 230 ppm. The 10-min value for AEGL-2 was extrapolated from the same aforementioned endpoint for this level, the EC_{50} for ataxia in rats. The AEGL-3 30-min value was also used for the 10-min value so as not to exceed the threshold for cardiac sensitization observed in dogs (Reinhardt et al., 1973). The resulting AEGL values are presented in the following table.

SUMMARY OF PROPOSED AEGL VALUES FOR 1,1,1-TRICHLOROETHANE (ppm [mg/m^3])

Classification	10-minute	30-minute	1-hour	4-hour	8-hour	Endpoint (Reference)
AEGL-1	230 (1252)	230 (1252)	230 (1252)	230 (1252)	230 (1252)	Eye irritation and slight dizziness in humans observed by Salvini et al. (1971)
AEGL-2	930 (5064)	670 (3650)	600 (3270)	380 (2070)	310 (1688)	EC_{50} for ataxia in rats, Mullin and Krivanek, (1982)
AEGL-3	4800[a] (26135)	4800 (26135)	3800 (20690)	2400 (13067)	1900 (10345)	LC_0 extrapolated from Bonnet et al. (1980)

[a] The 30-min value was used as the 10-min value so as not to exceed the threshold for cardiac sensitization observed in dogs (Reinhardt et al., 1973).

1,2-Dichloroethylene, CAS Reg. No. 540-59-0

Chemical Manager: Ernie Falke, USEPA
Author: Cheryl Bast, ORNL

Cheryl Bast reviewed previous NAC/AEGL deliberations, NAS/COT Subcommittee suggestions, and new data provided by industry representatives. The AEGL-1 was based on a no-effect-level for eye irritation in humans. An uncertainty factor of 3 was applied to protect sensitive individuals. This uncertainty factor of 3 was applied for AEGL-1 values for both the *cis*- and *trans*- isomers. Since data suggest that the *cis*-isomer is approximately twice as toxic as the *trans*- isomer, a modifying factor of 2 was applied in the derivation of the *cis*- isomer values only. The same value was applied across the 10- and 30-minute, 1-, 4-, and 8-hour exposure time points. For the *trans*- isomer, the motion was made by George Rodgers and seconded by Zarena Post. The motion passed (YES:14; NO:1; ABSTAIN:2)(Appendix I). For the *cis*- isomer, the motion was made by George Rodgers and seconded by Steve Barbee. The motion passed (YES:14; NO:2; ABSTAIN:2) (Appendix J).

The AEGL-2 for the 4- and 8-hour time points was based on narcosis observed in pregnant rats exposed to *trans*- isomer for 6 hours. Uncertainty factors of 3 each (total UF=10) were applied for both inter- and intraspecies differences. To obtain conservative and protective AEGL values in the absence of an empirically derived chemical-specific scaling exponent, 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 AEGL-2 for the 10- and 30-min and 1-hr time points was set as a ceiling based on a plateau for anesthetic effects in humans. Values extrapolated from animal data for the trans- isomer were divided by 2 to derive the *cis*- AEGL-2 values for 30 minutes to 8 hours. The 10-min value was set as the same ceiling as the trans-10-minute value. For the *trans*- isomer, the motion was made by Tom Hornshaw and seconded by George Rodgers. The motion passed (YES: 12; NO: 3; ABSTAIN: 3) (Appendix I*)*. For *cis*- isomer, the motion was made by Tom Hornshaw and seconded by George Rodgers. The motion was passed (YES: 13; NO: 2; ABSTAIN: 3) (Appendix J).
The AEGL-3 for the 4- and 8-hour time points was based on a 4-hr no-effect-level for death in rats exposed to *trans*- isomer. A total uncertainty factor of 10 was applied for AEGL-3 values for both the *cis*- and *trans*-isomers. To obtain conservative and protective AEGL values in the absence of an empirically derived chemical-specific scaling exponent, 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 AEGL-3 for

the 10- and 30-min and 1-hr time points was set as a ceiling based on a plateau for intracranial pressure, nausea, and severe dizziness in humans. *Cis*- values extrapolated from animal data for the *trans*-isomer were divided by 2 to derive the *cis*- AEGL-3 values for 30 minutes to 8 hours. The 10-min value was set as the same ceiling as the *trans*- 10-min value. For the *trans*-isomer, the motion was made by Bob Benson and seconded by Bob Snyder. The motion passed (YES: 13; NO: 4; ABSTAIN: 1) (Appendix I). For the *cis*-isomer, the motion was made by Mark McClanahan and seconded by Bob Snyder. The motion was passed (YES: 10; NO: 4; ABSTAIN: 2) (Appendix J).

After the meeting, it was noted that there was a logical inconsistency which is not rationally defensible for the 10-, 30-, and 60-minute AEGL-2 and -3 values for the *cis*- isomer. The rationale is as follows:

Values extrapolated from animal data for the *trans*- isomer were divided by 2 to derive the *cis*- AEGL-2 and values for 30 minutes to 8 hours. The 10-min value was set as the same ceiling as the *trans*- 10-minute value. This is reasonable for the 4-and 8-hour values. However, the extrapolated 10-, 30-, and 60-minute values from animal data were not used for the *trans*- isomer because there were conflicting human data. The rationale for the 4- and 8-hour values for the *cis*- isomer is consistent with the *trans*- argument. However, if the *trans*- values are to be used to derive the *cis*- values based upon the rationale that the *cis*- isomer is twice as toxic, then the 10-, 30-, and 60-minute values for the *cis*- isomer should be based upon the human data as they were for the *trans*- isomer. The rationale discussed at the meeting was that the concentration-response curves and partition coefficients were likely different for the two isomers, and thus, there might not be a 2-fold differential toxicity at shorter time points. However, we have insufficient data to either confirm or refute this assumption.

Cis- values extrapolated from animal data for the *trans*-isomer were divided by 2 to derive the *cis*- AEGL-3 values for 30 minutes to 8 hours. The 10-minute *cis*- value was set as the same ceiling as the *trans*- 10-minute value. This is reasonable for the 4- and 8-hour values. However, the extrapolated 30- and 60-minute values from animal data were not used for the *trans*- isomer because there were conflicting human data. The rationale for the 4- and 8-hour values for the *cis*- isomer is consistent with the *trans*- argument. However, if the *trans*- values are to be used to derive the *cis*- values based upon the rationale that the *cis*- isomer is twice as toxic, then the 10-, 30-, and 60-minute values for the *cis*- isomer should be based upon the human data as they were for the *trans*- isomer. The rationale discussed at the meeting was that the concentration-response curves and partition coefficients were likely different for the two isomers, and thus, there might not be a 2-fold differential toxicity at shorter time points. However, we have insufficient data to either confirm or refute this assumption.

Therefore, for consistency, it was proposed and approved by the Committee in a vote by E-mail that the AEGL-2 and AEGL-3 values for the *cis*- isomer be set at one-half the *trans*- value.

Thus, proposed values are as follows:

PROPOSED AEGL VALUES FOR TRANS-1,2-DICHLOROETHENE (ppm[mg/m^3])						
Classification	**10-min**	**30-min**	**1-hour**	**4-hour**	**8-hour**	**Endpoint (Reference)**
AEGL-1 (Nondisabling)	280 [1109]	280 [1109]	280 [1109]	280 [1109]	280 [1109]	Ocular irritation in humans (Lehman & Schmidt-Kehl, 1936)
AEGL-2 (Disabling)	1000 [3960]	1000 [3960]	1000 [3960]	690 [2724]	450 [1782]	Narcosis in rats:4- & 8-hr (Hurtt et al., 1993); Anesthetic effects in humans (Lehman & Schmidt-Kehl, 1936)

AEGL-3 (Lethal)	1700 [6732]	1700 [6732]	1700 [6732]	1200 [4752]	620 [2455]	No-effect-level for death in rats: 4- & 8-hr (Kelly, 1999); Nausea, intracranial pressure, and dizziness in humans (Lehman & Schmidt-Kehl, 1936)

PROPOSED AEGL VALUES FOR CIS-1,2-DICHLOROETHENE (ppm[mg/m^3])						
Classification	**10-min**	**30-min**	**1-hour**	**4-hour**	**8-hour**	**Endpoint (Reference)**
AEGL-1 (Nondisabling)	140 [554]	140 [554]	140 [554]	140 [554]	140 [554]	Ocular irritation in humans (Lehman & Schmidt-Kehl, 1936)
AEGL-2 (Disabling)	500 [1980]	500 [1980]	500 [1980]	340 [1346]	230 [911]	Narcosis in rats:4- & 8-hr (Hurtt et al., 1993); Anesthetic effects in humans (Lehman & Schmidt-Kehl, 1936)
AEGL-3 (Lethal)	850 [3366]	850 [3366]	850 [3366]	620 [2455]	310 [1228]	No-effect-level for death in rats: 4- & 8-hr (Kelly, 1999); Nausea, intracranial pressure, and dizziness in humans (Lehman & Schmidt-Kehl, 1936)

ADMINISTRATIVE ISSUES

Plans for future NAS/AEGL meeting dates were discussed. The following are proposed meeting dates:

March 16-17, 2000, Philadelphia, PA (preceding SOT meeting)
June 12-14, 2000, Washington, D.C. (Finalization of NAS-approved chemicals and SOPs)

Future NAS/COT meetings were also announced and included

June 5-6, 2000 (Irvine, CA)
September 14-15, 2000 (Woods Hole, MA)

Meeting highlights were prepared by Bob Young and Po-Yung Lu, Oak Ridge National Laboratory.

LIST OF ATTACHMENTS

The attachments were distributed during the meeting and will be filed in the EPA Docket Office.

1. NAC/AEGL Meeting No. 16 Agenda
2. NAC/AEGL Meeting No. 16 Attendee List
3. Memorandum from John Morawetz on exposure period and ceiling levels
4. Data Analysis for Ethylene Oxide - Kowetha Davidson
5. Data Analysis for Methyl Isocyanate - Carol Forsyth
6. Data Analysis for Otto Fuel II - Sylvia Talmage
7. Chemical Warfare Agents Reference Package & Overview of Chemical Agent Program
8. Chemical Warfare Agents, Symptoms, Effects and Characteristics - Annetta Watson
9. Summary of Existing Toxicity Data for Selected Chemical agents - Loren Koller
10. Data Analysis for Sulfur Mustard - Bob Young
11. Data Analysis for 1,1,1-Trichloroethane - Tessa Long
12. Data Analysis for 1,2-Dichloroethylene - Cheryl Bast

LIST OF APPENDICES

A. Approved NAC/AEGL-15 Meeting Highlights
B. Ballot for AEGL-1 definition modification
C. Ballot for SOP statement
D. Ballot for Ethylene Oxide
E. Ballot for Methyl Isocyanate
F. Ballot for Otto Fuel II
G. Ballot for Sulfur Mustard
H. Ballot for 1,1,1-Trichloroethane
I. Ballot for *Trans*-1,2-Dichloroethylenhe
J. Ballot for *Cis*-1,2-Dichloroethylene

National Advisory Committee for
Acute Exposure Guideline Levels for Hazardous Substances

Attachment 1

NAC/AEGL-16
December 6-8, 1999

U.S. Department of Transportation
DOT Headquarters/Nassif Building, Rooms 6200-6204
400 7th Street, SW
Washington, DC

AGENDA

Monday, December 6, 1999

10:00 AM	Introductory remarks and approval of NAC/AEGL-15 Highlights (George Rusch, Roger Garrett, and Paul Tobin)
10:15	Status Reports (Roger Garrett, George Rusch, and Ernest Falke) ✦ International matters ✦ NRC/COT AEGL Subcommittee Issues: • SOP Manual • Status of seven chemicals reviewed by NAS
11:30	Lunch
12:30 PM	Ethylene oxide: AEGL-2 (Kyle Blackman/Kowetha Davidson)
2:15	Break
2:30	Methyl isocyanate: AEGLs-1 & 2 (Loren Koller/Carol Forsyth)
3:45	Otto Fuel II (Propylene glycol dinitrate) : AEGL-3 (Bill Bress/Sylvia Talmage)
5:00	Administrative issues, future meetings
5:15	Adjourn for the day

Tuesday, December 7, 1999

8:30 AM	Introduction to DoD's Program (Roger Garrett)
8:35	Overview of US Chemical Warfare Agent Program (Veronique Hauschild/Annetta Watson) • Components of the program: stockpile and non-stockpile • Historic responsibilities for agent exposure standard-setting • Chemical, physical and toxicological properties of nerve and sulfur mustard vesicant agents • Issues surrounding application of chemical warfare agent emergency exposure guidelines
10:00	Break
10:15	NRC/COT review of acute human toxicity estimates for nerve and vesicant chemical warfare agents (Loren Koller)
10:30	Sulfur Mustard (Agent HD) (Ken Still/Bob Young)
11:30	Lunch
12:30 PM	Sulfur Mustard (Agent HD) (continued)
1:30	1,1,l-Trichloroethane (Mark McClanahan/Tessa Long)
2:30	Break
2:45	1,1,l-Trichloroethane (continued)
4:00	1,2-Dichloroethylene (Ernie Falke/Cheryl Bast)
5:30	Adjourn for the day

Wednesday, December 8, 1999

8:30 AM	Phosphine (Ernie Falke/Cheryl Bast)
10:00	Break
10:15	Bromine: AEGL-3 (Zarena Post, Larry Gephart/Sylvia Talmage)
11:30	Uranium hexafluoride (George Rusch/Cheryl Bast)
1:30 PM	Adjourn meeting

NAC/AEGL-16
Dec. 6-8, 1999

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Don Hansen	DOE-BNL	(516) 344-7535
Cheryl Bast	ORNL	865-574-7581
Tessa Long	ORNL	865-241 0051
Paul Dusaud	HSIA	202-775-0232
James Barter	PPG	412-434-2801

MEMORANDUM

TO: George Rusch

FROM: John Morawetz

DATE: December 1, 1999 FAXed 973-455-5405

RE: December 1999 AEGL meeting

I would like to suggest that the AEGL committee finalize our views on the industrial hygiene questions we have been discussing for the last year and a half. I would like a vote on the afternoon of December 7 or the morning of the 8th on this suggested SOP language in the following order:

1) Frequently exposure to a high level of a substance for a short time period can cause a toxic effect far more serious than exposure to a lower level for a longer period of time. In fact, while exposure to a chemical at a given level for 30 minutes might only result in a minimal toxic response, exposure to twice that level for 15 minutes could be lethal.

   A ceiling level not to be exceeded is the AEGL value with the shortest (least) time. For most chemicals, this will be the 30 minute value, unless a shorter period is determined (for example 10 minutes).

2) Each individual AEGL value and its corresponding exposure period represents a discrete dose-response threshold for humans for an adverse health effect based on a one time, episodic exposure at the specified concentration and exposure period. Therefore, the AEGL values are not intended to apply to subsequent exposures to the chemical at the same AEGL level or any other AEGL level, irrespective of whether the subsequent airborne concentrations are higher or lower and the exposures intermittent or continuous. For example, the AEGL-2 value for 30 minutes was not established with the consideration that additional exposures to the same chemical may occur in the future. This same example applies at all specified exposure levels.

Please let me know if you need any other additional material.

c: Frank D. Martino
Secretary/Treasurer's Office
Eric Bray
Michael Sprinker
Roger Garrett, EPA FAX 202-401-2863
Paul Tobin, EPA FAX 202-260-0981
Po-Yung Lu, ORNL FAX 423-241-0397

ACUTE EXPOSURE GUIDELINE LEVELS (AEGLs) FOR ETHYLENE OXIDE (ETO)

AEGL-2

ORNL STAFF SCIENTIST: KOWETHA A. DAVIDSON
CHEMICAL MANAGER: KYLE BLACKMAN

NAC/AEGL -16
DECEMBER 6-8, 1999
WASHINGTON, DC

Attachment 4

REASONS FOR RE-VISITING AEGL-2

- The study used to derive AEGL-2 resulted in dead implants (dominant lethality) in addition to the CNS effects.
- More appropriate study is needed for deriving AEGL-2 level.
- Genetic toxicity should be taken into account in the selection of AEGL-2 endpoint.

HUMAN DATA APPLICABLE TO AEGL-2

- Irritation to eyes and upper respiratory tract, wheezing, coughing, shortness of breath, apnea, immunological asthma
- Muscle weakness, muscle twitching, malaise, incoordination, peripheral neuropathy, dizziness, and gastrointestinal effects
- Concentrations at which these effects occurred exceeded 500 ppm

ANIMAL DATA APPLICABLE TO AEGL 2

DEVELOPMENTAL AND REPRODUCTIVE EFFECTS IN ANIMALS

Snellings et al., 1982; BRRC, 1993

- NOEL for developmental effects in rats: 33 ppm, 6 h/day, GD 6-15
- Minimal growth retardation (4% compared with controls) in rats at 50 ppm, 6 h/day, GD 6-15
- Slightly greater growth retardation (5–10% compared with controls) in rats at 100–225 ppm, 6 h/day, GD 6-15

OTHER DEVELOPMENTAL EFFECTS

Rutledge and Generoso, 1989

- Fetal deaths, hydrops, and other malformations at 1200 ppm 1.5 h, GD 1

Saillenfait et al., 1996

- No developmental effects in rats at 400, 800, 1200 ppm, 0.5 h/day or 0.5 h/day, 400 ppm, 3 × /day GD 6–15
- Growth retardation at 200, 800, and 1200 ppm, 0.5 h/day, 3 × /day, GD 6–15

Hackett et al., 1982

- No developmental effects in rabbits at 150 ppm, 7 h/day, GD 7–19

GENETIC EFFECTS IN GERM CELLS

- DNA strand breaks and unscheduled DNA synthesis in mice at 450 ppm for 4 h; 900 ppm for 2 h; or 1800 ppm for 1 h

- Dominant lethality in mice at 1000 ppm for 4 h; 400 or 500 ppm for 6 h/day, 4 days; 300 ppm 6 h/day, 600 ppm 3 h/day, or 1200 ppm for 1.5 h/day for 4 days.

- Heritable translocation in mice at 165–300 ppm 6 h/day, 5 day/week for 6 weeks then 7 days/week for 2.5 weeks.

AEGL-2 DERIVATION

Study: **BRRC, 1993**: S-D female rats exposed to 0, 50, 125, or 225 ppm ETO 6 h/day, on GD 6-15 inclusive. Measured concentrations within 3% of target. Fetal growth was retarded by 3-4%, 5%, and 10%, respectively, compared with the control group. The effect at the 50-ppm exposure level approximated the threshold for detection of fetal growth retardation and was used for deriving AEGL-2.

Uncertainty factors:

3 for intraspecies sensitivity

- polymorphism in the glutathione detoxification pathway for ETO; however, only 10% of ETO metabolism is via glutathione conjugation
- data suggest only a small impact of polymorphism in vivo in humans;
- 50 ppm is at least fivefold lower than the odor threshold and level that would cause sensory irritation.

Uncertainty factors continued:

1 for interspecies sensitivity

- systemic uptake, distribution, and modes of action are similar across species
- Rhomberg et al. (199) showed that the relationship between concentration of ETO in air and hemoglobin adduct formation (measure of internal dose) is linear for several species (mouse, rat, rabbit, and human);
- ETO is metabolized primarily by glutathione conjugation and nonenzymatic hydrolysis (ETO is not a substrate for epoxide hydrolase); 75% of ETO metabolism in the mouse is via glutathione conjugation, 50% in the rat, and only 10% in humans.
- ten Berge noted in his comments on the NAC/AEGL Standing Operating Procedures: ...."I think that man is the most unsensitive species for ethylene oxide and that a factor of 10 is not justified at all in case of acute toxic effects."

N-Value used to extrapolate across time periods

n = 1.2 based on lethality data for the rat.

AEGL-2 Values			
30 minutes	1 hour	4 hours	8 hours
132 ppm (238 mg/m^3))	74 ppm (133 mg/m^3)	23 ppm (41 mg/m^3)	13 ppm (23 mg/m^3)

Study: BRRC, 1993

Intraspecies UF = 3

Interspecies UF = 1

Scaling factor = 1.2 based on lethality study in rats

AEGL VALUES					
Class.	PROPOSED AEGL VALUES FOR ETHYLENE OXIDE				
	30 minutes	1 hour	4 hours	8 hours	Endpoint (Reference)
AEGL-1	No values derived				
AEGL-2	132 ppm (238 mg/m^3)	74 ppm (133 mg/m^3)	23 ppm (41 mg/m^3))	13 ppm (41 mg/m^3)	Developmental toxicity BRRC, 1993
AEGL-3	360 ppm (648 mg/m^3)	200 ppm 360 mg/m^3)	63 ppm (113 mg/m^3)	35 ppm (63 mg/m^3)	Lethality Jacobson et al., 1956

BHOPAL DISASTER

Immediate Effects:

- death
- coughing, pulmonary edema
- eye irritation, lacrimation, photophobia, corneal ulceration
- spontaneous abortion

Long-term Effects:

- cough, breathlessness, chest pain
- reduced pulmonary function
- eye irritation, reduction in vision, corneal opacity
- infant death

EFFECTS OF MIC IN ANIMALS

Death

Signs of irritation to mucus membranes

Histological lesions in lung

Decrements in pulmonary function

Litter resorption

Little species variation

SUMMARY OF EXPERIMENTAL STUDIES WITH MIC IN HUMANS

Concentration	Duration	Effects	Reference
0.4 ppm	1 - 5 min	NOEL	Kimmerle and Eben, 1964
0.3 and 1 ppm	1 min	NOEL	Mellon Institute, 1963a
0.5 ppm	10 min	eye, nose, and throat irritation, tearing	Mellon Institute, 1970
2 and 4 ppm	1 - 5 min	irritation	Kimmerle and Eben, 1964
21 ppm	"short"	intolerable	Kimmerle and Eben, 1964
1.75, 2, and 5 ppm	1 min	eye, nose, and throat irritation, tearing	Mellon Institute, 1970; 1963a
1 ppm	10 min	eye, nose, and throat irritation, tearing	Mellon Institute, 1963a

SUMMARY OF NONLETHAL ANIMAL DATA WITH MIC

IRRITATION LEVELS

Concentration	Duration	Species	Reference
8 ppm	6 hours	rats	IRDC, 1964
2.4 ppm	6 hours	guinea pigs, rats, mice	Dodd et al., 1985; 1986
230 ppm	0.1 hour	rats	Dow Chemical, 1990
35 ppm	1 hour	rats	Dow Chemical, 1990
5.4 ppm	4 hours	rats	Dow Chemical, 1990
9 ppm	3 hours	mice	Varma et al., 1988

REVERSIBLE HISTOPATHOLOGY

6 ppm	3 hours	guinea pig	Ferguson and Alarie, 1991
13 ppm	3 hours	guinea pig	Ferguson and Alarie, 1991

DEVELOPMENTAL TOXICITY DATA

Varma et al., 1990

Species: rats and mice

Exposure: 9 ppm for 3 hours on GD 10 (rats) or GD 8 (mice)

Results:

- decreased maternal, fetal, and placental weights
- increased resorptions/litter; 36% of rats and 70% of mice with complete litter resorption

Varma et al., 1987

Species: mice

Exposure: 2, 6, 9, or 15 ppm for 3 hours on GD 8

Results:

- decreased maternal, fetal, and placental weights at all concentrations
- 9 and 15 ppm: death of 2 dams
- complete litter resorption in 8/10 at 9 ppm and 12/16 at 15 ppm

DEVELOPMENTAL TOXICITY DATA - continued

Schwetz et al., 1987

Species: mice

Exposure: 1 or 3 ppm for 6 hr/day on GD 14-17

Results:

- 1 and 3 ppm: increased dead fetuses at birth
- 3 ppm: increased pup mortality during lactation

	Pups/litter (% dead)		
Day	0 ppm	1 ppm	3 ppm
0	10.4 (0.4)	8.7 (3.3)*	8.0* (6.4)*
1	10.3	8.7	7.8*
4 (0-4)	10.2 (2.0)	8.6 (0.8)	7.1* (11.3)*

DERIVATION OF n FROM RAT LC_{50} DATA

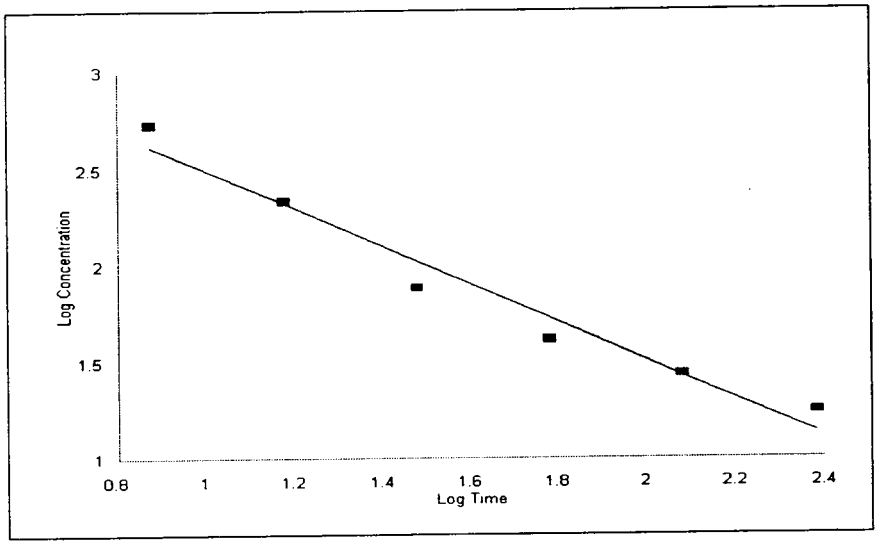
Reference: Mellon Institute, 1970

Duration	LC_{50}
7.5 min	541 ppm
15 min	216 ppm
30 min	76.6 ppm
60 min	41.3 ppm
120 min	27.4 ppm
240 min	17.5 ppm

Equation: $y = 3.48 - 1.01x$

$r^2 = 0.9642$

$n = 1.01$



Proposed AEGL-2 for Methyl Isocyanate

Key study: Varma, 1987

Exposure: 2 ppm for 3 hours on GD 8

Toxicity endpoint: decreased fetal body weight

Scaling: $C^1 \times t = k$

Estimate: exposure concentration reduced by a factor of 3 to estimate threshold for effect

Uncertainty factors: 10: 3 - sensitive individuals
3 - interspecies

Proposed AEGL-2 Values for MIC (ppm [mg/m^3])				
	30-min	1-hr	4-hr	8-hr
AEGL-2	0.13 [0.32]	0.067 [0.16]	0.017 [0.034]	0.008 [0.02]

Supporting data:

Exposures: 3 ppm for 2 hours - cardiac arrhythmias in rats (Tepper et al., 1987)

1 ppm for 10 minutes - eye irritation and tearing in humans (Mellon Institute, 1963a)

Interim AEGL-3 for Methyl Isocyanate

Key study: Schwetz et al., 1987

Exposure: 1 ppm for 6 hr/day on GD 14-17

Toxicity endpoint: increased number of dead fetuses at birth

Scaling: $C^1 \times t = k$

Uncertainty factors: 30: 10 - mechanism of systemic effects unknown
3 - interspecies

AEGL-3 Values for MIC (ppm [mg/m^3])				
	30-min	1-hr	4-hr	8-hr
AEGL-3	0.40 [0.95]	0.20 [0.47]	0.05 [0.12]	0.025 [0.06]

Supporting data:

Exposures: 9 ppm for 3 hours - increased resorptions in rats and mice (Varma, 1987; Varma et al., 1990)

Resulting AEGL-3 values: 1.8, 0.9, 0.23, and 0.11 ppm

Summary of Proposed AEGL Values (ppm [mg/m^3])				
AEGL Level	**30-minute**	**1-hour**	**4-hour**	**8-hour**
AEGL-1	**n/a**	**n/a**	**n/a**	**n/a**
AEGL-2	**0.13 [0.32]**	**0.067 [0.16]**	**0.017 [0.034]**	**0.008 [0.02]**
AEGL-3	**0.40 [0.95]**	**0.20 [0.47]**	**0.05 [0.12]**	**0.025 [0.06]**

ACGIH TLV-TWA: 0.02 ppm (0.047 mg/m^3) [skin] (ACGIH, 1991; 1998)

NIOSH TWA: 0.02 ppm (0.047 mg/m^3) [skin]; IDLH = 3 ppm (NIOSH, 1994; 1997; based on Kimmerle and Eben, 1964)

OSHA TWA: 0.02 ppm (0.047 mg/m^3) [skin] (OSHA, 1995)

ERPG levels 1, 2, and 3 are 0.025 ppm, 0.5 ppm, and 5 ppm, respectively (AIHA, 1998)

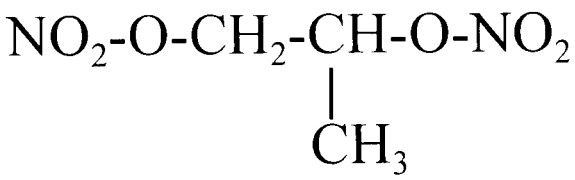
ACUTE EXPOSURE GUIDELINE LEVELS (AEGLs)

FOR

PROPYLENE GLYCOL DINITRATE

(Cas No. 6423-43-4)

(OTTO FUEL II; CAS No. 106602-80-6)



ORNL Staff Scientist: Sylvia Talmage
Chemical Manager: William Bress
Chemical Reviewers: Robert Snyder, William Pepelko, Kenneth Still
NAC-16 Meeting, December 6-8, 1999 - Consideration of AEGL-3 values

Attachment 6

The following AEGL-1 and AEGL-2 values were accepted at the NAC-15 meeting.

Classification	Exposure Duration			
	30-Minute	**1-Hour**	**4-Hour**	**8-Hour**
AEGL-1 (Nondisabling)	0.33 ppm (2.3 mg/m^3)	0.17 ppm (1.1 mg/m^3)	0.05 ppm (0.34 mg/m^3)	0.03 ppm (0.17 mg/m^3)
AEGL-2 (Disabling)	2.0 ppm (14 mg/m^3)	1.0 ppm (6.8 mg/m^3)	0.25 ppm (1.7 mg/m^3)	0.13 ppm (0.8 mg/m^3)

The AEGL-1 values are based on the threshold for mild headaches in 20 human volunteers: 0.1 ppm for 6 hours and 0.5 ppm for 1 hour (Stewart et al., 1974).

The AEGL-2 values are based on severe headaches in 3 subjects accompanied by dizziness in one subject and slight loss of equilibrium in two subjects after 6 hours of exposure to 0.5 ppm.

AEGL-1 and -2 values were time-scaled based on $c^n \times t = k$, where $n = 1$. The $n = 1$ relationship is based on concentrations and exposure durations that induced both mild and severe headaches.

No sensitive subpopulations were identified; an intraspecies uncertainty factor of 3 was applied.

Animal Studies - Consideration of AEGL-3

No deaths following single exposures of ≤8 hours

Monkeys:

70-100 ppm for 6 hours (Jones et al., 1972)

Convulsions, vomiting, pallor, cold extremities, semiconsciousness

10, 15, or 33 ppm for 90 days (Jones et al., 1972)

No toxic signs, normal weight gain

Some histological changes

2 ppm for 4 hours (Mattsson et al., 1981)

Some changes in VER

No change in cognitive behavior

Dogs, rats, guinea pigs:

10, 15, or 33 ppm for 90 days (Jones et al., 1972)

Methemoglobinemia (up to 23%); decreases in hemoglobin and hematocrit (dog)

Some histological changes

Rats:

199 ppm for 4 hours (Jones et al., 1972)

No toxic signs (methemoglobin level of 23.5%)

Derivation of AEGL-3

The proposed AEGL-3 values are based on the 70-100 ppm concentration for 6 hours which resulted in clonic convulsions, semi-consciousness, and other signs in monkeys. Although no deaths occurred, the signs are serious enough to be considered the threshold for death.

Interspecies uncertainty factor: 3

The monkey is an appropriate species for extrapolation to humans.

Both the monkey and humans showed changes in the VER at similar concentrations.

PGDN has some CNS depression properties; the threshold for CNS depression (for anesthetics) does not differ widely among species or individuals.

Intraspecies uncertainty factor: 3

Methemoglobin formation, observed at high concentrations in some animal studies, should not be a problem for humans at these low concentrations.

The 6-hour 70 ppm concentration was divided by a total uncertainty factor of 10 (3 for interspecies and 3 for intraspecies) and scaled across time. Because no data were available for time scaling with the endpoint of lethality, the more conservative time-scaling values of $n = 1$ for the 8-hour value and $n = 3$ for the 30 minute and 1- and 4-hour values were used.

ACCEPTED AEGL-1 AND AEGL-2 VALUES
PROPOSED AEGL-3 VALUES

Classification	Exposure Duration			
	30-Minute	**1-Hour**	**4-Hour**	**8-Hour**
AEGL-1 (Nondisabling)	0.33 ppm (2.3 mg/m^3)	0.17 ppm (1.1 mg/m^3)	0.05 ppm (0.34 mg/m^3)	0.03 ppm (0.17 mg/m^3)
AEGL-2 (Disabling)	2.0 ppm (14 mg/m^3)	1.0 ppm (6.8 mg/m^3)	0.25 ppm (1.7 mg/m^3)	0.13 ppm (0.8 mg/m^3)
AEGL-3 (Lethal)	16 ppm (114 mg/m^3)	12 ppm (86 mg/m^3)	8.0 ppm (57 mg/m^3)	5.3 ppm (38 mg/m^3)

AEGL-1 and -2 values were time-scaled based on $c^n \times t = k$, where $n = 1$.

Because no data were available for time scaling with the endpoint of lethality, the more conservative time-scaling values of $n = 3$ for the shorter time periods and $n = 1$ for the longer time period were used to derive the AEGL-3 values.

Potential Methemoglobin Formation in Infants (Calculations by Bob Benson)
Infants are more susceptible to methemoglobinemia than adults.

Calculation of N released from exposure to PGDN at the 8-hour AEGL concentrations:
Assumptions:

a breathing rate in infants of 4.5 m^3/day (U.S. EPA Exposure Factors Handbook)
100% of the PGDN that enters the lung is absorbed into the circulatory system
1 molecule of N per molecule of PGDN (M.W. = 14/166)

4.5 m^3/24 hours x 8 hours/24 hours x 0.17 mg/m^3 = 0.26 x 14/166 = 0.02 mg
4.5 m^3/24 hours x 8 hours/24 hours x 0.8 mg/m^3 = 0.1.2 x 14/166 = 0.10 mg
4.5 m^3/24 hours x 8 hours/24 hours x 38 mg/m^3 = 57 x 14/166 = 4.8 mg

EPA's reference dose for nitrate-nitrogen (NO_3^-) is based on a clinical study in newborn infants. That study showed that ingestion of 10 mg/day of nitrate-nitrogen did not cause an increase in the measured amount of methemoglobin. Therefore, there should be no problem if the N is released as nitrate. There are no data, however, for nitrite-nitrogen (NO_2^-). EPA applied a modifying factor of 10 to derive a reference dose (chronic) for nitrite nitrogen of 1 mg/day. Metabolism studies with PGDN show that released nitrite-nitrate is rapidly converted to nitrate. It is unlikely that methemoglobin levels from nitrite would approach lethal levels.

Acute Emergency Guideline Levels (AEGLs) for Chemical Warfare Agents

OVERVIEW OF US CHEMICAL AGENT PROGRAM

Presentation to NAC/AEGL
December 7, 1999

Veronique Hauschild, MPH
Environmental Health Risk Assessment and Risk Communication Program
US Army Center for Health Promotion and Preventive Medicine
(USACHPPM), APG, MD 410-436-5213

1

Acute Emergency Guideline Levels (AEGLs) for Chemical Warfare Agents

WHY:

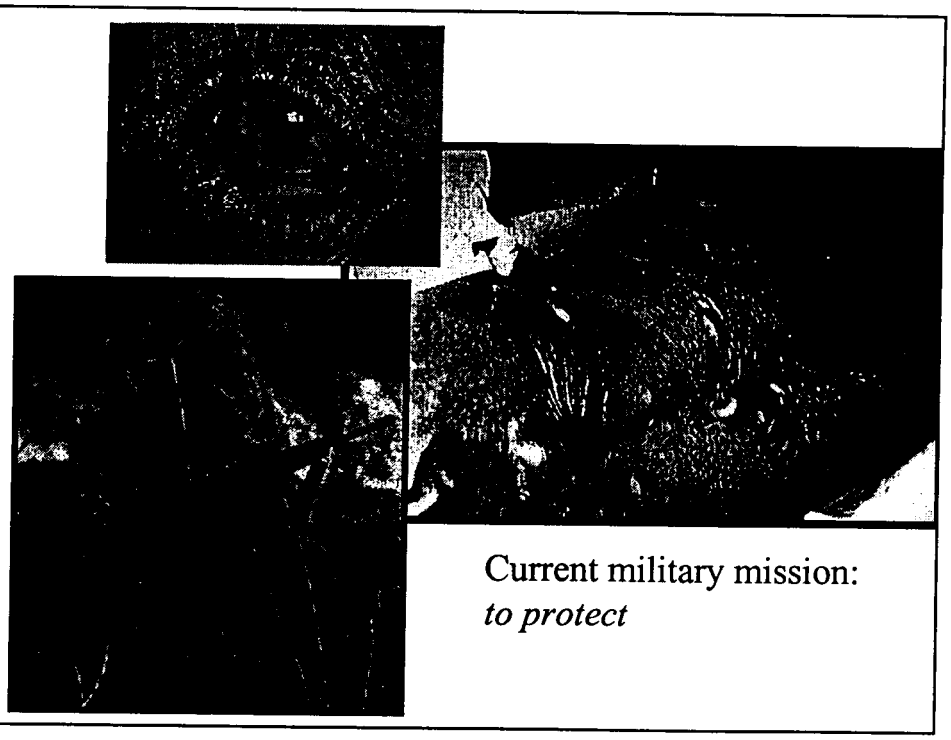
Although the 1990 Bilateral Destruction Agreement and more recent Chemical Weapons Convention have effectively ended production of all chemical warfare munitions (CWM) in the U.S., the potential for a chemical agent incident, particularly at Army storage installations, continues to exist.

2

Chemical Warfare Agents in the US

- Nerve Agents
  - G-agents (GA, GB, GD)
  - VX
- Vesicants/Blister Agents
  - Sulfur Mustard (H, HD)
  - Lewisite
  - Mixtures (HT, HL)

3



Current military mission:
to protect

"Incidents" May involve Accidental or Deliberate Releases of Agent

- Spill
  - Onto ground or other surface
  - Exposures may result from direct contact or from evaporation and drift of vapor
- Explosion
  - Example – from unstable munition
  - May cause formation of airborne droplets
  - Smaller droplets (aerosols) and vapors may travel far
- Fire
  - Aerosols and vapors formed
  - Agent lofted by heated air, increased capacity to travel

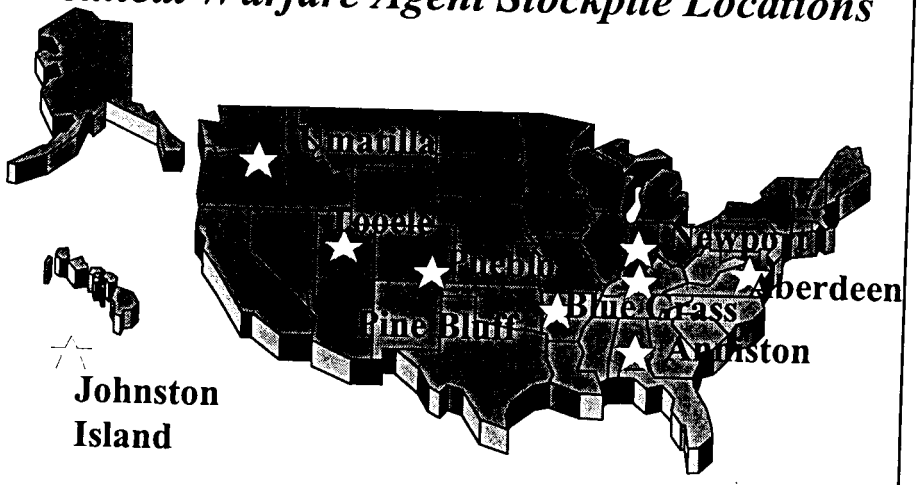
5

Types of Potential Chemical Warfare Agent Releases

- STOCKPILE (8 States + Johnston Island)
- NON- STOCKPILE SITES*
  - Installations (ex: Ft. Polk, Raritan Army Ammunition Plant)
  - Formerly Used Defense Sites (FUDS) (Spring Valley-American University, Wash D.C.)
- ACTS OF TERRORISM
  - EX: Tokyo subway incident
  - Atlanta Olympics

6

Chemical Warfare Agent Stockpile Locations



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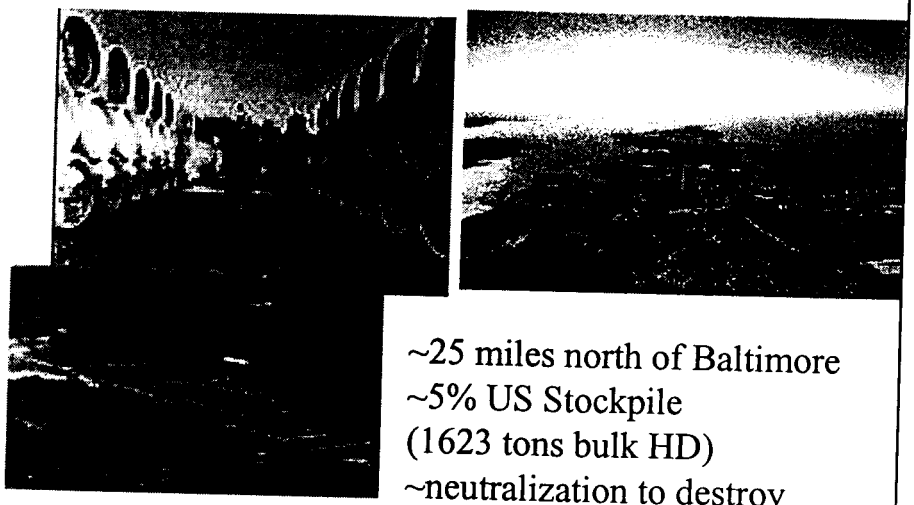
Aberdeen Proving Ground (Edgewood), Maryland



~25 miles north of Baltimore
~5% US Stockpile
(1623 tons bulk HD)
~neutralization to destroy

8

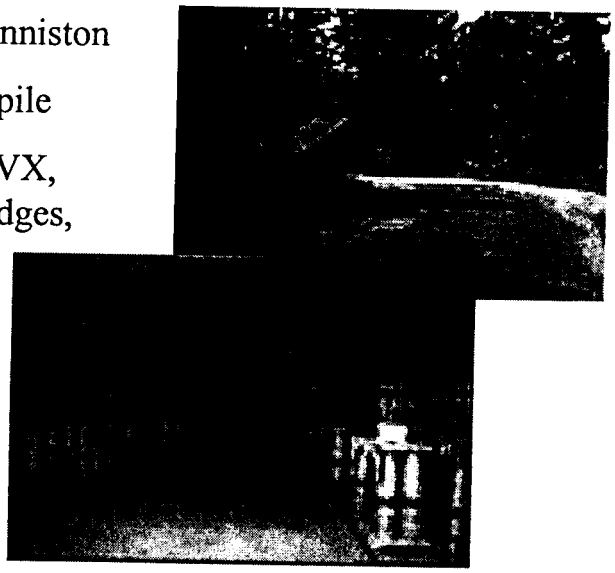
Anniston, Alabama

~8 miles west Anniston

~7.4% US Stockpile

(2254 tons: GB, VX, HD; mines/cartridges, projectiles)

~incineration to destroy



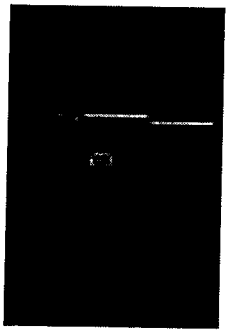
Pueblo, Colorado

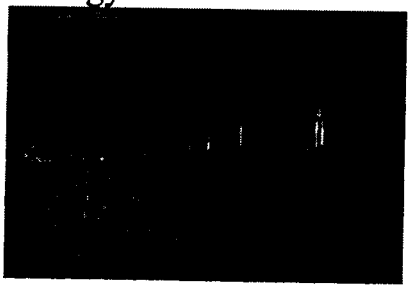
~14 miles east Pueblo

~storage since the 50's

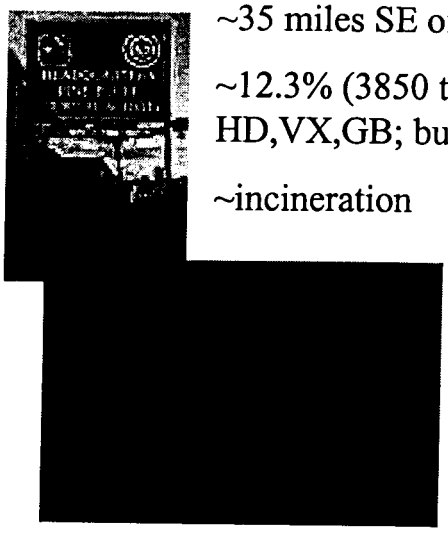
~8.5% (2611 tons:HD projectiles, mortar rounds)

~destruction technology undetermined





Pine Bluff, Arkansas

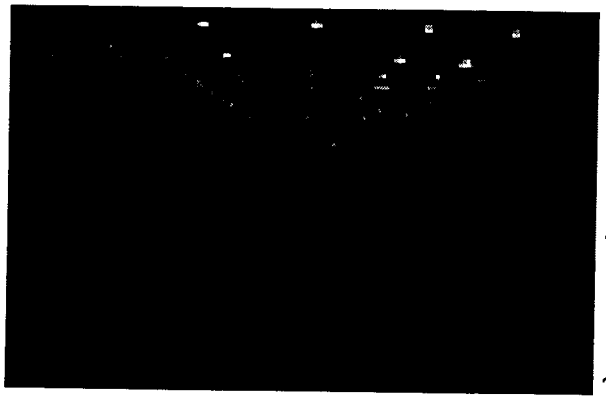


~35 miles SE of Little Rock

~12.3% (3850 tons: HD,VX,GB; bulk, rockets)

~incineration

Newport, Indiana

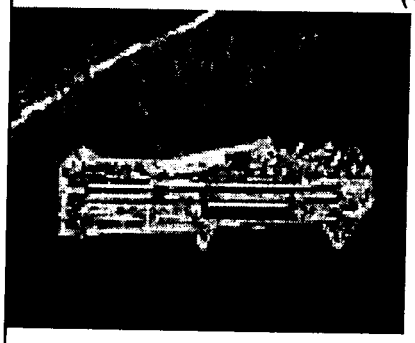


~2 miles south of Newport/western Indiana

~4 % stockpile (1269 ton VX bulk)

~Neutralization technology to destroy

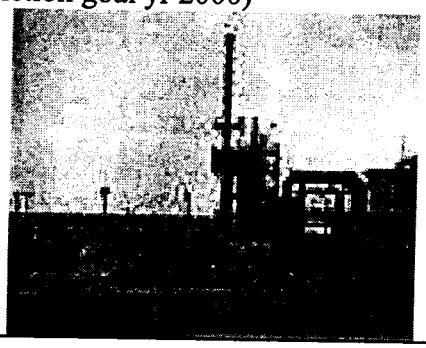
Johnston Island, Johnston Atoll (Pacific)



~Built 1985, 825 mi south Hawaii

~ all agents/items, stored since 70s (shipped from Germany, Solomon Islds)

~80% of original stockpile destroyed (completion goal yr 2000)

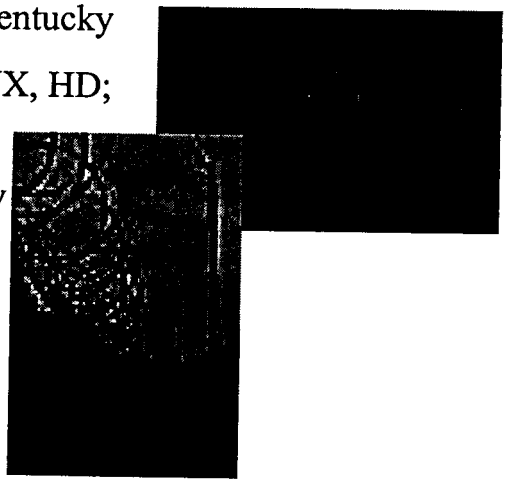


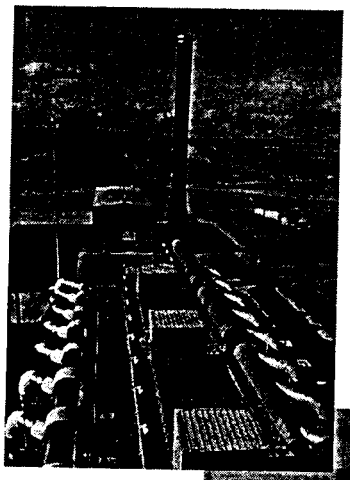
Lexington-Blue Grass (Richmond), Kentucky

~250 acres in central Kentucky

~1.7% (523 tons:GB, VX, HD; rockets, projectiles)

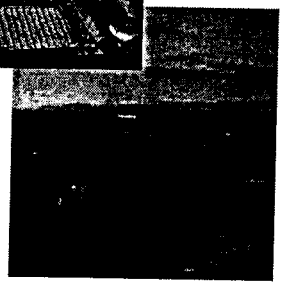
~destruction technology undetermined



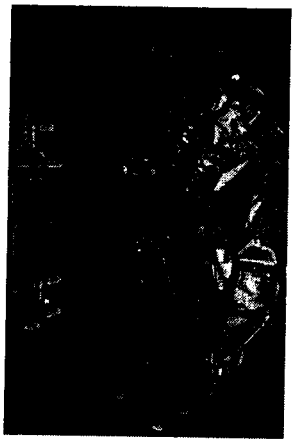


Deseret (Tooele), Utah

- 22 miles south of Tooele
- 44.5% (13,616 tons – GA,GB, VX, HD, Lewisite)
- Already destroyed over 3 million pounds (incineration)



Umatilla, Oregon



~7 miles west Hermiston

~11.6% (3717 tons: GB, VX projectiles, mines, bombs and bulk HD)

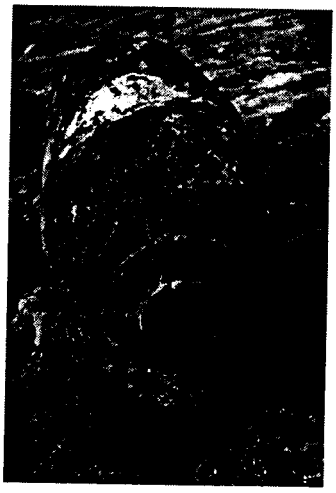
~destruction to be incineration

NonStockpile Sites: A Growing Problem

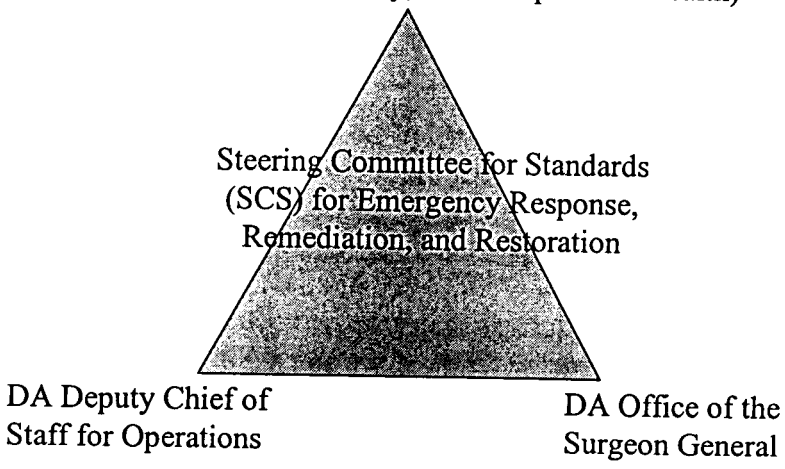
- Numerous sites, many still unknown
  - 96 locations (224 sites) [1996 survey]
    - Army – 37
    - Navy – 5
    - Air Force –6
    - Defense Logistics Agency - 3
    - Formerly Used Defense Sites (FUDS)- 45
  - 38 States plus Virgin Islands and District of Columbia
    - 1996 Survey added 5 States to 1993 survey
- No controlled destruction technology yet available (pilot tests ongoing)
- Potential for human exposures and environmental releases

17

Non-Stockpile



Policy Making for Chemical Warfare Agent Health Standards



Key Organizations: Army 'Chemical' Community

- U.S. Army Soldier Biological and Chemical Command (SBCCOM)
  - Technical Escort Unit(s) (TEU)
  - Edgewood Chemical and Biological Center (ECBC)
  - Chemical Stockpile Emergency Preparedness Program (CSEPP)
- Program Manager for Chemical Demilitarization (PMCD)
- Project Manager for NonStockpile Chemical Materiel (PMNSCM)
- US Army Chemical School (Chem School)
- US Army Chemical and Nuclear Agency (USANCA)

20

Organizations Involved with Health/Environmental Issues:

US Army:

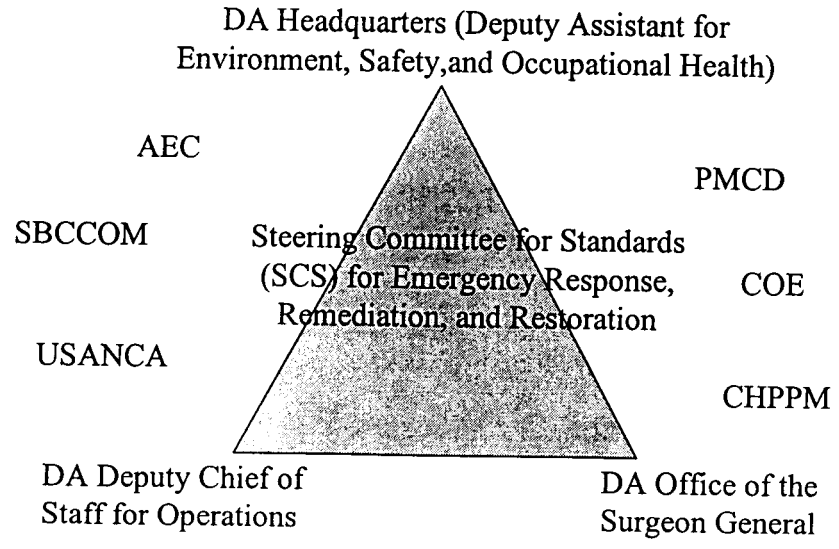
- Center for Health Promotion and Preventive Medicine (CHPPM)
- US Army Medical Research Institute for Chemical Defense (MRICD)
- Army Environmental Center (AEC)
- Corps of Engineers (COE)

Other Federal:

- US Department of Health and Human Services - Centers for Disease Control and Protection (CDC)
- US Environmental Protection Agency (EPA)
- Federal Emergency Management Agency (FEMA)

21

Policy Making for Chemical Warfare Agent Health Standards



Some "Issues" Regarding the CWA AEGLs and their (Potential) Applications

23

"Incidents" May involve Accidental or Deliberate Releases of Agent

- Spill
  - Onto ground or other surface
  - Exposures may result from direct contact or from evaporation and drift of vapor
- Explosion
  - Example – from unstable munition
  - May cause formation of airborne droplets
  - Smaller droplets (aerosols) and vapors may travel far
- Fire
  - Aerosols and vapors formed
  - Agent lofted by heated air, increased capacity to travel

24

The Hazard of Primary Interest for Catastrophic Events

- Most anticipated exposures to a population are expected to be VAPORS
- Vapors pose hazard when inhaled and/or contact with skin and eyes
- Agent vapors inhalation poses greatest potential for serious injury because rapidly absorbed by respiratory tract tissues; lethality may result
- Skin is a barrier to agent absorption
- Lethal cumulative exposure for agent vapor inhalation is several times lower than lethal cumulative exposure for vapor contact with skin

25

Current "Emergency" Levels

- Referred to by Army as "No effect levels" or "No significant effect levels"
- "Endorsed" by CDC ('1994 Thacker letter') as "Acute Threshold Effects Levels"

Recommended Acute Threshold Effects Levels for Determining Emergency Evacuation Distances in the CSEPP Program (CDC, 94)

Chemical Agent	Level (mg-min/m^3)
Mustard (H, HT, HD)	2.0
Lewisite (L)	2.0
Sarin (GB)	0.5
VX	0.4

26

Anticipated "Uses" of an AEGL

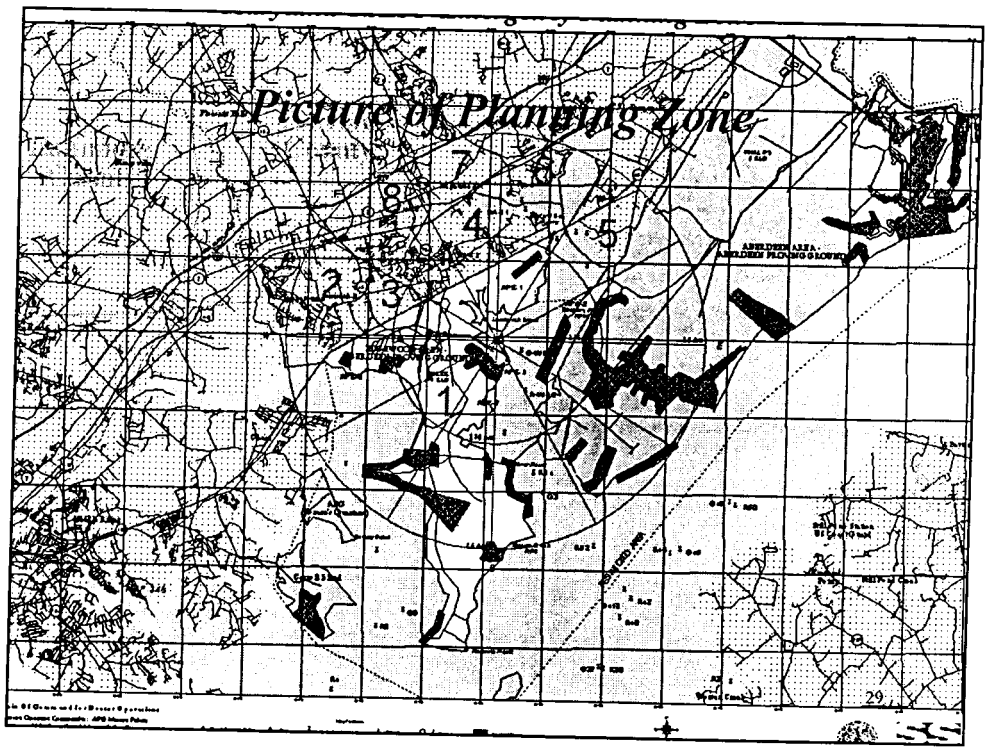
- Update currently used values;
- Provide scientifically and legally defensible values
- Assess requirements for new modeling/re-vamping emergency plans for fixed Stockpile sites

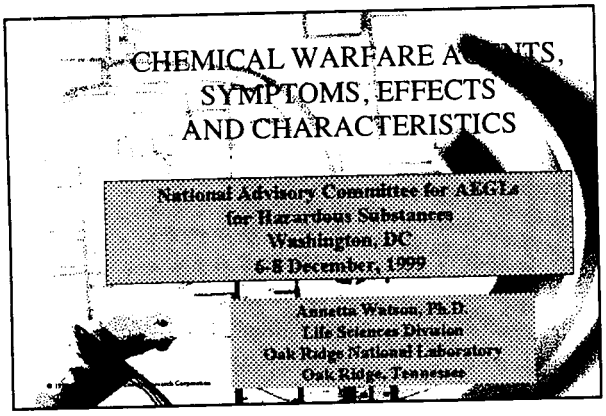
27

Possible "Impacts" of an AEGL -1

- Increased planning zone areas
- Requests for additional resources (State, counties)
  - New roads/bridges
  - New 'safe houses'
  - More medical supplies/antidotes (that become outdated)
- General Public Outcry
  - General concern/worry
  - Property values

28


Picture of Planning Zone



ACKNOWLEDGMENT

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C02

GA GB VX

NERVE AGENTS

- Attacks body's nervous system
- Scientific classification: Organophosphate
  - Organophosphates also include insecticides Malathion and Parathion

C03

SPECIFIC NAMES

Abbreviation	Common Name	Referred to As
VX	VX	VX
GB	Sarin	GB or G-agent
GA*	Tabun	GA or G-agent

*Small amount known to be stored at Deseret Chemical Depot, Utah

CO4

PHYSICAL PROPERTIES

- Usually liquid in normal state
- Becomes volatile and generates vapors if heated
- Potential for release if in vapor or aerosol form
- All nerve agents originally in liquid form (includes thickened agent)
- Most distinguishable factors are consistency and color

CO3

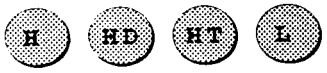
G-AGENTS

- GB usually colorless, watery
- GA may be pale to dark amber
- Pure form has almost no odor
- GB only major G-agent in unitary stockpile

CO5

- Oily liquid
- Resembles 20-weight motor oil
- Pale amber color
- Persistent; designed to cling to whatever it splatters on
  - Persistence is weather-dependent

CO1



BLISTER AGENTS (VESICANTS)

- Poisons that destroy cells
- Blister most noticeable effect
- Sulfur Mustard and Lewisite

CO2

SPECIFIC NAMES

Abbreviation	Common Name	Referred to As
H, HD, HT	Sulfur Mustard	H, HD, HT
L	Lewisite	L

CO3

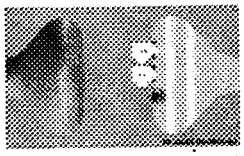
MUSTARD PHYSICAL PROPERTIES

- Liquid or solid form in normal state
- Becomes volatile and generates vapors if heated
  - Burns well once ignited
- Pale amber brown color in liquid form
- Colorless gas when vaporized
- Mustard-garlic smell

CO10

HOW NERVE AGENTS WORK
Normal Neural Transmission

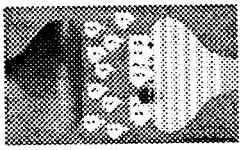
- Acetylcholine crosses synapse between nerve endings
  - How impulses travel between nerve cells
- If junction with skeletal muscle, muscles cells contract
- If junction with smooth muscles, muscles move rhythmically
- If junction with gland, glandular cells secrete
- Acetylcholine inactivated by acetylcholinesterase in readiness for next transmission



CO11

HOW NERVE AGENTS WORK
Abnormal Neural Transmission After Nerve Agent Intoxication

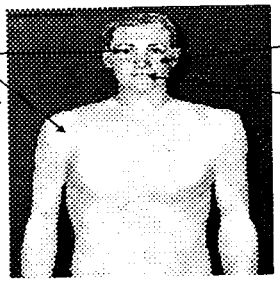
- Nerve agent blocks acetylcholinesterase so it cannot destroy acetylcholine
  - Acetylcholine accumulates and continue to stimulate target nerve
  - Muscles twitch uncontrollable and repetitively
  - Excess secretions of glands



CO12

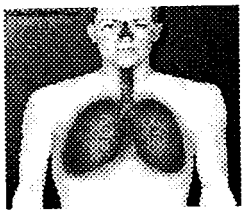
ROUTES OF EXPOSURE

- Direct Contact
- Inhalation
- Ingestion



CO13

INHALATION

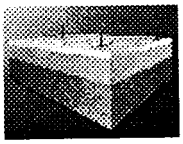


- Nerve agent enters through respiratory system
- Rapidly and effectively enters into blood stream

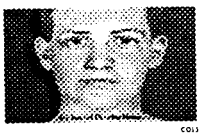
Respiratory failure chief cause of death after severe exposure

CO14

DIRECT CONTACT



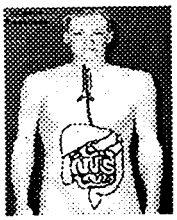
- Skin or eyes are touched with agent vapor or liquid
- All nerve agent absorbed through skin
  - VX remains on skin and absorbed more completely
  - GB evaporates quickly, but still threat
- Scrapes or cuts or other skin damage presents immediate entry points
  - Freshly shaven skin, sunburn, insect bites, rashes
- Eyes most sensitive organ for nerve agent effects



CO15

INGESTION

- Ingestion of contaminated food or drink, incidental hand to mouth or eye contact, smoking
- Unlikely agent will contaminate food or drink



CO16

SIGNS AND SYMPTOMS

- Signs are objective evidence of a medical condition
- Signs are observed
- Symptoms are subjective evidence (salivation, miosis, runny nose, etc.)
- Symptoms are usually verbally communicated (headache, eye pain, nausea, etc.)

Not all signs and symptoms may appear...

Dose, duration, and route of entry make a difference

CO17

SIGNS AND SYMPTOMS OF NERVE AGENT EXPOSURE

- Miosis
- Dim Vision
- Respiratory Trouble
- Difficulty in Breathing
- Increased Oral/Nasal Secretions
- Localized Sweating
- Nausea and Vomiting
- Abdominal Cramping
- Involuntary Urination or Defecation
- Heartbeat Irregularities
- Generalized Weakness
- Twitching or Muscles Spasms
- Convulsions and Coma

CO18

OTHER SIGNS AND SYMPTOMS OF NERVE AGENT EXPOSURE

- Noted with early or mild exposure:
  - headache
  - anxiety
  - restlessness
  - giddiness
  - irritability

CO19

FACTORS AFFECTING SIGNS AND SYMPTOMS

- Time onset may appear immediately or be delayed
- Reaction depends on
  - which agent
  - amount of agent patient exposed to
  - dose (how much patient absorbed)
  - duration
  - route of exposure
  - sensitivity of person's system

CO20

FACTORS AFFECTING SIGNS AND SYMPTOMS

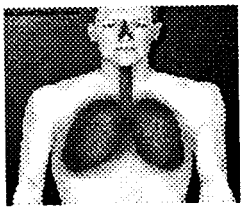
- General rule:

Immediate	**if**	**moderate to large amounts are inhaled**
	if	**moderate to large amounts are spilled onto the skin**
Delayed	**if**	**small amounts are involved**
	if	**agent has been absorbed through skin in small localized area**

CO21

INHALATION PEAK EFFECTS

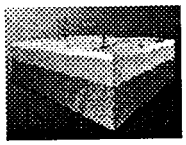
- Effects can occur after single breath
- Immediate response within seconds
- Peak effects usually within 15 - 20 minutes
- After approximately 20 minutes or more, effects usually maximized and will not worsen



CO22

DERMAL PEAK EFFECTS

- Absorption may continue for hours even after decontamination
- Effects may not occur for 1 to 18 hours
- Later effects usually not lethal



CO23

NERVE AGENT EXPOSURE LEVELS

- Mild (May also be effects of initial reaction leading to more serious reaction)

eyes	miosis, pain (deep in eye or head), dim or blurred vision
nose	runny
lungs	"tightness in chest"; bronchoconstriction, secretions in airways, cough, moderate difficulty in breathing

CO26

NERVE AGENT EXPOSURE LEVELS

- Moderate (May also include symptoms under Mild)

eyes:	miosis, pain, dim or blurred vision
nose:	runny (severe), nasal congestion
lungs:	"tightness in chest"; breathing more difficult; secretions more copious
muscles:	feeling of generalized weakness, generalized twitching of large muscle groups
GI:	nausea, vomiting, diarrhea, cramps

CO25

NERVE AGENT EXPOSURE LEVELS

- Severe (May develop symptoms under Mild and Moderate or go directly to these symptoms)

muscles:	convulsions, weakness with eventual loss of muscle tone and capability to function (flaccid paralysis)
lungs:	cessation of respiration
all:	loss of consciousness, coma, death

CO26

NERVE AGENT EXPOSURE LEVELS

- Symptoms may occur after little more than 1 breath of nerve agent vapor
- Large amounts may cause reactions within seconds
- Effects do not worsen appreciably after approximately 20 minutes following cessation of exposure

CO27

NERVE AGENT SKIN EXPOSURE LEVELS

- Mild (May also be effects of initial reaction leading to more serious reaction)

skin	sweating at exposure site
muscles	localized, unorganized contraction of muscle fibers at exposure site ("bag of worms") [fasciculation]

CO28

NERVE AGENT SKIN EXPOSURE LEVELS

- Moderate (May also include symptoms under Mild)

muscles	generalized (at random, all over) fasciculation and twitching, generalized weakness that increases with any form of activity
GI	nausea, vomiting, diarrhea

CO29

NERVE AGENT SKIN EXPOSURE LEVELS

- Severe (May develop from symptoms under Mild and Moderate or go directly to these symptoms)

muscles	extremely weak, convulsions (seizures) with eventual flaccid paralysis
lungs	cessation of respiration
all	sudden loss of consciousness and collapse, death

CO30

NERVE AGENT SKIN EXPOSURE LEVELS

- Larger exposure, shorter onset time
- Large exposure may cause reactions within minutes
- After asymptomatic period, first effect may be loss of consciousness
- Onset time may be as long as 18 hours; however, in such cases effects usually not lethal

CO31

DIFFERENTIAL DIAGNOSIS: NON-AGENT OR AGGRAVATING CAUSES

- Signs and symptoms may also be caused by
  - epilepsy
  - gastroenteritis
  - exposure to agricultural insecticides
  - emphysema
  - cerebrovascular accidents
  - head trauma
  - drug overdose
  - heat illnesses
  - Allergy
  - Upper respiratory malady

CO32

NERVE AGENT INITIAL FIRST AID TREATMENT

- Immediate removal of agent
- Decontamination
  - Ideal decontamination solution is chlorine bleach
- Antidote administration
- Airway management support as necessary
- Must be provided by properly trained and equipped personnel

CO33

NERVE AGENT ANTIDOTES

- Atropine
  - Administered to block receptor sites of acetylcholine
- 2-PAM chloride
  - Restores acetylcholinesterase
- Diazepan (Valium®)
  - Anticonvulsant; controls seizures

CO34

BLISTER AGENT EXPOSURE

CO35

OBJECTIVE

- Identify the specific signs and symptoms of blister agent exposure

CO36

BLISTER (VESICANT) AGENTS

- Destroy individual cells in target tissue
- Blisters most noticeable effect
- Sulfur Mustard and Lewisite in Army's inventory

CO37

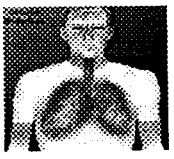
HOW BLISTER AGENTS WORK

- Designed to inflict wartime casualties
- Affect skin tissue and especially harsh on soft membranes
  - Eyes
  - Surface of Eye
  - Lung tissue
  - Mouth
  - Throat
- Greatest effect on warm, moist surfaces
  - Mucous membranes
  - Armpits
  - Knees
  - Groin
  - Buttock
  - Elbows
  - Fold of neck

CO38

BLISTER AGENT EXPOSURE

- Liquid and vapors create extreme hazard
- Greater absorbed dose, greater severity of skin and tissue damage
- Delayed reaction with little or no pain*
- Burning, stinging, redness or blisters usually delayed between 2 to 36 hours*

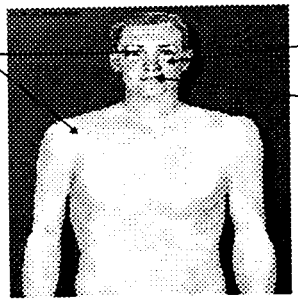


*Except with Lewisite, immediate pain

CO39

ROUTES OF EXPOSURE

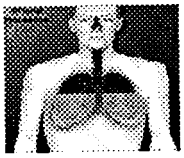
- Direct Contact
- Inhalation
- Ingestion



CO40

INHALATION

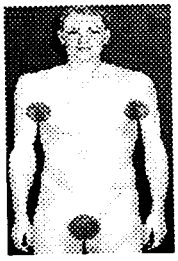
- Inhaled vapors enter body through respiratory system
- Direct access to lining of nose, throat, bronchial tubes
- Prolonged exposure destroys mucous membrane lining
  - Internal inflammation
  - Hemorrhaging
  - Airways and lungs may later become infected
- Most damage to upper airways
  - Heavy exposure; air sacs in lungs are injured and fill with fluids



CO41

DIRECT CONTACT

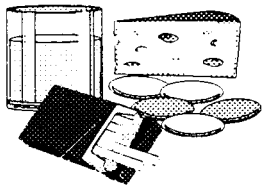
- Skin surface or eye touches liquid or surface on which agent was deposited
  - Secondary contamination
  - Blister fluid non-irritating and does not cause blisters
- Warmth and moisture increase effects
  - Lining around eyelids
  - Inside mouth and nose
  - Between toes
  - Behind knees
  - Groin, armpits, anal area
  - Behind ears



CO42

BLISTER AGENT INGESTION

- Contact with contaminated food, drink, or incidental hand-to-mouth (cigarettes)
  - Mouth
  - Throat
  - Esophagus



CO43

SIGNS AND SYMPTOMS

- Severity of symptoms and how rapidly they develop greatly influenced by weather conditions
  - Hot, humid weather increases action of sulfur mustard
- Onset of sulfur mustard clinical signs and symptoms characteristically delayed for hours
- Onset of Lewisite clinical signs and symptoms immediately on contact

("Lewisite hurts")

CO44

SIGNS AND SYMPTOMS OF SULFUR MUSTARD AGENT EXPOSURE

- Eye Irritation/Inflammation
- Photophobia
- Erythema
- Blisters
- Inflammation of Respiratory Tract
- Systemic and Gastrointestinal Effects

CO45

FACTORS AFFECTING SULFUR MUSTARD SIGNS AND SYMPTOMS

- Characteristically delayed
  - May appear quickly with large exposure
- Reactions depends on
  - which agent
  - amount of agent patient exposed to
  - dose (how much patient absorbed)
  - duration
  - route of exposure
  - sensitivity of person's system
- Inhalation quicker reaction than direct contact

CO46

FACTORS AFFECTING SULFUR MUSTARD SIGNS AND SYMPTOMS

- Inhalation exposure, effects occur after few hours
  - Accompanied by sneezing, coughing, tracheobronchitis
- Direct contact exposure, effects usually delayed
  - Absorption may continue for hours even after decontamination

Not all signs and symptoms may appear...

Dose, duration, and route of entry make a difference

CO47

SULFUR MUSTARD AGENT EXPOSURE LEVELS

- Mild

Skin	no immediate clinical effects (no burning, stinging, or redness); agent becomes "fixed" to tissue within minutes; blisters appear about 2 to 36 hours later
Eyes	within 4 to 12 hours after exposure, itching, tearing, conjunctivitis, sensation of grit in eye, burning and photophobia, some swelling of eyelids

CO48

SULFUR MUSTARD AGENT EXPOSURE LEVELS

- Moderate

Skin	no immediate clinical effects, blisters appear sooner and are more severe than in cases of mild dose
Eyes	within 3 to 6 hours after exposure, increase intensity from mild symptoms: edema of lids to point of near closure, spasms of muscles surrounding eye, increased photophobia, blurred vision, possible discharge, miosis may also occur; severe inflammation of conjunctiva and cornea

CO49

SULFUR MUSTARD AGENT EXPOSURE LEVELS

- Severe

Skin	no immediate clinical effects, blisters appear sooner and are large, death to tissue, skin sloughing may be evident
Eyes	severe pain, increased swelling of lids to point of closure, discharge, possible damage to cornea
Muscles	large amounts may affect nerve endings (Note: This is a systemic effect that may occur after large dose through skin or inhalation or combination)

CO50

SULFUR MUSTARD INHALATION/INGESTION EXPOSURE LEVELS

- Mild

Nose, throat, windpipe	burning sensation, sinus pain, cough
GI	nausea and vomiting

CO51

SULFUR MUSTARD INHALATION/INGESTION EXPOSURE LEVELS

- Moderate

Nose, throat, windpipe	burning sensation
Lungs	chest tightness, severe cough
GI	nausea and vomiting, stomach pains

CO32

SULFUR MUSTARD INHALATION/INGESTION EXPOSURE LEVELS

- Severe

Nose, throat, Windpipe	severe burning
Lungs	difficulty breathing due to airway damage
GI	nausea, vomiting, bloody diarrhea (rare), stomach pains
Muscles	large amounts may affect nerve endings (Note: This is a systemic effect that may occur after large dose through skin or inhalation or combination)

CO33

SULFUR MUSTARD EXPOSURE ONSET OF SIGNS/SYMPTOMS

- Initial signs/symptoms: 2 - 36 hours acute tracheobronchitis
- Approximate for moderate exposure:
  - 2 - 4 hours — chest tightness, hacking cough, hoarseness, sneezing
  - 4 - 16 hours — sinus pain, increased respiration rate
  - 16 - 48 hours — severe cough, unable to speak, very rapid breathing
  - 24 - 48 hours — severe dyspnea, lung tissue hemorrhage, bronchopneumonia

CO34

DIFFERENTIAL DIAGNOSIS: NON-AGENT OR AGGRAVATING CAUSES OF OBSERVED SIGNS/SYMPTOMS

- Hay fever
- Chemical or thermal burns
- Tear gas exposure
- Poison ivy, poison oak, and other contact allergies

CO35

SULFUR MUSTARD INITIAL FIRST AID TREATMENT

- Immediate removal
- Decontamination through washing and diluting, and removal of clothing
- Treatment provided by properly trained and equipped personnel

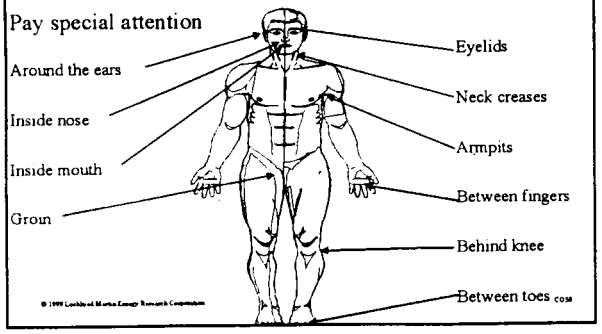
CO36

TREATMENT FOR SULFUR MUSTARD EYE CONTACT

- Speed Critical
  - Flush eyes immediately with water
    - Tilt head to side
    - Pulling eyelids apart with uncontaminated fingers
    - Pouring water slowly into eyes
- Do not cover eyes with bandages
- Dark or opaque glasses shield eyes from light and provide relief from photophobia

CO37

SULFUR MUSTARD: DECONTAMINATION FOR SKIN CONTACT



Attachment 9

REVIEW OF EXISTING TOXICITY DATA AND HUMAN ESTIMATES FOR SELECTED CHEMICAL AGENTS AND RECOMMENDED HUMAN TOXICITY ESTIMATES APPROPRIATE FOR DEFENDING THE SOLDIER--CEDPAT--(REUTTER--WADE REPORT).

REVIEW OF ACUTE HUMAN-TOXICITY ESTIMATES FOR SELECTED CHEMICAL-WARFARE AGENTS--
NRC-COT

REPORT OF THE WORKSHOP ON CHEMICAL AGENT ANALYSIS--- IDA.

EVALUATION OF AIRBORNE EXPOSURE LIMITS FOR G-AGENTS: OCCUPATIONAL AND GENERAL
POPULATION EXPOSURE CRITERIA-- U.S. ARMY--EDGEWOOD.

EVALUATION OF AIRBORNE EXPOSURE LIMITS FOR VX: OCCUPATIONAL AND GENERAL POPULATION EXPOSURE CRITERIA--U.S. ARMY--EDGEWOOD.

EVALUATION OF AIRBORNE EXPOSURE LIMITS FOR SULFUR MUSTARD: OCCUPATIONAL AND GENERAL POPULATION EXPOSURE CRITERIA--U.S. ARMY--EDGEWOOD.

REVIEW OF ACUTE HUMAN-TOXICITY ESTIMATES FOR SELECTED CHEMICAAL-WARFARE AGENTS
NRC--COT.

COMMITTEE ON REVIEW AND EVALUATION OF THE ARMY CHEMICAL STOCKPILE DISPOSAL PROGRAM--NRC.

Army's Office of Surgeon General asked the Army's Chemical Defense Equipment Process Action Team (CDEPAT) to review the toxicity data for the nerve agents:

GA - tabun
GB - sarin
GD - soman
GF -
VX -
HD - sulfur mustard

- Purpose - to establish a set of exposure limits that would be useful in protecting soldiers from toxic exposures to the nerve agents.

CDEPAT Report (Reutter-Wade Report)

- Review of existing toxicity data and human estimates for selected chemical agents and recommended human toxicity estimates appropriate for defending the soldier
  - Authored by: Dr. Sharon Reutter
    Colonel (Dr.) John Wade
  - Classified document

NRC - COT Subcommittee Charge:

- Review the scientific protocols and quality of the toxicity data used in revising the human-toxicity estimates for acute exposures
- Review the toxicity estimates for mild and non-severe effects and for severe and lethal effects
- Review the methods used in driving the human-toxicity estimates for acute exposures
- Determine the appropriateness of the assumptions made in deriving the human-toxicity estimates for acute exposure

*The COT Subcommittee was not asked to recommend new toxicity estimates.

Problem with the data:

- Database developed from 1930's to 1960's
- Human toxicity estimates based on experiments performed 30-40 years ago
- Quality of relevant toxicity data is marginal
- Data available for only a few adverse health effects
- By current standards, toxicity database is inadequate

*The Subcommittee recommended that the Army convene an expert panel to develop a research strategy for deriving more scientifically sound toxicity values for the agents.

Exposure reviewed for each agent:

- Percutaneous vapor (30 minute exposures without clothing)
  LCT 50 (Lethal effects)
  ECT 50 (for threshold effects)

- Inhalation vapor exposure (2 minute exposure)
  LCT 50 (lethal effects)
  ECT 50 (for severe effects)
  ECT 50 (for mild effects)

- Percutaneous liquid exposure (applied to 70 kg man)
  LD 50 (lethal effects)
  ED 50 (severe effects)

Conclusions:

- Some estimates were judged to be scientifically valid
- Some estimates were adequate to serve as interim values
- Some estimates needed to be lowered
- Some estimates need to be raised

TABLE 2 Evaluation of Human-Toxicity Estimates for GB

Toxicity Type	Route and Form of Exposure	Human-Toxicity Estimates for GB: Existing Estimates	Human-Toxicity Estimates for GB: CDEPAT's Proposed Estimates	Subcommittee's Evaluation of Proposed Estimates for GB	Rationale for Subcommittee's Evaluation
LCt_{50}[a]	Percutaneous, vapor	15,000 mg-min/m^3	10,000 mg-min/m^3	Proposed estimate is scientifically valid	Proposed estimate supported by studies in monkeys and humans
	Inhalation, vapor	70 mg-min/m^3	35 mg-min/m^3	Proposed estimate should be lowered	Estimate too high because human studies show 100% lethality at 40 mg-min/m^3
ECt_{50}[b]					
Threshold effects	Percutaneous, vapor	None	1,200 mg-min/m^3	Proposed estimate is scientifically valid	Estimate supported by studies of ChE inhibition in humans; further research recommended
Severe effects	Inhalation, vapor	35 mg-min/m^3	25 mg-min/m^3	Proposed estimate should be lowered	ECt_{50}/LCt_{50} ratio of 0.7 used to develop estimate; LCt_{50} for this route of exposure was lowered; therefore, ECt_{50} should be lowered correspondingly; further research recommended
Mild effects	Inhalation, vapor	2 mg-min/m^3	0.5 mg-min/m^3	Proposed estimate should be raised	No effects in humans at 0.5 mg-min/m^3; effects begin to appear at $\approx$2 mg-min/m^3; further research recommended
LD_{50}[c]	Percutaneous, liquid	1,700 mg for 70-kg man	1,700 mg for 70-kg man	Low confidence in proposed estimate; proposed estimate should serve as interim value	Estimate based on a ratio of ChE inhibition in rabbits and humans; however, human data concerning the relation between ChE inhibition and adverse effects are inconsistent; further research recommended
ED_{50}[d]					
Severe effects	Percutaneous, liquid	None	1,000 mg for 70-kg man	Proposed estimate should serve as interim value	In the absence of adequate data on GB for this effect, CDEPAT assumed that the ratio of ID_{50}[e]/LD_{50} is 0.6 and used that to estimate the ED_{50} values; further research recommended

[a]LCt_{50}: Vapor exposure that produces lethality in 50% of the exposed animals. Ct refers to the product of concentration (c) and exposure time (t). Note that Ct is not necessarily a constant.

[b]ECt_{50}: Percutaneous vapor exposure or inhalation vapor exposure causing a defined effect (e.g., incapacitation, severe effects, mild effects, threshold effects).

[c]LD_{50}: Liquid dose causing lethality in 50% of the exposed animals.

[d]ED_{50}: Liquid dose causing a defined effect in 50% of the exposed animals.

[e]ID_{50}: Liquid dose causing incapacitation in 50% of the exposed population.

Institute for defense analysis workshop (May 1998)

- Reach a consensus on interim toxicity parameters for the six nerve agents
- Specify guidelines for their use
- Identify high priority areas of research to improve the estimates

Workshop focused on:

- Acute exposures/effects
- 70 kg male soldier
- Military scenarios
- Evaluate the six nerve agents
- Developing "consensus values"

Table 2. GB Toxicity Values

mg-mm/m³ CDEPAT NRC

Agent	Parameter	Route of Entry	Value		
GB	LCt50	Percutaneous vapor	12000	10,000	Valid
GB	LCt50	Inhalation vapor	35	35	Lowered
GB	ECt50, threshold {2}	Percutaneous vapor	1200	1200	Valid
GB	ECt50, severe {4}	Percutaneous vapor	8000		
GB	ECt50, severe {4}	Inhalation vapor	25	25	Lowered
GB	ECt50, mild {5}	Inhalation vapor	1	0.5	Raised
GB	LD50	Percutaneous liquid	1700	1700	Interim
GB	ED50, severe {4}	Percutaneous liquid	1000	1000	Interim

Recommended Research:

- Longer exposures and lower concentrations
- The effect of clothing
- Mixed populations (male/female, soldiers/civilians)

Table 3. Characteristic Clinical Signs/Symptoms Associated with Graded Levels of Severity of G-agent Toxicity (From Vojvodic, 1981)

Severity	Clinical Sign/Symptoms of Poisoning
Mild	CNS: Restlessness, emotional lability, increased irritability, disturbances in sleep, frontal headache. Visual: slight reduction of vision, especially at dusk and in artificial light, pain in the eyes, especially on convergence. Miosis, pupils react weakly to light, sometimes anisocoria. The changes in the eyes can be absent if the eyes are not directly exposed to the nerve gas. Respiratory: sensation of pressure and tightness in the chest, slight difficulty in breathing, rhinorrhea. Cardiovascular: pulse can be slightly slowed. Gastrointestinal: pain in the region of the stomach, mild heartburn with disturbances in appetite, stool normal or watery, urination normal.
Moderate	In addition to the symptoms reported for mild poisoning, there is also a feeling of fear which can result in panic. Headache, inadequate reactions to the environment, increased reflex sensitivity, fibrillation, and fasciculation of the muscles. The pupils are narrowed to a "pin head," do not react to light, and lacrimation is increased. The other ocular symptoms are the same as in mild poisoning, but more pronounced. Rhinorrhea, labored breathing involving auxiliary respiratory musculature. The pulse is rhythmic, slow, and heart chamber filling is good. The blood pressure can be increased slightly. There are intensive gastric pains, nausea, increased salivation, and vomiting. The stool is liquid, and urination is frequent. The body temperature is decreased slightly.
Severe	The symptoms are the same as in moderate poisoning, but more pronounced. The feeling of fear is replaced by terror. Vertigo, headache, speech disturbances, loss of orientation, paresthesia, loss of consciousness. Signs include: muscular fibrillation, tremor which initially involves the head, then the upper extremities, and finally, the entire body. Muscular hypertonicity, spastic contractions of the individual muscles, then entire groups of muscles, and finally, generalized clonic-tonic convulsions. After a phase of central nervous system excitation, there is a phase of inhibition with coma. Copious-perspiration and pronounced cyanosis are visible on the skin. The changes in the eyes are initially the same as in the moderate form. However, as poisoning rapidly develops, miosis can be totally absent, replaced by mydriasis and exophthalmos. If miosis is present, it decreases gradually and disappears at death. The respiratory disorders are very pronounced, rhythm is disturbed, the respiratory excursions are irregular, respiration is noisy ("harsh and wheezing"). The pulse is initially slowed (sometimes accelerated when the blood pressure is slightly increased). As the intoxication progresses, the blood pressure drops, the pulse becomes weak, and filling decreases. The heart sounds are muffled and indistinct. Defecation and urination are involuntary. Blood cholinesterase activity is decreased to 10-20% of baseline (to 1-5% in the case of death), and serum activity is less than 10% of the normal value.

Table 11. Existing, Recalculated/Developed, and Recommended Airborne Exposure Limits (AELs) for GA, GB, GD, and GF for Occupational and General Populations

Criteria	GA	GB	GD	GF	Application
Occupational Worker Population AEL (WPL) (mg/m^3)					
Existing	0.0001	0.0001	0.00003	NF	WPL (TWA; 8 hr/day, 40 hr/wk)
	0.2	0.2	0.06	NF	IDLH (30 min)
Recalculated or Developed*	0.000033	0.000033	0.000016	0.000016*	WPL (TWA; 8 hr/day, 40 hr/wk)
	0.1	0.1	0.05	0.05**	IDLH (30 min)
	0.002*	0.002*	0.001*	0.001*	STEL (TWA;15 min x 4 /day)
Recommended	0.0001	0.0001	0.00003	0.00003	WPL (TWA 8 hr/day; 40 hr/wk)
	0.1	0.1	0.05	0.05	IDLH (30 min)
	0.002	0.002	0.001	0.001	STEL (TWA;15 min x 4 /day)
General Population AEL (GPL) (mg/m^3)					
Existing	0.000003	0.000003	0.000003	NF	WPL (TWA; 24 hr x 7 days/wk)
Recalculated or Developed*	0.0000011	0.0000011	0.0000006	0.0000006	WPL (TWA; 24 hr x 7 days/wk)
	0.0024*	0.0024*	0.0012*	0.0012*	AEGL-1(30 min)
	0.0012*	0.0012*	0.0006*	0.0006*	AEGL-1(1 hr)
	0.0003*	0.0003*	0.0001*	0.0001*	AEGL-1(4 hr)
Recommended	0.000003	0.000003	0.000001	0.000001	WPL (TWA; 24 hr x 7 days/wk)
	0.0024	0.0024	0.0012	0.0012	AEGL-1(30 min)
	0.0012	0.0012	0.0006	0.0006	AEGL-1(1 hr)
	0.0003	0.0003	0.0001	0.0001	AEGL-1(4 hr)

NF = No AELs were found.
* = Developed (no existing criteria)
NF = No criteria for this exposure time could be found
WPL = Occupational AEL (no observable adverse effects)
GPL = General Population AEL (no observable adverse effects)
IDLH- = Immediately Dangerous to Life or Health
STEL = Short Term Exposure Limit
AEGL-1 = Acute Exposure Guideline - Level 1
TWA = Time Weighted Average

SULFUR MUSTARD (AGENT HD) AEGL

CAS No. 505-60-2

NAC/AEGL-16
U.S. Dept. Of Transportation
DOT Headquarters/Nassif Bldg. Rms 6200-6204
400 7th Street, SW
Washington, D.C.

December 6-8, 1999

Effects of Acute Exposure to Sulfur Mustard (Agent HD) in Human Volunteers (Reed, 1918)			
Nominal Conc. (mg/m^3)	Exposure Duration (min)	No. of Subjects	Results
0.1	10	6	no detectable effect
0.1	15	2	1 of 2 slight conjunctival injection
0.1	30	5	1 of 5 marked bilateral conjunctival injection 1 of 5 slight conjunctival injection
0.5	10	5	2 of 5 conjunctival injection
0.5	15	3	1 of 3 slight conjunctival injection
0.5	30	8	1 of 8 conjunctivitis, rhinitis 1 of 8 severe conjunctivitis, marked skin burn 1 of 8 marked conjunctivitis, slight facial burn
0.5	45	1	no effect
1.0	5	1	1 of 1 marked conjunctivitis, photophobia, rhinitis, laryngitis, pulmonary congestion
1.0	10	2	1 of 2 slight conjunctivitis
1.0	15	2	no effect
1.0	20	1	1 of 1 severe conjunctivitis
1.0	45	1	1 of 1 very severe conjunctivitis, photophobia, skin burns, mucosal exfoliation in nasopharynx
2.6	5	1	no effect
4.3	10	1	1 of 1 marked conjunctivitis, no pain

Human Exposure Study (Anderson, 1942)

- 3-4 human volunteers per exposure
- hot, humid atmospheric conditions (a worst case scenario)
- remarkably consistent ocular response among individuals
- Ct product found to be a useful and valid index

- 12 mg·min/m^3 - threshold for demonstrable ocular effect (no symptoms)
- 12-30 mg·min/m^3 - conjunctivitis, minor irritation; no functional decrement
- 20-30 mg·min/m^3 - mild conjunctivitis, some edema, irritation
- 60-70 mg·min/m^3 - marked conjunctivitis, photophobia, chemosis, "casualty"
- 75-90 mg·min/m^3 - serious casualties likely (several weeks treatment)
- $\geq$100 mg·min/m^3 - 100% casualty level

Acute Lethality of Sulfur Mustard in Laboratory Species		
Species	**Lethality Value**	**Reference**
Rat	2-min LCt_{50}: 1512 mg · min/m^3 30-min LCt_{50}: 990 mg · min/m^3 60-min LCt_{50}: 840 mg · min/m^3	Fuhr and Krakow, 1945 (not verified)
Mouse	2-min LCt_{50}: 4140 mg · min/m^3 30-min LCt_{50}: 1320 mg · min/m^3 60-min LCt_{50}: 860 mg · min/m^3	Fuhr and Krakow, 1945 (not verified)
Mouse	60-min LC_{50}: 42.5 mg/m^3	Vijayaraghavan, 1997
Guinea pig	5-min LCt_{50}: 800 mg · min/m^3	Langenberg et al., 1998

SPECIAL CONSIDERATIONS/ISSUES

- **Latency period**
- **Temperature/humidity**
- **Eye most sensitive organ/tissue**
- **Carcinogenic potential**

AEGL-1

	30 min	1 hr	4 hrs	8 hrs
AEGL-1	0.10 mg/m^3	0.05 mg/m^3	0.01 mg/m^3	0.006 mg/m^3

Key study: Anderson (1942)

Toxicity endpoint: 30 mg · min/m^3 represented the upper range for mild ocular effects (conjunctival injection and minor discomfort with no functional decrement) for human volunteers exposed to agent HD at varying exposure regimens.

Time scaling: n = 1 based upon analysis of ocular responses in human volunteers

Uncertainty factors: 3
Interspecies = 1 (human subjects)
Intraspecies = 3 (direct contact effect)

Modifying factor: 3 (latency/persistence issue)

AEGL-2

AEGL-2	30 min	1 hr	4 hrs	8 hrs
	0.24 mg/m^3	0.12 mg/m^3	0.03 mg/m^3	0.01 mg/m^3

Key study: Anderson (1942)

Toxicity endpoint: 70.5 mg-min/m^3 (15-min exposure to 4.7 mg/m^3) induced ocular irritation (well marked, generalized conjunctivitis, edema, photophobia, and irritation) resulting in performance decrement and necessitating medical treatment

Time scaling: n = 1 based upon analysis of ocular responses in human volunteers

Uncertainty factors: 3
Interspecies = 1 (human subjects)
Intraspecies = 3 (direct contact effect)

Modifying factor: 3 (latency/persistence issue)

AEGL-3

	30 min	1 hr	4 hrs	8 hrs
AEGL-3	3 mg/m^3	1.5 mg/m^3	0.38 mg/m^3	0.19 mg/m^3

Key study: Vijayaraghavan (1997)

Toxicity endpoint: Lethality threshold estimated as 3-fold reduction in lower bound 95% confidence interval (13.5 mg/m^3 ÷ 3 = 4.5 mg/m^3) for mouse 1-hr LC_{50} of 42.5 mg/m^3.

Time scaling: n = 1 based upon analysis of ocular responses in human volunteers

Uncertainty factors:

Interspecies = 1 (data do not support greater sensitivity of humans)

Intraspecies = 3 (direct contact pulmonary injury)

Modifying factor: 1 (14-day post exposure observation period)

ACUTE EXPOSURE GUIDELINES FOR SULFUR MUSTARD
(CAS NO. 505-60-2)

AEGL-1 VALUES			
30 minutes	1 hour	4 hours	8 hours
0.10 mg/m^3	0.05 mg/m^3	0.013 mg/m^3	0.006 mg/m^3

Reference: Anderson, J.S. 1942. The effect of mustard gas vapour on eyes under Indian hot weather conditions. CDRE Report No. 241. Chemical Defense Research Establishment (India).

Test Species/Strain/Number: 3-4 human volunteers

Exposure Route/Concentrations/Durations: Inhalation exposure to varying concentrations (1.7- 15.6 mg/m^3) for varying durations (2-33 minutes)

Effects: Ocular effects ranging from mild injection to notable conjunctivitis, photophobia, lacrimation, blepharospasm

Endpoint/Concentration/Rationale: Conjunctival injection with minor discomfort in the absence of functional decrement following exposure to a Ct of 30 mg-min/m^3.

Uncertainty Factors/Rationale:

Interspecies: 1 (human subjects)

Intraspecies: A factor of 3 was applied for intraspecies variability (protection of sensitive populations). This factor was limited to three under the assumption that the primary mechanism of action of agent HD involves a direct effect on the ocular surface and that this response will not vary greatly among individuals.

Modifying Factor: A modifying factor of 3 was applied due to uncertainties regarding the latency and persistence of the irritant effects of low-level exposure to agent HD

Animal to Human Dosimetric Adjustment: Not applicable

Time Scaling: $C^n \times t = k$, where $n = 1$ based on analysis of available human exposure data for ocular effects.

Confidence and Support for AEGL Levels: The key study was conducted using human volunteers thus avoiding uncertainties associated with animal studies. Ocular irritation is considered the most sensitive endpoint for assessing the effects of acute exposure to sulfur mustard. The AEGL-1 values are considered to be adequately protective of human health and the confidence rating for the AEGL-1 values is considered to be medium.

ACUTE EXPOSURE GUIDELINES FOR SULFUR MUSTARD
(CAS NO. 505-60-2)

AEGL-2 VALUES			
30 minutes	1 hour	4 hours	8 hours
0.24 mg/m^3	0.12 mg/m^3	0.03 mg/m^3	0.01 mg/m^3

Reference: Anderson, J.S. 1942. The effect of mustard gas vapour on eyes under Indian hot weather conditions. CDRE Report No. 241. Chemical Defense Research Establishment (India).

Test Species/Strain/Sex/Number: 3-4 human volunteers

Exposure Route/Concentrations/Durations: Inhalation exposure to varying concentrations (1.7- 15.6 mg/m^3) for varying durations (2-33 minutes)

Effects: Ocular effects ranging from mild injection to notable conjunctivitis, photophobia, lacrimation, blepharospasm

Endpoint/Concentration/Rationale: Ocular irritation (well marked, generalized conjunctivitis, edema, photophobia, and irritation) resulting in effective performance and necessitating medical treatment in three human subjects following exposure to 70.5 mg-min/m^3 (15-min exposure to 4.7 mg/m^3)

Uncertainty Factors/Rationale:

Interspecies: 1 (human subjects)

Intraspecies: A factor of 3 was applied for intraspecies variability (protection of sensitive populations). This factor was limited to three under the assumption that the primary mechanism of action of agent HD involves a direct effect on the ocular surface and that this response will not vary greatly among individuals.

Modifying Factor: A modifying factor of 3 was applied due to uncertainties regarding the latency and persistence of the irritant effects of low-level exposure to agent HD

Animal to Human Dosimetric Adjustment: Not applicable

Time Scaling: $C^n \times t = k$, where $n = 1$ based on analysis of available human exposure data for ocular effects.

Confidence and Support for AEGL Levels: The key study was conducted using human volunteers thus avoiding uncertainties associated with animal studies. The AEGL-2 values are based upon ocular effects that would be considered severe enough to impair vision and escape. Confidence in the AEGL-2 values is medium.

ACUTE EXPOSURE GUIDELINES FOR SULFUR MUSTARD
(CAS NO. 505-60-2)

AEGL-3 VALUES			
30 minutes	1 hour	4 hours	8 hours
3 mg/m^3	1.5 mg/m^3	0.38 mg/m^3	0.19 mg/m^3

Reference: Vijayaraghavan, R. 1997. Modifications of breathing pattern induced by inhaled sulphur mustard in mice. Arch.Toxicol. 71: 157-164.

Test Species/Strain/Sex/Number: Swiss mice/female/4 per exposure group

Exposure Route/Concentrations/Durations: Head-only inhalation exposure for 1 hr to sulfur mustard (>99% purity) at 8.5, 16.9, 21.3, 26.8, 42.3, or 84.7 mg/m^3; observed for up to 14 days

Effects: Lethality assessed up to 14 days post exposure

Endpoint/Concentration/Rationale: 1-hr LC_{50} = 42.5 mg/m^3 (95% c.i. 13.5-133.4 mg/m^3). A lethality threshold was based upon a 3-fold reduction in the lower 95% c.i. for the lethal response (i.e., 1.3 $mg/m^3 \div 3 = 4.5$ mg/m^3).

Uncertainty Factors/Rationale:

Total uncertainty factor: 3

Interspecies: An uncertainty factor for interspecies variability was not applied because available data suggest that humans are not more sensitive than animal species. A lethality estimate based upon animal data results in exposures that do not approach those reported as causing human fatalities.

Intraspecies: Intraspecies variability was limited to 3 because lethality appears to be a function of extreme pulmonary damage resulting from direct contact of the agent with epithelial surfaces.

Modifying Factor: No modifying factor was applied because the basis of lethality estimate was from a study utilizing a 14-day observation period with which to assess the lethal response from a 1-hour exposure.

Animal to Human Dosimetric Adjustment: Insufficient data

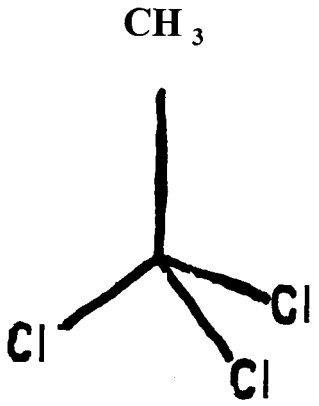
Time Scaling: $C^n \times t = k$ where n = 1 based upon analysis of human exposure data for ocular effects.

Confidence and Support for AEGL Levels: The confidence in the precision of the AEGL-3 values is low to medium due to data deficiencies for defining a lethality threshold. The key study appeared to be a well-designed and properly conducted study but considerable variability was associated with the calculated LC_{50}. Based upon the available data and the approach used for their development, the AEGL-3 values are considered to represent a conservative estimate for the threshold for lethal responses to acute sulfur mustard exposure.

1,1,1-TRICHLOROETHANE AEGLs

CAS Reg. No. 71-55-6

C2H3Cl3
133.40



Mark McClanahan
Tessa Long

1,1,1-TRICHLOROETHANE

- PROPERTIES
  Volatile, colorless liquid
  Nonflammable
  Sweet pungent odor

- USES
  Metal degreasing
  Degreasing of various plastics and electrical equipment as well
  Other uses: Correction fluids, spot removers, stain repellents, drain cleaners, shoe polishes, textile processing (dry cleaning), aerosols, and pesticides

- PRODUCTION
  1994 U.S. Sales, 166,055,000 kg
  Dow Chemical Co., PPG Industries, Inc., and Vulcan Materials Co., Chemical Div.

- AVAILABLE DATA
  - Human Inhalation Exposures
    Abuse data (lethal and nonlethal)
    Accidental (lethal and nonlethal)
    Occupational (nonlethal)
    Experimental (nonlethal, low conc. exposures)
  - Animal Inhalation Exposures
    Acute LC_{50}s
    Acute Neurobehavioral
    Developmental/Reproductive
    Subchronic and Chronic

LETHALITY IN HUMANS

ABUSE SITUATIONS and ACCIDENTAL EXPOSURES

- Cardiac arrest
- Respiratory arrest
- Severe CNS depression
- Asphyxia
- Autopsies show congestion of all major organs and signs of asphyxia

LETHALITY IN ANIMALS

LC_{50} DATA

- Initial excitation phase followed by CNS depression, narcosis, and death
- Lack of Interspecies Variability

- Rat and mouse show equal sensitivity
  - six hr rat LC_{50} 10,305 ppm
  - six hr mouse LC_{50} 13,414 ppm
  - one hr EC_{50} for disabling effects 6000 ppm in rat and mouse

SUBLETHAL EFFECTS IN HUMANS

◆ PRIMARY EFFECT - CNS depression

Acute inhalation exposures

- fail to produce residual organ damage
- produce sleepiness, incoordination, and impaired performance on neurobehavioral tasks

Chronic inhalation exposures

- CNS disturbances and impaired neuromuscular function
- Peripheral nervous system effects
- Disappear with cessation of exposure

- SYSTEMIC EFFECTS
  - Sensory irritation, nausea
  - Cardiovascular
  - Hepatic

- DEVELOPMENTAL AND REPRODUCTIVE EFFECTS
  - Inadequate database for evaluation

- GENOTOXICITY/CARCINOGENICITY
  - IARC stated 1,1,1-trichloroethane is not classifiable as to its carcinogenicity to humans, based on inadequate data in humans and animals

SUBLETHAL EFFECTS IN ANIMALS

PRIMARY EFFECT - CNS depression

- Initial hyperactivity (⇑ responding)
- Decrease in activity (⇓ responding)
- Ataxia
- Loss of righting reflex
- Narcosis

SYSTEMIC EFFECTS

- Cardiac
- Liver
- ⇓ Body weight (subchronic, chronic)
- Hematological
- Respiratory

DEVELOPMENTAL/REPRODUCTIVE

- No reproductive effects have been identified in rodents
- Developmental delays at concentrations that produce maternal toxicity

GENOTOXICITY/CARCINOGENICTY

- Reports suggest 1,1,1-trichloroethane does not have genotoxic/carcinogenic potential in rodents

DERIVATION OF *n*

n=3
R^2=0.88
Correlation
coeff. = 0.93

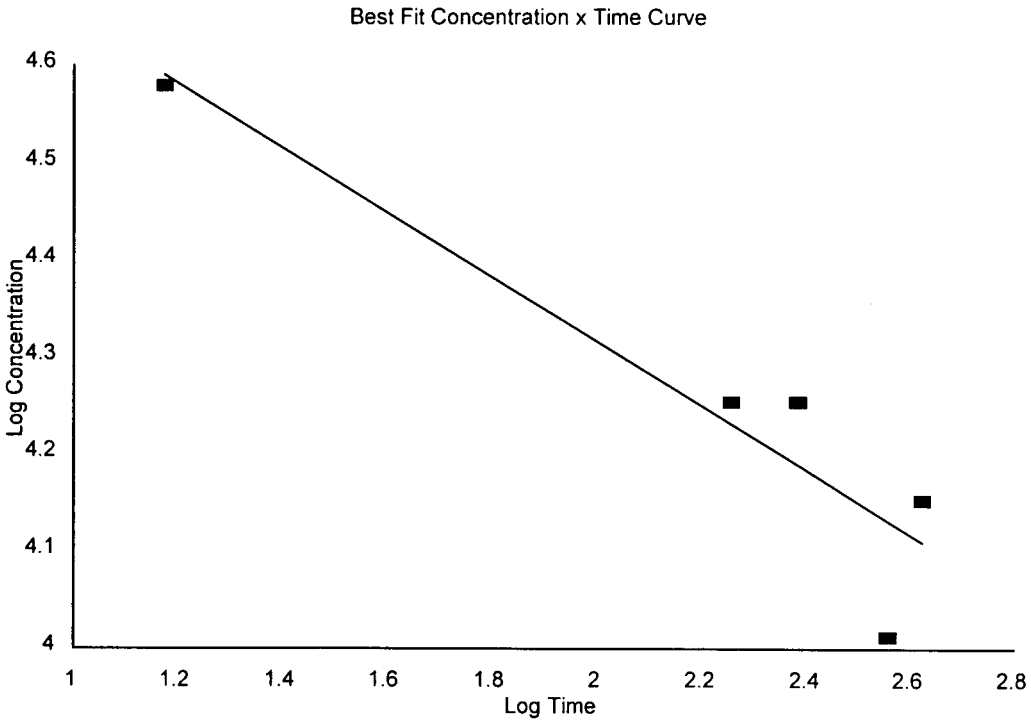


FIGURE 1. Regression curve for rat lethality data used for derivation of n.

- *n* is based on 5 LC_{50} conc./time points
- 15 min. Clark and Tinston, 1982
- 180 min. Adams et al., 1950
- 240 min. Calhoun et al., 1988
- 360 min. Bonnet et al., 1980
- 420 min. Adams et al., 1950

TABLE 1: AEGL-1 VALUES FOR 1,1,1-TRICHLOROETHANE (ppm [mg/m^3])				
AEGL level	30-min	1-hr	4-hr	8-hr
AEGL-1	300 [1630]	240 [1300]	150 [820]	120 [650]

Species: Human (six healthy subjects)
Conc.: 450 ppm
Time: 4 hr
Endpoint: Eye irritation, slight dizziness, mental fatigue
Reference: Salvini et al., 1971

n = 3

Uncertainty Factor = 3

Intraspecies = 3

Supporting data:

Stewart et al., 1969

Human subjects, 6.5 to 7 hr/5 days at 500 ppm, mild sleepiness (inconsistent complaints of eye irritation and headache)

Torkelson et al., 1958

Human subjects, 1.5 hr at 450-710 ppm, no untoward effects

Stewart et al., 1961

Human subjects, 1.3 hr at 500 ppm, eye irritation 3/6 subjects

3.1 hr 500 ppm no subjective or functional abnormalities

Geller et al., 1988

Baboons exposed to 1800 ppm for 4 hr had decreased no. of trials on neurobehavioral tasks, time scaling gives 360, 290, 180, and 140 ppm for the 30 min, 1,4, and 8 hr (UF=10)

TABLE 2: AEGL-2 VALUES FOR 1,1,1-TRICHLOROETHANE (ppm [mg/m^3])				
AEGL level	30-min	1-hr	4-hr	8-hr
AEGL-2	670 [3650]	600 [3270]	380 [2070]	300 [1633]

Species: Rat (groups of six males)
Concentration: 6740, 6000, 3780 ppm
Time: 0.5, 1, and 4 hr
Endpoint: EC_{50} for ataxia
Reference: Mullin and Krivanek, 1982

n = 3
Uncertainty Factor = 10
Intraspecies = 3
Interspecies = 3

Supporting Data:

Torkelson et al., 1958

Human subjects, 920 ppm for 1.3 hr, loss of equilibrium and feelings of lightheadedness in 3/4 subjects
1740-2180 ppm 5 min. loss of equilibrium and one subject unable to stand

Stewart et al., 1961

Human subjects, 1.3 hr at 955 ppm with only 1/3 subjects exhibiting a positive Romberg test

TABLE 3: AEGL-3 VALUES FOR 1,1,1-TRICHLOROETHANE (ppm [mg/m^3])				
AEGL level	30-min	1-hr	4-hr	8-hr
AEGL-3	1600 [8710]	1270 [6920]	800 [4360]	640 [3490]

Species: Rat (12 males/conc.)
Concentration: 7000 ppm
Time: 6 hr
Endpoint: Threshold for lethality
Reference: Bonnet et al., 1980

n = 3
Uncertainty Factor = 10
Interspecies = 3
Intraspecies = 3

TABLE 4. SUMMARY OF PROPOSED AEGL VALUES (ppm)					
Classification	**30-minute**	**1-hour**	**4-hour**	**8-hour**	**Endpoint (Reference)**
AEGL-1	300	240	150	120	Eye irritation, slight dizziness, mental fatigue in humans (Salvini et al., 1971)
AEGL-2	670	600	380	300	EC_{50} ataxia in rats (Mullin and Krivanek, 1982)
AEGL-3	1600	1270	800	640	Threshold for lethality, rat 6 hr (Bonnet et al., 1980)

Chemical Toxicity - TSD All Data

1,1,1-Trichloroethane

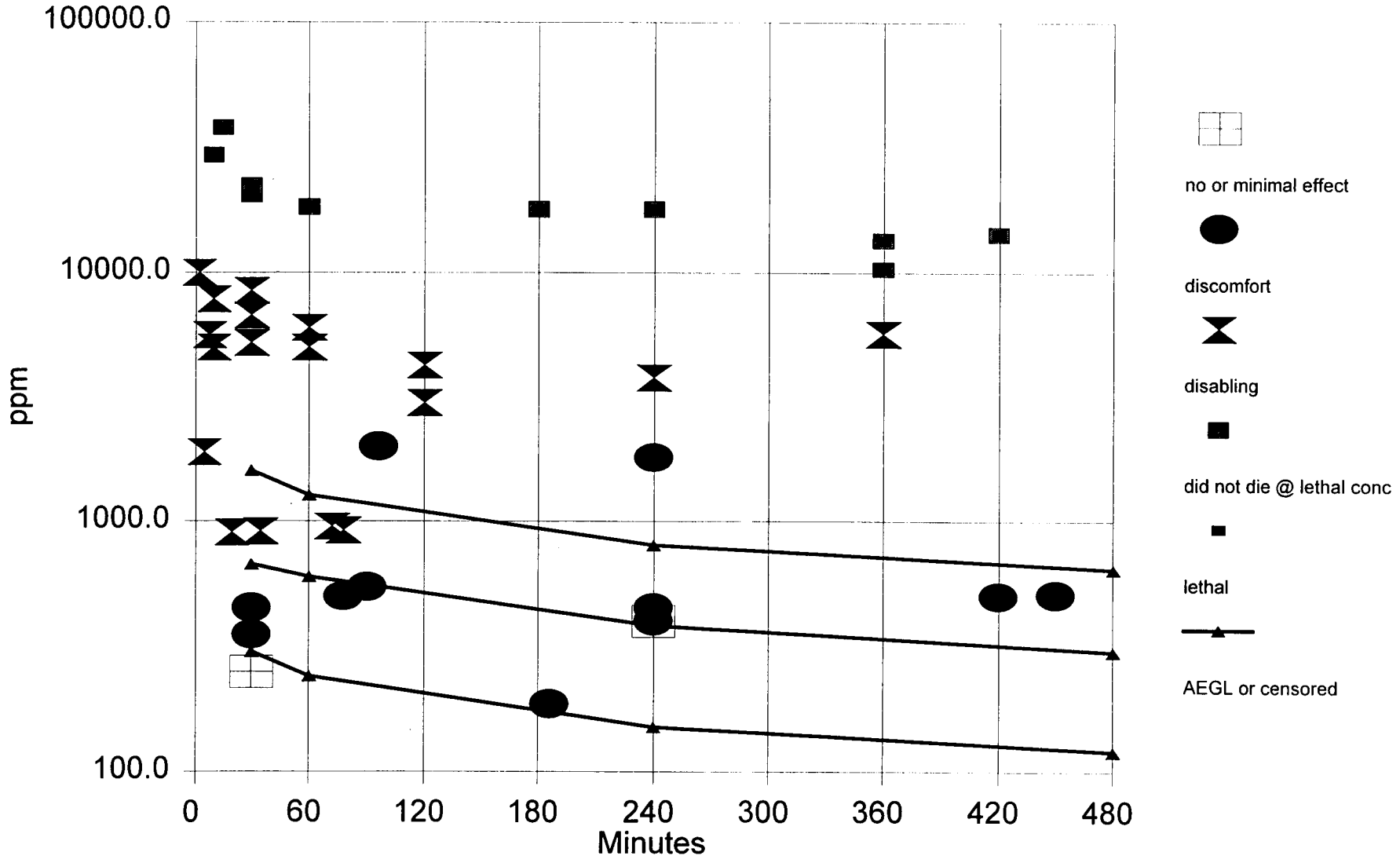


TABLE 5. STANDARDS AND GUIDELINES FOR 1,1,1-TRICHLOROETHANE	
ACGIH TLV-TWA (ACGIH 1998)	350 ppm
ACGIH TLV-STEL (ACGIH 1998)	450 ppm
OSHA PEL-TWA (NIOSH 1997)	350 ppm
OSHA Ceiling (NIOSH 1997)	350 ppm
NIOSH REL-TWA (NIOSH 1997)	350 ppm
NIOSH STEL (NIOSH 1997)	450 ppm
NIOSH IDLH (NIOSH 1994)	700 ppm
ERPG-1 (AIHA-ERPG, 1998)	350 ppm
ERPG-2 (AIHA-ERPG, 1998)	700 ppm
ERPG-3 (AIHA-ERPG, 1998)	3500 ppm

Attachment 12

ACUTE EXPOSURE GUIDELINE LEVELS FOR 1,2-DICHLOROETHENE

RESPONSE TO COT SUGGESTIONS NAC/AEGL-17 DECEMBER 6-8, 1999

CHEMICAL MANAGER: ERNIE FALKE
ORNL STAFF SCIENTIST: CHERYL BAST

INTRODUCTION- 1,2-DICHLOROETHENE

- **Exists in both *cis*- and *trans*- forms and as a mixture of these two isomers. Only the *trans*- isomer is produced and used in this country**

- **Colorless, flammable liquid used as an intermediate in the production of chlorinated solvents and as a low-temperature extraction solvent for decaffeinated coffee, dyes, perfumes, lacquers, and thermoplastics**

- **Produced by direct chlorination of acetylene or by the reduction of 1,1,2,2-tetrachloroethane with fractional distillation used to separate the isomers**

- **Ethereal, slightly acrid odor; Odor threshold is 17 ppm**

DATA SUMMARY- 1,2-DICHLOROETHENE

- **Human Data**

  - **Short-term inhalation experiments conducted with *trans*-1,2-dichloroethene. Two doctoral candidates self-administered the chemical as a vapor.**

  - **Effects included dizziness, burning of eyes, drowsiness, intracranial pressure, and nausea with increasing concentrations of chemical.**

DATA SUMMARY- 1,2-DICHLOROETHENE

- **Animal Data**

  - **Ocular irritation at low concentrations**

  - **Narcotic observations indicated a progression from equilibrium effects, followed by lethargy, light narcosis (loss of limb reflex and maintenance of corneal reflex), deep narcosis (loss of corneal reflex), and death**

  - **Data suggest that the *cis*- isomer is approximately twice as toxic as the *trans*- isomer with respect to narcosis and lethality**

ACUTE EXPOSURE GUIDELINES FOR 1,2-DICHLOROETHENE (CAS NO. 540-59-0)

AEGL-1 VALUES			
30 minutes	1 hour	4 hours	8 hours
19 ppm	13 ppm	6.6 ppm	4.7 ppm

Reference: Lehman, K. B., and Schmidt-Kehl, L. 1936. The thirteen most important chlorinated aliphatic hydrocarbons from the standpoint of industrial hygiene. Arch. Fur Hygiene. 116: 9-268.

Test Species/Strain/Number: Human subjects/ 2

Exposure Route/Concentrations/Durations: Inhalation: 275, 825, 950, 1000, 1200, 1700, or 2200 ppm for 5-30 minutes

Effects:

275 ppm	no effects (5 min. Total exposure); determinant for AEGL-1
825 ppm	slight dizziness after 5 min. (10 min. exposure)
950 ppm	slight burning of eyes (5 min.)
1000 ppm	dizziness after 10 min; slight burning of eyes (30 min exposure)
1200 ppm	Dizziness after 5 min; drowsiness; slight burning of eyes (10 min exposure)
1700 ppm	Dizziness after 3 min; slight burning of eyes; intracranial pressure; nausea (5 min exposure)
2200 ppm	Severe dizziness; intracranial pressure; nausea (5 min exposure)

Endpoint/Concentration/Rationale: 275 ppm for 5 min.; no effect level for narcosis; odor present.

Uncertainty Factors/Rationale:
Total uncertainty factor: 3
Interspecies: Not applicable, human data used.
Intraspecies: 3 - the mechanism of narcosis is not expected to differ greatly among individuals, including sensitive individuals.

Modifying Factor: 2; differential isomer toxicity, the *cis*-isomer has been reported to be approximately twice as toxic as the trans isomer in producing narcosis. It is thought that commercial products may contain a significant amount of *cis*-isomer.

Animal to Human Dosimetric Adjustment: Not applicable; human data used

Time Scaling: $C^n \times t = k$ where $n = 2$; The concentration-exposure time relationship for many irritant and systemically acting vapors and gases may be described by $C^n * t = k$, where the exponent n ranges from 1 to 3.5 (ten Berge et al., 1986). In the absence of chemical specific data, an approximate midpoint value of n=2 was used as a default for scaling across time.

Confidence and Support for the AEGL Values: Although the values developed are considered to be protective, confidence in the AEGL-1 values is moderate due to only two subjects and differential toxicity of the *cis*- and *trans*- isomers.

ACUTE EXPOSURE GUIDELINE FOR 1,2-DICHLOROETHENE (CAS NO. 540-59-0)

AEGL-2 VALUES

30 minutes	1 hour	4 hours	8 hours
56 ppm	40 ppm	20 ppm	14 ppm

Reference: Lehman, K. B., and Schmidt-Kehl, L. 1936. The thirteen most important chlorinated aliphatic hydrocarbons from the standpoint of industrial hygiene. Arch. Fur Hygiene. 116: 9-268.

Test Species/Strain/Number: Human subjects/ 2

Exposure Route/Concentrations/Durations: Inhalation: 275, 825, 950, 1000, 1200, 1700, or 2200 ppm for 5-30 minutes

Effects:	275 ppm	no effects (5 min.)
	825 ppm	slight dizziness after 5 min. (10 min. exposure); determinant for AEGL-2
	950 ppm	slight burning of eyes (5 min.)
	1000 ppm	dizziness after 10 min; slight burning of eyes (30 min exposure)
	1200 ppm	Dizziness after 5 min; drowsiness; slight burning of eyes (10 min exposure)
	1700 ppm	Dizziness after 3 min; slight burning of eyes; intracranial pressure; nausea (5 min exposure)
	2200 ppm	Severe dizziness; intracranial pressure; nausea (5 min exposure)

Endpoint/Concentration/Rationale: 825 ppm for 5 min.; slight dizziness was observed.

Uncertainty Factors/Rationale:
Total uncertainty factor: 3

Interspecies:	Not applicable - human data used.
Intraspecies:	3 - the mechanism of narcosis is not expected to differ greatly among individuals, including sensitive individuals.

Modifying Factor: 2; differential isomer toxicity, the *cis*-isomer has been reported to be approximately twice as toxic as the trans isomer in producing narcosis. It is thought that commercial products may contain a significant amount of *cis*-isomer.

Animal to Human Dosimetric Adjustment: Not applicable; human data used

Time Scaling: $C^n \times t = k$ where $n = 2$;The concentration-exposure time relationship for many irritant and systemically acting vapors and gases may be described by $C^n * t = k$, where the exponent n ranges from 1 to 3.5 (ten Berge et al., 1986). In the absence of chemical specific data, an approximate midpoint value of n=2 was used as a default for scaling across time.

Confidence and Support AEGL Values: Although the values developed are considered to be protective, confidence in the AEGL-2 values is moderate due to only two subjects and differential toxicity of the *cis*- and *trans*- isomers.

ACUTE EXPOSURE GUIDELINES FOR 1,2-DICHLOROETHENE (CAS NO. 540-59-0)

AEGL-3 VALUES

30 minutes	1 hour	4 hours	8 hours
200 ppm	141 ppm	71 ppm	50 ppm

Reference: Freundt et al. 1977.Toxicity studies on 1,2-dichloroethylene. Toxicology. 7: 141-153.

Test Species/Strain/Sex/Number: Female SPF Wistar rats, 6/exposure group

Exposure Route/Concentrations/Durations: Inhalation: 0, 200, 1000, 3000 ppm for 8 hours

Effects: Increased incidence of fatty liver degeneration, pulmonary capillary hyperemia, alveolar septum distension (200, 1000, 3000 ppm)
Fibrous swelling and hyperemia of cardiac muscle with poorly maintained striation (3000 ppm) determinant for AEGL-3

Endpoint/Concentration/Rationale: 3000 ppm for 8 hours. The LOAEL for fibrous swelling and hyperemia of cardiac muscle with poorly maintained striation, this effect was not seen at 1000 ppm.

Uncertainty Factors/Rationale:
Total uncertainty factor: 30
Interspecies: 10, The physiology and metabolism leading to the induction of cardiac pathology is unknown. Given an unknown mechanism and the potential for differences in metabolism between species, an uncertainty factor of 10 was chosen.
Intraspecies: 3, although a factor of 10 might be used, the total UF would drive the AEGL-3 values down to AEGL-2 values. Since AEGL-2 values are based on human data and thus considered most appropriate, an intraspecies UF of 3 has been applied

Modifying Factor: 2; differential isomer toxicity, the *cis-* isomer has been reported to be approximately twice as toxic as the trans isomer in producing narcosis. It is thought that commercial products may contain a significant amount of *cis-* isomer.

Animal to Human Dosimetric Adjustment: Insufficient data

Time Scaling: $C^n \times t = k$ where $n = 2$;The concentration-exposure time relationship for many irritant and systemically acting vapors and gases may be described by $C^n * t = k$, where the exponent n ranges from 1 to 3.5 (ten Berge et al., 1986). In the absence of chemical specific data, an approximate midpoint value of $n=2$ was used as a default for scaling across time.

Confidence and Support for AEGL Values: Although the values developed are considered to be protective, confidence in the AEGL-3 values is moderate due to species variability and differential toxicity of the *cis-* and *trans-* isomers.

ISSUES- 1,2-DICHLOROETHENE

- **Derivation of AEGL-1 and AEGL-2 values**
  - **Extrapolation from 5 minutes to 8 hours**
- **New industry study suggests derived values may be too low**
- **Cardiac pathology is not reproducible**

AEGL-1 FOR 1,2-DICHLOROETHENE (ppm [mg/m^3])				
	30-min	1-hr	4-hr	8-hr
trans-	458 [1814]	363 [1437]	229 [907]	150 [594]
cis-	229 [907]	182 [719]	115 [454]	75 [297]

Species: Rat
Concentration: 2000 ppm *trans*-1,2 dichloroethene
Time: 6 hr.
Endpoint: Ocular irritation
Reference: Hurtt et al., 1993

n = 3 (30 min., 1 hr., 4 hr.)
n = 1 (8 hr.)

Uncertainty Factor: 3 x 3 = 10

Interspecies = 3 (Ocular irritation not likely to vary greatly)
Intraspecies = 3 (Ocular irritation not likely to vary greatly)

Total UF of 10 was applied to both *trans*- and *cis*-values

Modifying Factor: 2 (applied to *cis*- isomer only)

Narcosis and lethality data suggest that the *cis*- isomer is twice as toxic as the *trans*- isomer

AEGL-2 FOR 1,2-DICHLOROETHENE (ppm [mg/m^3])				
	30-min	1-hr	4-hr	8-hr
trans-	1374 [5441]	1091 [4320]	688 [2724]	450 [1782]
cis-	687 [2721]	546 [2160]	344 [1362]	225 [891]

Species: Rat
Concentration: 6000 ppm *trans*-1,2 dichloroethene
Time: 6 hr.
Endpoint: Narcosis
Reference: Hurtt et al., 1993

n = 3 (30 min., 1 hr., 4 hr.)
n = 1 (8 hr.)

Uncertainty Factor: 3 x 3 = 10

Interspecies = 3 (Narcosis not likely to vary greatly)
Intraspecies = 3 (Narcosis not likely to vary greatly)

Total UF of 10 was applied to both *trans*- and *cis*-values

Modifying Factor: 2 (applied to *cis*- isomer only)

Narcosis and lethality data suggest that the *cis*- isomer is twice as toxic as the *trans*- isomer

AEGL-3 FOR 1,2-DICHLOROETHENE (ppm [mg/m^3])				
	30-min	1-hr	4-hr	8-hr
trans-	2460 [9742]	1952 [7730]	1230 [4870]	615 [2435]
cis-	1230 [4871]	976 [3865]	615 [2435]	308 [1218]

Species: Rat
Concentration: 12,300 ppm *trans*-1,2 dichloroethene
Time: 4 hr.
Endpoint: NOEL for death
Reference: Kelly, 1999

n = 3 (30 min., 1 hr., 4 hr.)
n = 1 (8 hr.)

Uncertainty Factor: 3 x 3 = 10

Interspecies = 3 (Rat and mouse data show little species variability with regard to death)
Intraspecies = 3

Total UF of 10 was applied to both *trans*- and *cis*-values

Modifying Factor: 2 (applied to *cis*- isomer only)

Narcosis and lethality data suggest that the *cis*- isomer is twice as toxic as the *trans*- isomer

RELATIONAL COMPARISON OF AEGL VALUES FOR *TRANS*-1,2-DICHLOROETHENE (ppm [mg/m^3])				
Classification	30-min	1-hour	4-hour	8-hour
AEGL-1 (Nondisabling)	458 [1814]	363 [1437]	229 [907]	150 [594]
AEGL-2 (Disabling)	1374 [5441]	1091 [4320]	688 [2724]	450 [1782]
AEGL-3 (Lethality)	2460 [9742]	1952 [7730]	1230[4870]	615 [2435]

RELATIONAL COMPARISON OF AEGL VALUES FOR *CIS*-1,2-DICHLOROETHENE (ppm [mg/m^3])				
Classification	30-min	1-hour	4-hour	8-hour
AEGL-1 (Nondisabling)	229 [907]	182 [719]	115 [454]	75 [297]
AEGL-2 (Disabling)	687 [2721]	546 [2160]	344 [1362]	225 [891]
AEGL-3 (Lethality)	1230 [4871]	976 [3865]	615 [2435]	308 [1218]

ACGIH (TLV-TWA): 200 ppm (790 mg/m^3), *cis-/trans-* mixture (ACGIH, 1991)
NIOSH (TWA): 200 ppm (790 mg/m^3), *cis-/trans-* mixture

Appendix A

NATIONAL ADVISORY COMMITTEE (NAC)
FOR ACUTE EXPOSURE GUIDELINE LEVELS (AEGLs)
FOR HAZARDOUS SUBSTANCES

Final Meeting 15 Highlights
Green Room, 3rd Floor, Ariel Rios Building
Washington, D.C.

September 14-15, 1999

INTRODUCTION

George Rusch, NAC/AEGL Chairman, opened the meeting and welcomed the committee members. The meeting agenda (Attachment 1) and the attendee list (Attachment 2) are attached. Expansion on the conclusions of Ed Calabrese's single- exposure cancer database were provided by George Alexeeff and will be included in the revision. The revised NAC/AEGL-14 Highlights are attached (Appendix A). Later, the NAC-14 meeting highlights were accepted (moved by Mark McClanahan and seconded by John Hinz, [Appendix B]).

Roger Garrett, Program Director, addressed international matters, citing the importance of making the AEGL guidelines international.

TECHNICAL DISCUSSIONS
Summary of Initiatives

International Involvement

He also provided an overview regarding the involvement of the European community with the AEGL Program and that there will be new NAC members representing OECD. Mark Ruitjen of the Netherlands was introduced and made a presentation (Attachment 3) about how emergency exposure values and issues of concern (e.g., carcinogenicity, reproductive/developmental effects) are applied and indicated that there was a desire for active participation in the AEGL Program. It was stated that AEGL values would likely replace temporary values and would serve as the primary values for situations needing acute exposure assessments. Peter Griem, a toxicologist with a private consulting company in Germany and Mark Ruijten of Rotterdam Municipal Health Service were present at the meeting.

AEGL/NAS Procedure

Roger Garrett discussed seven issues that came out of the last Subcommittee meeting: (1) how to handle/derive values for carcinogenic substances, (2) the development of AEGL-1 values when data are lacking, (3) use of data involving routes of exposure other than inhalation, (4) citation of primary vs. secondary references, (5) changes to the AEGL-1 and AEGL-2 definitions, (6) use of NOELs in AEGL development, and (7) inclusion of the benchmark dose approach in AEGL development (Attachments 4 and 5). Following extensive discussion, the committee voted to accept NOAELs for AEGL-1 development where no toxic effect is established and to footnote such values as being based on no-effects below the summary table. The NAC also agreed to not develop AEGL-1 values where data

were lacking. The need to develop AEGL-1 numbers is a risk management rather than a risk assessment decision. Based on U.S. EPA guidance, the carcinogenicity adjustment factor will be changed from 2.8 to between 2 and 6.

Further NAS issues involved rewording or reworking some of the language and use of terms in the Standing Operating Procedures (SOP). For example, the NAS/COT/AEGL Subcommittee questioned the use of the term AEGL-NOEL in the SOP. The NAC decided to delete such terms as part of each AEGL definition and to use the terms NOEL, LOEL, NOAEL, and LOAEL only for describing the literature. For the definition, a narrative description will be used instead of the term AEGL-NOEL. The definition of the AEGL-3 will be revised to reflect the three endpoints now used (benchmark LC_{01}, the highest nonlethal dose, and the $LC_{50}/3$). The benchmark dose discussion in the SOP will be expanded to include information of Fowles et al. (1999) which involves using the 95% lower confidence limits on the dose causing a 5% response. The fit of the data to the line is determined by a chi square test.

AEGLs in NAS/COT Review

Seven chemicals (aniline, hydrazine, methylhydrazine, dimethylhydrazine [1,1- and 1,2-], chlorine, fluorine, arsine, and hydrogen cyanide) were reviewed by the COT AEGL Subcommittee at the August 23-24, 1999, meeting. Aniline passed with the need for only minor revisions. Robert Young (ORNL) explained the Subcommittee's suggestion of development of AEGL-1 values for the hydrazines and arsine. Following a discussion of the lack of available data and the steep dose-response curve for these chemicals, the NAC voted unanimously not to develop AEGL-1 values. Sylvia Talmage (ORNL) presented the Subcommittee's questions involving chlorine: consideration of a time-scaling value of n=1 based on the best lethality studies and whether the present values which are based on adult asthmatics protect pediatric asthmatics (Attachment 6). Marc Ruijten volunteered to locate a paper which would support a time-scaling n value of 1. Following a review of numerous papers on chlorine exposure and asthmatics, George Rodgers reported that there was no information on the greater or lesser sensitivity of pediatric asthmatics compared with adult asthmatics. These conclusions will be reported back to the AEGL Subcommittee.

Application of AEGLs

Bill Dunn of Argonne National Laboratory presented examples of the modeling conducted for the Department of Transportation in which the derived numbers are applied to transportation accidents (Attachment 7). He discussed spills in general, noting that liquefied gases are more problematic than compressed gases and ordinary liquids. Most accidents involve ammonia, chlorine, fuming sulfuric acid, fuming nitric acid, hydrogen fluoride and sulfur dioxide and most exposures are of short durations— about 5-15 minutes. Furthermore, exposures are not to constant concentrations. Having used ERPG numbers in the past, he noted that ERPG/TLV-TWA ratios average 8, and that one-tenth the LC_{50} is a good surrogate for the ERPG-2.

Benchmark Dose Methodology

Judy Strickland of the U.S. EPA National Center for Environmental Assessment made a presentation on the EPA benchmark dose software application to ethylene oxide. A beta version (1.1b) of the U.S. Environmental Protection Agency (EPA) Benchmark Dose Software (BMDS) can be found at the Web site URL: http://www.epa/gov.ncea/bmds.htm. An updated document will be available in February of 2000. Her discussion focused on the use of the appropriate model for several data sets and the goodness of fit of the data to the line as measured by p values.

AEGL PRIORITY CHEMICALS

Hydrogen Sulfide, CAS Reg. No. 7783-06-4

Chemical Manager: Steven Barbee, Arch Chemical, Inc.
Author: Cheryl Bast, ORNL

Cheryl presented data provided by the state of Texas involving exposure to a mixture of chemicals downwind of an oil refinery and relevant to development of AEGL-1 values. The concentrations of the other chemicals emitted from the refinery during the exposure were considered minor and below an effect level. The AEGL-1 was based on an exposure to hydrogen sulfide of 0.090 ppm for up to 5 hours which resulted in discomfort (headache, nausea, eye irritation, throat irritation, and persistent odor) in six staff members of the Texas Natural Resource Conservation Commission. An intraspecies uncertainty factor of 3 was applied to protect sensitive individuals. The 0.03 ppm concentration was flatlined across all exposure durations. The value is supported by a state of California level of annoyance of 0.04 ppm which is five times the odor threshold. Ernest Falke moved to accept the values; the motion was seconded by Richard Niemeier. The motion passed (YES: 20, NO: 2, ABSTAIN: 0) (Appendix C).

Furan, CAS Reg. No. 110-00-9

Chemical Manager: George Rodgers, University of Louisville (AAPCC)
Author: Claudia Troxel, ORNL

George Rodgers provided a brief discussion of furan in cigarette smoke. There was no revision to the TSD.

Otto Fuel II (Propylene Glycol Dinitrate), CAS Reg. No. 6423-43-4

Chemical Manager: William Bress, Vermont Department of Health
Author: Sylvia Talmage, ORNL

Sylvia Talmage reviewed background data, monitoring data, and data from the key references (Attachment 9). Data from a key study with healthy human subjects were sufficient to derive AEGL-1 and AEGL-2 values as well as to derive the time-scaling exponent of 1 based on the endpoints for the AEGL-1 and AEGL-2. The AEGL-1 was based on the threshold for mild headaches at two time points, 0.5 ppm for 1 hour and 0.1 ppm for 6 hours (only one of several subjects was affected). The 0.5 ppm concentration was used to derive the 30-minute and 1-hour values and the 0.1 ppm concentration was used to derive the 4- and 8-hour values, respectively No sensitive subpopulations were identified at these low concentrations of propylene glycol dinitrate and its metabolite nitric oxide. Therefore, the values were adjusted by an intraspecies uncertainty factor of 3. It was moved and seconded by George Rodgers and Richard Niemeier, respectively to adopt the proposed AEGL-1 values. The motion passed (YES: 16, NO: 0, ABSTAIN:0) (Appendix D).

The AEGL-2 values were based on a concentration of 0.5 ppm which caused severe headaches

accompanied by dizziness in one subject and slight loss of equilibrium in two subjects in one of several sensitive equilibrium tests after 6 hours of exposure. This concentration-exposure duration was considered the threshold for impaired ability to escape. The 0.5 ppm concentration was adjusted by an intraspecies uncertainty factor of 3 to protect sensitive individuals and scaled across time using the $C^1 \times t = k$ relationship as for the AEGL-1 above. It was moved and seconded by George Rodgers and Richard Neimeier, respectively, to adopt the proposed AEGL-1 values. The motion passed (YES: 16, NO: 0, ABSTAIN:0) (Appendix D).

The proposed AEGL-3 values, based on exposure of squirrel monkeys to concentrations of 70-100 ppm for 6 hours which resulted in vomiting, pallor, cold extremities, semiconsciousness, and colic convulsions will be considered at the next NAC/AEGL meeting in December.

Because propylene glycol dinitrate is the most toxic and volatile component of Otto Fuel II, the NAC decided to derive AEGL values for propylene glycol dinitrate with a footnote to the technical support document title suggesting that the values are appropriate for Otto Fuel II.

SUMMARY OF PROPOSED AEGL VALUES FOR PROPYLENE GLYCOL DINITRATE

Classification	30-Minute	1-Hour	4-Hour	8-Hour	Endpoint
AEGL-1	0.33 ppm (2.3 mg/m^3)	0.17 ppm (1.1 mg/m^3)	0.05 ppm (0.34 mg/m^3)	0.03 ppm (0.17 mg/m^3)	Threshold for mild headache, humans
AEGL-2	2.0 ppm (14 mg/m^3)	1.0 ppm (6.8 mg/m^3)	0.25 ppm (1.7 mg/m^3)	0.13 ppm (0.8 mg/m^3)	Severe headache and slight imbalance, humans

ADMINISTRATIVE ISSUES

Because of Hurricane Floyd, the NAC/AEGL-15 meeting was concluded at the end of the second day on September 15, 1999. The remaining agenda items that were not covered will be addressed at the December meeting.

This report was prepared by Sylvia Talmage, Robert Young, and Po-Yung Lu, ORNL.

LIST OF ATTACHMENTS

The attachments were distributed during the meeting and will be filed in the EPA Docket Office.

1. NAC/AEGL Meeting No. 15 Agenda
2. NAC/AEGL Meeting No. 15 Attendee List
3. Netherlands Temporary Emergency Number Program - Marc Ruijten
4. Principal Issues to Resolve with NAS/COT/AEGL Subcommittee - Roger Garrett
5. Technical Issues from NAS/COT/AEGL Subcommittee - Roger Garrett
6. Chemical Specific Comment Responses to NAS/COT/AEGL: Chlorine -Sylvia Talmage
7. Health Criteria Needs for Risk Assessment and Emergency Response Planning - William Dunn
8. Benchmark Dose Procedures: Application to Ethylene Oxide - Judy Strickland
9. Data Analysis for Otto Fuel II - Sylvia Talmage

LIST OF APPENDICES

A. Approved NAC-AEGL-14 Meeting Highlights
B. Ballot for Minutes approval
C Ballot for Hydrogen sulfide
D. Ballot for Otto Fuel II

( ) = ABSENT

12/6/99

NAC/AEGL Meeting 16: 12/6-8/99 **Chemical:** 20/30 present > 13 votes = Consensus

Appendix B

	NAC Member	AEGL 1	AEGL 2	AEGL 3	NAC Member	AEGL 1	AEGL 2	AEGL 3	
X	George Alexeeff				Loren Koller				✓
✓	Steven Barbee				Glenn Leach	present ~ 11	00		X
✓	Lynn Beasley				Mark A. McClanahan				✓
X	David Belluck				John S. Morawetz				✓
✓	Robert Benson				~~Deirdre L. Murphy~~				
X	Jonathan Borak				Richard W. Niemeier				X
✓	William Bress				William Pepelko				✓
✓	George Cushmac				Zarena Post				✓
✓	Ernest Falke				George Rodgers				✓
X	Larry Gephart				George Rusch, Chair				✓
✓	John Hinz				Michelle Schaper				✓
✓	Jim Holler				Bob Snyder				✓
✓	Thomas C. Hornshaw				Thomas Sobotka NOTE:	present 11:20 AM			X
✓	Nancy Kim				Kenneth Still				✓
X	MARINELLE PAYTON				Richard Thomas				X
					Thomas Tuccinardi/ Doan Hansen				
					TALLY				

PPM, (mg/m³)	30 Min	60 Min	4 Hr	8Hr
AEGL 1	, ( )	, ( )	, ( )	, ( )
AEGL 2	, ( )	, ( )	, ( )	, ( )
AEGL 3	, ( )	, ( )	, ( )	, ( )

AEGL 1 **Motion:** _____ **Second:** _____

AEGL 2 **Motion:** _____ **Second:** _____

AEGL 3 **Motion:** _____ **Second:** _____

Approved by Chair: _____ **DFO:** _____ **Date:** _____

Appendix C

JOHN MORAWETZ PROPOSAL

NAC/AEGL Meeting 16: 12/6-8/99 **Chemical:** VOTE ON: ①

NAC Member	~~AEGL~~ 1	~~AEGL~~ 2	~~AEGL~~ 3	NAC Member	~~AEGL~~ 1	~~AEGL~~ 2	~~AEGL~~ 3
George Alexeeff	A			Loren Koller			
Steven Barbee				Glenn Leach	A		
Lynn Beasley				Mark A. McClanahan			
David Belluck	A			John S. Morawetz			
Robert Benson				Deirdre L. Murphy			
Jonathan Borak	A			Richard W. Niemeier	A		
William Bress				William Pepelko			
George Cushmac				Zarena Post			
Ernest Falke				George Rodgers	OPPOSED		
Larry Gephart	A			George Rusch, Chair			
John Hinz				Michelle Schaper			
Jim Holler				Bob Snyder			
Thomas C. Hornshaw				Thomas Sobotka	A		
Nancy Kim				Kenneth Still			
MARIELLE PAYTON	A			Richard Thomas	A		
				Thomas Tuccinardi/ Doan Hansen	A A		
ADOPT THE FOLLOWING...				TALLY			

"A ceiling value not to be exceeded is the AEGL value with the shortest (least) time. For most chemicals, this will be the 30min. value, unless a shorter period is determined (for example 10 minutes)." BY SHOW OF HANDS, ONLY NO VOTE WAS GEORGE RODGERS

PPM, (mg/m^3)	30 Min	60 Min	4 Hr	8Hr
AEGL 1	, ( )	, ( )	, ( )	, ( )
AEGL 2	, ( )	, ( )	, ( )	, ( )
AEGL 3	, ( )	, ( )	, ( )	, ( )

AEGL 1 **Motion:** R. Snyder **Second:** J. Hinz

AEGL 2 **Motion:** _____ **Second:** _____

AEGL 3 **Motion:** _____ **Second:** _____

Approved by Chair: [signature] **DFO:** Paul S. Tobin **Date:** 12/6/99

75-21-8
ETHYLENE OXIDE

NAC/AEGL Meeting 16: 12/6-8/99 **Chemical:** ~~METHYL ISOBUTYL KETONE~~

Appendix D

NAC Member	AEGL 1	AEGL 2	AEGL 3
George Alexeeff		A	
Steven Barbee		Y	
Lynn Beasley		Y	
David Belluck		A	
Robert Benson		P	
Jonathan Borak		A	
William Bress		Y	
George Cushmac		Y	
Ernest Falke		N	
Larry Gephart		A	
John Hinz		Y	
Jim Holler		Y	
Thomas C. Hornshaw		Y	
Nancy Kim		Y	

NAC Member	AEGL 1	AEGL 2	AEGL 3
Loren Koller		N	
Glenn Leach		A	
Mark A. McClanahan		Y	
John S. Morawetz		N	
~~Deirdre L. Murphy~~			
Richard W. Niemeier		A	
William Pepelko		A	
Zarena Post		Y	
George Rodgers		Y	
George Rusch, Chair		Y	
Michelle Schaper		Y	
Bob Snyder		N	
Thomas Sobotka		N	
Kenneth Still		Y	
Richard Thomas		A	
Thomas Tuccinardi/ Doan Hansen		A A	
TALLY		14/19	

PPM, (mg/m^3)	30 Min	60 Min	4 Hr	8Hr
AEGL 1	, ( )	, ( )	, ( )	, ( )
AEGL 2	80 , ( )	45 , ( )	14 , ( )	7.9 , ( )
AEGL 3	, ( )	, ( )	, ( )	, ( )

AEGL 1 **Motion:** _____ **Second:** _____

AEGL 2 **Motion:** G. Rodgers **Second:** J. Hinz

AEGL 3 **Motion:** _____ **Second:** _____

Approved by Chair: George M Rusch **DFO:** Paul S. Tobin **Date:** 12/6/99

NAC/AEGL Meeting 16: 12/6-8/99 **Chemical:** METHYL ISOCYANATE

NAC Member	AEGL 1	AEGL 2	AEGL 3	NAC Member	AEGL 1	AEGL 2	AEGL 3
George Alexeeff		A		Loren Koller		Y	
Steven Barbee		Y		Glenn Leach		A	
Lynn Beasley		Y		Mark A. McClanahan		Y	
David Belluck		A		John S. Morawetz		Y	
Robert Benson		Y		~~Deirdre L. Murphy~~			
Jonathan Borak		A		Richard W. Niemeier		A	
William Bress		Y		William Pepelko		A	
George Cushmac		Y		Zarena Post		Y	
Ernest Falke		Y		George Rodgers		Y	
Larry Gephart		A		George Rusch, Chair		Y	
John Hinz		Y		Michelle Schaper	P	P	
Jim Holler		Y		Bob Snyder		Y	
Thomas C. Hornshaw		P		Thomas Sobotka		N	
Nancy Kim		Y		Kenneth Still		Y	
				Richard Thomas		A	
				Thomas Tuccinardi/ Doan Hansen		A A	
				TALLY		17/18	

* AEGL-1 unanimous to accept with one abstain -M. SCHAPER

PPM, (mg/m^3)	30 Min	60 Min	4 Hr	8Hr
AEGL 1	N/A ,( )	N/A ,( )	N/A ,( )	N/A ,( )
AEGL 2	0.13 ,( )	0.67 ,( )	0.017 ,( )	0.008 ,( )
AEGL 3	,( )	,( )	,( )	,( )

Not ~~Determined~~ Applicable, AEGL-1 irritation levels would exceed AEGL-1

AEGL 1 **Motion:** E. Falke **Second:** M. McClanahan

AEGL 2 **Motion:** L. Koller **Second:** M. McClanahan

AEGL 3 **Motion:** _____ **Second:** _____

Approved by Chair: _____ **DFO:** _____ **Date:** 12/6/99

106602-80-6
↳ 6423-43-4 → NO_2-OCH_2 CH − ONO_2 / CH_3

NAC/AEGL Meeting 16: 12/6-8/99 **Chemical:** OTTO FUEL II (PROPYLENE GLYCOL DINITRATE)

Appendix F

NAC Member	AEGL 1	AEGL 2	AEGL 3
George Alexeeff	A	A	A
Steven Barbee	Y	Y	Y
Lynn Beasley	Y	Y	Y
David Belluck	A	A	A
Robert Benson	Y	Y	Y
Jonathan Borak	A	A	A
William Bress	Y	N	Y
George Cushmac	Y	Y	Y
Ernest Falke	Y	Y	Y
Larry Gephart	A	A	A
John Hinz	Y	Y	Y
Jim Holler	A	A	A
Thomas C. Hornshaw	Y	Y	Y
Nancy Kim	Y	N	Y
MICHELLE PAYTON	A	A	A

NAC Member	AEGL 1	AEGL 2	AEGL 3
Loren Koller	A	A	A
Glenn Leach	A	A	A
Mark A. McClanahan	Y	Y	Y
John S. Morawetz	N	N	Y
~~Deirdre L. Murphy~~			—
Richard W. Niemeier	Y	Y	Y
William Pepelko	A	Y	A
Zarena Post	Y	N	Y
George Rodgers	Y	N	Y
George Rusch, Chair	Y	Y	Y
Michelle Schaper	Y	N	Y
Bob Snyder	Y	Y	Y
Thomas Sobotka	A	A	A
Kenneth Still	A	A	A
Richard Thomas	A	A	A
Thomas Tuccinardi/ Doan Hansen	A A	A A	A A
TALLY	16/19	12/18	17/17

PPM, (mg/m³) ppm	30 Min	60 Min	4 Hr	8Hr
AEGL 1 0.33	,( )	,( )	,( )	,( )
AEGL 2 6.0	,( )	,( )	,( )	,( )
AEGL 3 23	16 ,( )	13 ,( )	8.0 ,( )	5.3 ,( )

AEGL 1 **Motion:** Benson **Second:** Falke

AEGL 2 **Motion:** Snyder **Second:** John Hinz

AEGL 3 **Motion:** Falke **Second:** McClanahan

Approved by Chair: [signature] ~~**DFO:**~~ Paul S. Tobin **Date:** 12/8/99

12/7/99 e

NAC/AEGL Meeting 16: 12/6-8/99 **Chemical:** 505-60-2 SULFUR MUSTARD

Appendix G

NAC Member (10 Min AEGL 1,2,3)	AEGL 1	AEGL 2	AEGL 3
George Alexeeff A A A	A	A	A
Steven Barbee Y Y Y	Y	Y	Y
Lynn Beasley Y Y Y	Y	Y	Y
David Belluck A A A	A	A	A
Robert Benson Y N N	Y	N	Y
Jonathan Borak A A A	A	A	A
William Bress Y Y Y	Y	Y	Y
George Cushmac Y Y Y	Y	Y	Y
Ernest Falke Y Y Y	Y	Y	Y
Larry Gephart A A A	A	A	A
John Hinz Y P P	Y	N	Y
Jim Holler A A A	A	A	A
Thomas C. Hornshaw Y Y Y	Y	Y	Y
Nancy Kim Y Y Y	Y	Y	Y

NAC Member	AEGL 1	AEGL 2	AEGL 3
Loren Koller Y Y Y	Y	Y	Y
Glenn Leach Y Y Y	Y	Y	Y
Mark A. McClanahan Y N N	Y	N	Y
John S. Morawetz N Y P	N	Y	Y
~~Deirdre L. Murphy~~			
Richard W. Niemeier Y Y Y	Y	Y	P
William Pepelko Y N Y	Y	Y	Y
Zarena Post N Y Y	Y	Y	Y
George Rodgers P P P	Y	Y	N
George Rusch, Chair Y Y Y	Y	P	Y
Michelle Schaper A A A	A	A	A
Bob Snyder Y Y Y	Y	Y	Y
Thomas Sobotka Y N N	Y	Y	Y
Kenneth Still Y Y Y	Y	Y	Y
Richard Thomas A A A	A	A	A
Thomas Tuccinardi/ A A A Doan Hansen A N Y	A P	A N	A Y
18/19, 15/20, TALLY	20/21	17/21	20/21

~~PPM~~, (mg/m³)	10 Min	30 Min	60 Min	4 Hr	8Hr
AEGL 1	0.040 mg/m³	0.13 mg/m³, ( )	0.067, ( )	0.017, ( )	0.008, ( )
AEGL 2	0.6	0.20, ( )	0.10, ( )	0.025, ( )	0.013, ( )
AEGL 3	6.1	4.2, ( )	2.1, ( )	0.53, ( )	0.27, ( )

10min Benson — L Koller

AEGL 1 **Motion:** L Koller — **Second:** K Still

10min Bress — G Leach

AEGL 2 **Motion:** Snyder — **Second:** Pepelko

10min Bress — G. Leach

AEGL 3 **Motion:** Benson — **Second:** W. Pepelko

Approved by Chair: [signature] **DFO:** [signature] **Date:** 12/7/99

Appendix H

NAC/AEGL Meeting 16: 12/6-8/99 **Chemical:** 1,1,1-TRICHLOROETHANE 71-55-6 Cl_3C-CH_3

NAC Member (10 MIN AEGL 1,2,3)	AEGL 1 (1) (2)	AEGL 2	AEGL 3
George Alexeeff AAA	A A	A	A
Steven Barbee YYY	N Y	N	Y
Lynn Beasley YYY	Y Y	Y	Y
David Belluck AAA	A A	A	A
Robert Benson YYY	Y Y	Y	Y
Jonathan Borak AAA	A A	A	A
William Bress YYY	N Y	N	Y
George Cushmac YYY	Y Y	Y	Y
Ernest Falke YYY	Y Y	Y	Y
Larry Gephart AAA	A A	A	A
John Hinz YYY	P N	N	Y
Jim Holler AAA	A A	A	A
Thomas C. Hornshaw YYP	N Y	Y	P
Nancy Kim YNP	Y Y	Y	P
Marinelle Payton AAA	A	A	A

NAC Member	AEGL 1	AEGL 2	AEGL 3
Loren Koller AAA	A A	A	A
Glenn Leach AAA	A A	A	A
Mark A. McClanahan YYY	N N	N	Y
John S. Morawetz YNN	Y Y	N	N
Deirdre L. Murphy			
Richard W. Niemeier YNY	Y Y	Y	Y
William Pepelko YYY	A A	A	A
Zarena Post YNN	Y Y	N	N
George Rodgers YNY	Y Y	Y	Y
George Rusch, Chair YYY	N Y	Y	Y
Michelle Schaper PPP	A A	A	A
Bob Snyder YYY	Y Y	Y	Y
Thomas Sobotka AAA	N Y	A	A
Kenneth Still AAA	Y Y	Y	Y
Richard Thomas AAA	A A	A	A
Thomas Tuccinardi/ Doan Hansen AAA / AAA	A A / N N	A / Y	A / Y
(17/17) (2/10) (13/15) TALLY	*11/18 #6/19	12/18	14/16

10 MIN AEGL-1 10 MIN AEGL-2 10 MIN AEGL-3

(1) * DOES NOT PASS 2/3 CONSENSUS
(2) # DOES PASS 2/3 CONSENSUS

PPM, (mg/m³) 10 MIN	30 Min	60 Min	4 Hr	8Hr
AEGL 1 230	(1) ~~150~~ (2) 230 ,( )	~~150~~ 230 ,( )	~~150~~ 230 ,( )	~~150~~ 230 ,( )
AEGL 2 930	670 ,( )	600 ,( )	380 ,( )	310 ,( )
AEGL 3 4800	4800 ,( )	3800 ,( )	2400 ,( )	1900 ,( )

AEGL 1 **Motion:** LOST (10 min) **Second:** ROGERS
10 min: McCLANAHAN / MORAWETZ

AEGL 2 **Motion:** RODGERS (10 min) **Second:** HANSEN
10 min: FALKE / HINZ

AEGL 3 **Motion:** McCLANAHAN (10 min) **Second:** HANSEN
10 min: RODGERS / HINZ

Approved by Chair: [signature] **DFO:** [signature] **Date:** 12/7/99 - 12/8/99

~~130-60-5~~ 12/6/17

Appendix I

NAC/AEGL Meeting 16: 12/6-8/99 **Chemical:** trans-1,2-DICHLOROETHYLENE

NAC Member	AEGL 1	AEGL 2	AEGL 3 ① ②	NAC Member	AEGL 1	AEGL 2	AEGL 3
George Alexeeff	A	A	A A	Loren Koller	A	A	A A
Steven Barbee	Y	N	Y N	Glenn Leach	A	A	A A
Lynn Beasley	Y	Y	Y Y	Mark A. McClanahan	Y	N	Y N
David Belluck	A	A	A A	John S. Morawetz	Y	P	N Y
Robert Benson	N	Y	Y Y	~~Deirdre L. Murphy~~			
Jonathan Borak	A	A	A A	Richard W. Niemeier	Y	N	Y N
William Bress	Y	Y	Y Y	William Pepelko	Y	Y	N Y
George Cushmac	Y	Y	Y Y	Zarena Post	Y	Y	N Y
Ernest Falke	Y	Y	Y Y	George Rodgers	Y	Y	N Y
Larry Gephart	A	A	A A	George Rusch, Chair	Y	Y	Y Y
John Hinz	P	P	Y N	Michelle Schaper	P	P	P P
Jim Holler	A	A	A A	Bob Snyder	Y	Y	Y Y
Thomas C. Hornshaw	N	Y	N Y	Thomas Sobotka	A	A	A A
Nancy Kim	Y	Y	N Y	Kenneth Still	A	A	A A
Michelle Pattan	A	A	A	Richard Thomas	A	A	A A
				Thomas Tuccinardi/ Doan Hansen	A A	A A	A A A A
				TALLY	14/15	12/15	*11/17 #13/17

* DOES NOT PASS 2/3 CONSENSUS
\# DOES PASS 2/3 CONSENSUS

PPM, (mg/m³) 10 MIN	30 Min	60 Min	4 Hr	8Hr
AEGL 1 280	280 ,( )	280 ,( )	280 ,( )	280 ,( )
AEGL 2 2000	1000 ,( )	1000 ,( )	700 ,( )	450 ,( )
AEGL 3 ② ~~1700~~ 2500 ① ~~2500~~	~~2500~~ 2500 ,( )	~~1700~~ 2000 ,( )	~~1200~~ 1200 ,( )	~~620~~ 620 ,( )

AEGL 1 **Motion:** ~~R. Snyder~~ Rodgers **Second:** ~~M. McClanahan~~ Post

AEGL 2 **Motion:** ~~Benson~~ McClanahan Hornshaw **Second:** ~~Snyder~~ Rodgers

AEGL 3 **Motion:** ① Snyder ② ~~Benson~~ McClanahan **Second:** Snyder

Approved by Chair: [signature] **DFO:** Paul S. Tobin **Date:** 12/8/99

156-59-2 10/0177

Appendix J

NAC/AEGL Meeting 16: 12/6-8/99

Chemical: cis- 1,2-DICHLOROETHYLENE

NAC Member	AEGL 1	AEGL 2	AEGL 3 ①	AEGL 3 ②
George Alexeeff	A	A	A	A
Steven Barbee	Y	Y	N	Y
Lynn Beasley	Y	Y	Y	Y
David Belluck	A	A	A	A
Robert Benson	N	N	Y	N
Jonathan Borak	A	A	A	A
William Bress	Y	Y	Y	N
George Cushmac	Y	Y	Y	Y
Ernest Falke	Y	Y	Y	Y
Larry Gephart	A	A	A	A
John Hinz	P	P	N	N
Jim Holler	A	A	A	A
Thomas C. Hornshaw	N	Y	Y	Y
Nancy Kim	Y	Y	Y	Y
MICHELLE PAYTON	A	A	A	

NAC Member	AEGL 1	AEGL 2	AEGL 3 ①	AEGL 3 ②
Loren Koller	A	A	A	A
Glenn Leach	A	A	A	A
Mark A. McClanahan	Y	Y	N	Y
John S. Morawetz	Y	P	N	P
~~Deirdre L. Murphy~~		\		
Richard W. Niemeier	Y	Y	N	Y
William Pepelko	Y	Y	Y	Y
Zarena Post	Y	N	P	N
George Rodgers	Y	Y	N	Y
George Rusch, Chair	Y	Y	Y	Y
Michelle Schaper	P	P	P	P
Bob Snyder	Y	Y	Y	Y
Thomas Sobotka	A	A	A	A
Kenneth Still	A	A	A	A
Richard Thomas	A	A	A	A
Thomas Tuccinardi/ Doan Hansen	A A	A A	A A	A A
TALLY	14/16	13/15 *	10/16 *	# 10/16

* DOES NOT PASS 2/3 CONSENSUS
# DOES PASS CONSENSUS

PPM, (mg/m³) 10 MIN	30 Min	60 Min	4 Hr	8Hr
AEGL 1 140	140 ,( )	140 ,( )	140 ,( )	140
AEGL 2 1000	690 ,( )	550 ,( )	340 ,( )	230
AEGL 3 ② 1700 ① 1700	1200 1700 ,( )	980 1700 ,( )	620 1220 ,( )	310 620

AEGL 1 Motion: Rodgers Second: Barbee

AEGL 2 Motion: ~~McClanahan~~ Hornshaw Second: Rodgers

AEGL 3 Motion: Falke Second: McClanahan Snyder Benson

Approved by Chair: [signature] DFO: Paul S. Tobin Date: 12/8/99

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