National Advisory Committee (NAC)
for Acute Exposure Guideline Levels (AEGLs) for Hazardous Substances

February 1-3, 2006

Final Meeting-39 Highlights

U.S. Department of Labor
Rooms 5515 1A and 1B
200 Constitution Ave., N.W.
Washington, DC 20210

INTRODUCTION

Chairman George Rusch welcomed the committee, and announced that the NAC AEGL committee was well represented at the Toxicology Forum held January 31 in Washington, D. C. Participants in the AEGL session of the Toxicology Forum included Drs. Rusch, Don Gardner (chairman of the AEGL COT subcommittee), Ernest Falke, Bob Benson, Marc Ruijten, and George Woodall.

The chair also noted that as a consequence of political concerns the AEGL meeting for December, 2005, had to be canceled, and the agenda for this meeting was severely shortened. He stated that it was unfortunate that these political concerns interfered with the technical responsibility of the AEGL Committee to provide additional guidance to emergency responders.

Dr. Rusch also thanked retiring NAC members Jonathan Borak, Bill Bress, Tom Hornshaw, Nancy Kim, and John Morawetz for their many years of service to the committee.

The draft NAC/AEGL-38 meeting highlights were reviewed. Marc Ruijten suggested including a statement that a white paper regarding the use of RD_{50} for AEGL value derivation would be prepared and included as part of the SOP. This suggestion was incorporated into the highlights. A motion was made by George Rodgers and seconded by Nancy Kim to accept the meeting highlights as presented with the aforementioned revision. The motion passed unanimously by a show of hands (Appendix A). The final version of the NAC/AEGL-38 meeting highlights is attached (Appendix B).

The highlights of the NAC/AEGL-39 meeting are summarized below along with the Meeting Agenda (Attachment 1) and the Attendee List (Attachment 2). The subject categories of the highlights do not necessarily follow the order listed in the NAC/AEGL-39 Agenda.

HUMAN STUDIES ISSUES

Ernest Falke presented a synopsis of the Final Rule on Protections for Subjects in Human Research (Attachment 3) regarding use of third party human pesticide data including how this may impact the AEGL program. The Final Rule was expected to be published within one week. The Agency has interpreted this law to include both pesticides and industrial chemicals. Dr. Falke pointed out that the most important Section impacting the AEGL program is Subpart Q-Ethical Standards for Assessing Whether to Rely on the Results of Human Research in EPA Actions.

AEGL DATA BASES

Richard Williams, intern with the AEGL program, provided information and demonstrations of the AEGL Expert System data base and AEGL Derivation data base (Attachment 4). The AEGL Expert System data base is designed to examine AEGL chemicals using a chemical class approach and to compile a broad range of safety and emergency data (Federal and nongovernmental) for these chemicals. The AEGL Derivation data base is designed to store and categorize data pertaining to the development of AEGL values. The AEGL expert system data base will be publically available; whereas, the Derivation data base will be available to AEGL program staff and NAC members. Both data bases were well received by NAC members. Several suggestions for improvement were offered and are presented in Attachment 5.

USE OF OCCUPATIONAL STANDARDS AND RECOMMENDATIONS IN SETTING AEGL VALUES

John Morawetz discussed the use of occupational standards in the context of derivation of AEGL values (Attachment 6). Different occupational standards were defined, and Mr. Morawetz pointed out that occupational values provide no specific information that AEGL-1 effects will not occur in the public at recommended occupational exposure limits.

REVIEW of PRIORITY CHEMICALS

Cyclohexyl Isocyanate (CAS No. 3173-53-3)

Staff Scientist: Carol Wood, ORNL
Chemical Manager: Marc Ruijten, RIVM

Cheryl Bast presented this chemical on behalf of Carol Wood. AEGL-3 values (0.14 ppm for 10- and 30- min, 0.11 ppm for 1-hr, 0.072 ppm for 4-hrs, and 0.047 ppm for 8-hrs) for cyclohexyl isocyanate were derived at NAC-38 (September, 2005). The point-of-departure (1.88 ppm) was a calculated $BMCL_{05}$ from a 6-hour rat study (Eastman Kodak, 1990; 1992) (Attachment 7). However, the $BMCL_{05}$ was calculated incorrectly; the correct value is 1.67 ppm, yielding AEGL-3 values of 0.13 ppm for 10- and 30- min, 0.10 ppm for 1-hr, 0.064 ppm for 4-hrs, and 0.042 ppm for 8-hrs. A motion was made by Richard Niemier and seconded by George Woodall to adopt the revised AEGL-3 values based on the $BMCL_{05}$ of 1.67 ppm. Uncertainty factors (3 each for inter- and intraspecies extrapolation), modifying factor (3 for sparse data base), and time scaling (default values of n = 1 or n =3) remained unchanged. The motion carried (YES: 21; NO: 0; ABSTAIN: 0) (APPENDIX C).

Summary of AEGL Values for Cyclohexyl Isocyanate						
Classification	**10-minute**	**30-minute**	**1-hour**	**4-hour**	**8-hour**	**Endpoint (Reference)**
AEGL–1	NR	NR	NR	NR	NR	Not recommended: Insufficient data
AEGL–2	NR	NR	NR	NR	NR	Not recommended: Insufficient data
AEGL–3	~~0.14 ppm~~ 0.13 ppm	~~0.14 ppm~~ 0.13 ppm	~~0.11 ppm~~ 0.10 ppm	~~0.072 ppm~~ 0.064 ppm	~~0.047 ppm~~ 0.042 ppm	6-hr $BMCL_{05}$ in rats (Eastman Kodak, 1990; 1992)

Silane (CAS No. 7803-62-5)

Staff Scientist: Dana Glass, ORNL
Chemical Manager: Bob Benson, U.S. EPA

Bob Benson, chemical manager, made a few introductory remarks about the issues regarding silane. The data base is limited. There are only limited data that could be used to determine the value of n for time scaling. In addition, there are no data that can be used to estimate the intrahuman variability in response. Dana Glass then discussed the data summarized in the TSD (Attachment 8). The key study for determining the AEGL-3 values is Takebayashi et al. (1993). This study was conducted in mice with exposures at 0, 2500, 5000, or 10,000 ppm for 4 hours. At

5000 ppm there was no mortality but the animals showed renal lesions even after a two week recovery period. At 10,000 ppm, 6 of 8 animals died. AEGL-3 values were determined from the 5000 ppm exposure for 4 hours using a total uncertainty factor of 30, the default scaling procedure (n = 3 for shorter durations and n = 1 for longer durations), with the 10 minute value set at the 30 minute value because the primary study used an exposure duration of 4 hours. The interspecies uncertainty factor was 3 because other data (MacEwen and Vernot, 1972) identified the mouse as the most sensitive species. The intraspecies uncertainty factor was set at the default value of 10 as there are no data to estimate intrahuman variability and the chemical is not acting as a direct chemical irritant. The calculated values are 300 ppm for 10 and 30 minutes, 270 ppm for 1 hour, 170 ppm for 4 hours, and 80 ppm for 8 hours. After discussion, a motion was made by Bob Benson and seconded by Ernest Falke to adopt AEGL-3 values as proposed. The motion carried (YES: 19; NO: 0; ABSTAIN: 3) (APPENDIX D).

The key study for determining AEGL-2 values is also Takebayashi et al. (1993). At an exposure of 2500 ppm for 4 hours, the animals showed reversible renal lesions. Renal lesions that were present after a two day recovery period were not present after a 2 week recovery period. This is considered the no effect level for irreversible effects and is used to derive quantitative values using the uncertainty factors and time scaling as described above. The calculated values are 170 ppm for 10 and 30 minutes, 130 ppm for 1 hour, 80 ppm for 4 hours, and 42 ppm for 8 hours. A motion was made by Bob Benson and seconded by Richard Thomas to adopt AEGL-2 values as proposed. The motion carried (YES: 21; NO: 0; ABSTAIN: 1) (APPENDIX D).

The key study for determining AEGL-1 values is Omae et al. (1992). In this study, mice were exposed to 0 or 1000 ppm for 1, 2, 4, or 8 hours. Additional animals were exposed for 6 hours/day, 5 days/week for 2 and 4 weeks. Signs of minor irritation were observed (increased face washing and mild irritation in the nasal cavity after 4 weeks of exposure). No renal lesions were observed in the study. Mark Ruijten made a motion to base AEGL-1 values on the 1000 ppm exposure with a total uncertainty factor of 10 and no time scaling. The interspecies and intraspecies uncertainty factors were both 3 because the only effect observed is mild irritation and this response is not expected to vary greatly among species or among humans. Because of the conflict with AEGL-2 at longer times, AEGL-1 values for 4 and 8 hours were not recommended. The AEGL-1 values are 100 ppm for 10, 30, and 60 minutes. Steve Barbee seconded the motion. The motion passed. The motion carried (YES: 13; NO: 3; ABSTAIN: 6) (APPENDIX D).

Summary of AEGL Values for Silane

Classification	10-minute	30-minute	1-hour	4-hour	8-hour	Endpoint (Reference)
AEGL–1	100 ppm	100 ppm	100 ppm	NR	NR	NOEL for irritation in mice (Omae et al., 1992)
AEGL–2	170 ppm	170 ppm	130 ppm	80 ppm	42 ppm	Reversible renal lesions in mice (Takebayashi , 1993)
AEGL–3	300 ppm	300 ppm	270 ppm	170 ppm	80 ppm	NOEL for lethality in mice (Takebayashi , 1993)

Trimethoxysilane (CAS No. 2487-90-3)

Staff Scientist: Dana Glass, ORNL
Chemical Manager: Bob Benson, U.S. EPA

Bob Benson, chemical manager, made a few introductory remarks about the issues regarding trimethoxysilane. The data base is limited. In the only single exposure study available (Nachreiner and Dodd, 1988), the effects observed at the lowest exposure tested were more severe than the definition of AEGL-2. It might be possible to use a repeated dose study to derive AEGL-1 values. The data for deriving the value of n for time scaling are also limited. Dana Glass then discussed the data summarized in the TSD (Attachment 9). The key study for determining the AEGL-3 values is Nachreiner and Dodd (1988). In this study rats were exposed for 1 hour to 68, 155, 342, or 643 ppm and for 4 hours to 19, 39, 71, or 166 ppm. No deaths were observed at the lowest exposures, but there were severe lung lesions at this exposure. The $BMCL_{05}$ for 1 hour is 60 ppm and for 4 hours is 22 ppm. AEGL-3 values were calculated using the $BMCL_{05}$ values, a total uncertainty factor of 30, and the default time scaling procedure (n = 3 for shorter durations and n = 1 for longer durations). The interspecies uncertainty factor of 3 was used because another study (Dow Corning, 1981) showed similar effects in rats, mice, and hamsters. The default value of 10 was used as the intraspecies uncertainty factor as there are no data to estimate intrahuman variability and it is not clear that trimethoxysilane is acting as a simple chemical irritant in the lung. The proposed AEGL-3 values were 3.6 ppm for 10 minutes, 2.5 ppm for 30 minutes, 2.0 ppm for 1 hour, 0.73 ppm for 4 hours, and 0.37 ppm for 8 hours. Mark Ruitjen had used the original data on mortality and the ten Berge program to calculate an n value of 1.45. Using this as the value of n, the calculated AEGL-3 values are 8.8 ppm for 10 minutes, 4.1 ppm for 30 minutes, 2.5 ppm for 1 hour, 0.98 ppm for 4 hours, and 0.61 ppm for 8 hours. Ernie Falke made a motion to accept the values based on the time scaling exponent of n= 1.45. Richard Thomas seconded the motion. The motion passed (YES: 18; NO: 2; ABSTAIN: 1) (APPENDIX E).

As noted above, the lowest exposure from Nachreiner and Dodd (1988) gave effects more severe than the definition of AEGL-2. Because of the limited data and the steep dose response curve, Bob Benson made a motion to derive the AEGL-2 values by dividing the AEGL-3 values by 3. (2.9 ppm for 10 minutes, 1.4 ppm for 30 minutes, 0.83 ppm for 1 hour, 0.33 ppm for 4 hours, and 0.20 ppm for 8 hours). John Hinz seconded the motion. The motion passed (YES: 21; NO: 1; ABSTAIN: 0) (APPENDIX E).

There are no single exposure studies with endpoints consistent with the definition of AEGL-1. There was some discussion of using a repeat dosing study to derive these values. A four week study at 0.5 ppm showed no effects. However, because trimethodysilane does not have good warning properties based on odor and because the resulting calculated values would be very low,

this option was not further discussed. Bob Benson made a motion to not recommend derivation of AEGL-1 values. Richard Thomas seconded the motion. The motion passed (YES: 18; NO: 1; ABSTAIN: 2) (APPENDIX E).

Summary of AEGL Values for Trimethoxysilane						
Classification	**10-minute**	**30-minute**	**1-hour**	**4-hour**	**8-hour**	**Endpoint (Reference)**
AEGL–1	NR	NR	NR	NR	NR	Not Recommended due to insufficient data
AEGL–2	2.9 ppm	1.4 ppm	0.83 ppm	0.33 ppm	0.20 ppm	⅓ the AEGL-3 values
AEGL–3	8.8 ppm	4.1 ppm	2.5 ppm	0.98 ppm	0.61 ppm	$BMCL_{05}$ in rats (Nachreiner and Dodd , 1988)

Tetramethoxysilane (CAS No. 681-84-5)

Staff Scientist: Dana Glass, ORNL
Chemical Manager: Bob Benson, U.S. EPA

Bob Benson, the chemical manager, made a few introductory remarks about the issues regarding tetramethoxysilane. The data base is limited. In the only single exposure study available (Dow Corning, 1992), the effects observed at the lowest exposure were more severe than the definition of AEGL-2. The options to be considered include setting the AEGL-2 values based on 1/3 of the AEGL-3 values or using a repeat exposure study as the basis of AEGL-2. It might also be possible to use the repeat exposure study to derive AEGL-1 values. There are no data to derive a value of n for time scaling. Dana Glass then discussed the data summarized in the TSD (Attachment 9). The key study for deriving AEGL-3 values is Dow Corning (1992). Rats were exposed to 31, 50, or 88 ppm for 4 hours. There were no deaths at 31 ppm. Deaths were observed at both higher exposures. At 31 ppm there was lung damage in all animals. The lung damage was more severe at higher exposure. The $BMCL_{05}$ for 4 hours is 26 ppm. Based on the $BMCL_{05}$ for 4 hours of 26 ppm, a total uncertainty factor of 30, and the default time scaling procedure (n = 3 for shorter durations and n = 1 for longer durations), the calculated AEGL-3 values are 1.7 ppm for 10 and 30 minutes, 1.4 ppm for 1 hour, 0.87 ppm for 4 hours, and 0.43 ppm for 8 hours. The interspecies uncertainty factor of 3 was used because in studies with trimethoxysilane, rats, mice, and hamsters show similar effects. The default value of 10 was used as the intraspecies uncertainty factor as there are no data to estimate intrahuman variability and it is not clear that tetramethoxysilane is acting as a simple chemical irritant in the lung. Bob

Benson made a motion to accept these AEGL-3 values. Nancy Kim seconded the motion. The motion passed (YES: 20; NO: 1; ABSTAIN: 1) (APPENDIX F). .

As noted above, the lowest exposure from Dow Corning (1992) gave effects more severe than the AEGL-2 definition. A repeat exposure study (Kolesar et al. 1989) exposed rats for 6 hours/day, 5 days/week for 28 days at 0, 1, 5, or 10 ppm (phase 1) and 0, 15, 30, or 45 ppm (phase 2). At 30 ppm there were changes in the respiratory tract in most of the animals. In the nasal cavity there was ulceration in 18/20 animals; mild squamous metaplasia in the lung in 15/20 animals; and bilateral corneal lesions including desquamation of the central corneal epithelium. These effects are more severe than the definition of AEGL-2. At 15 ppm there was minimal acute inflammation of the respiratory epithelium in 2/20 animals; no lesions in the lung and only minimal acute inflammation in the larynx in 1/20 animals; and minimum acute keratitis in the corneal epithelium. Clinical observations at 15 ppm included lethargy, rough coat, and eye squinting. From this study, 15 ppm is considered a no effect level for irreversible effects. There were no significant respiratory or ocular changes reported at 10 ppm. Based on the point of departure of 15 ppm for 6 hours, a total uncertainty factor of 30, and the default time scaling, the calculated AEGL-2 values are 1.1 ppm for 10 and 30 minutes, 0.91 ppm for 1 hour, 0.57 ppm for 4 hours, and 0.38 ppm for 8 hours. These values are greater than those derived by dividing AEGL-3 values by 3. The rationales for the uncertainty factor and time scaling are the same as described for AEGL-3 above. Bob Benson made a motion to accept these AEGL-2 values. Ernie Falke seconded the motion. The motion passed (YES: 14; NO: 2; ABSTAIN: 6) (APPENDIX F).

There was discussion of using the 10 ppm level from the repeat exposure study of Kolesar et al. (1989) to derive AEGL-1 values. However, as there would be very little difference between AEGL-1 and AEGL-2 using this approach and considering that tetramethoxysilane does not have good odor warning properties, this approach was not adopted. Bob Benson made a motion to adopt AEGL-1 values of not recommended due to inadequate data. Bill Bress seconded the motion. The motion passed (YES: 14; NO: 0; ABSTAIN: 1) (APPENDIX F).

Summary of AEGL Values for Tetramethoxysilane						
Classification	**10-minute**	**30-minute**	**1-hour**	**4-hour**	**8-hour**	**Endpoint (Reference)**
AEGL–1	NR	NR	NR	NR	NR	Not Recommended due to insufficient data
AEGL–2	1.1 ppm	1.1 ppm	0.91 ppm	0.57 ppm	0.38 ppm	NOEL for irreversible effects in rats (Kolesar et al., 1989)
AEGL–3	1.7 ppm	1.7 ppm	1.4 ppm	0.87 ppm	0.43 ppm	4-hr rat $BMCL_{05}$ (Dow Corning , 1992)

Sulfuryl Chloride (CAS No. 7791-25-5)

Staff Scientist: Robert Young, ORNL
Chemical Manager: Steven Barbee, Arch Chemical

Steve Barbee, chemical manager, provided introductory remarks regarding the discrepancy in the 1-hr (Stauffer Chemical) and 4-hr (DuPont) data sets for sulfuryl chloride. Bob Young reviewed the data for sulfuryl chloride (Attachment 10). AEGL-1 values were not recommended because of insufficient data. Proposed AEGL-2 values (4.7 ppm for 10-min, 4.7 for 30-min, 3.7 ppm for 1-hr, 2.3 ppm for 4-hr, and 1.2 ppm for 8-hr) were derived by dividing the AEGL-3 values by 3. Proposed AEGL-3 values (14 ppm for 10-min, 14 for 30-min, 11 ppm for 1-hr, 7.0 ppm for 4-hr, and 3.5 ppm for 8-hr) were based on a 4-hour $BMCL_{05}$ in rats of 70.1 ppm (Du Pont, 1982). Uncertainty factors of 3 each were applied for inter- and intraspecies extrapolation because sulfuryl chloride is a direct contact irritant. Time scaling was accomplished using the default values of n =1 or n = 3; the 30-min value was adopted as the 10-min value. After a thorough discussion, a motion was made by Marc Ruijten and seconded by Richard Niemier to accept AEGL-3 values as proposed. The motion passed (YES: 15; NO: 1; ABSTAIN: 1) (APPENDIX G). A motion was then made by George Woodall and seconded by Bob Benson to accept AEGL-2 values as proposed. The motion passed (YES: 14; NO: 4; ABSTAIN: 0) (APPENDIX G). A statement will be added to the revised TSD stating that sulfuryl chloride and phosgene have similar modes of action and that the ratio of the data-derived AEGL-3 to AEGL-2 values for phosgene is approximately 3. This will strengthen the justification of the sulfuryl chloride AEGL-2 values. A motion was then made by Bob Benson and seconded by Ernest Falke to not recommend AEGL-1 values because of insufficient data. The motion passed unanimously by a show of hands (APPENDIX G).

Summary of AEGL Values for Sulfuryl Chloride

Classification	10-minute	30-minute	1-hour	4-hour	8-hour	Endpoint (Reference)
AEGL–1	NR	NR	NR	NR	NR	Not Recommended due to insufficient data
AEGL–2	4.7 ppm	4.7 ppm	3.7 ppm	2.3 ppm	1.2 ppm	⅓ the AEGL-3 values
AEGL–3	14 ppm	14 ppm	11 ppm	7.0 ppm	3.5 ppm	4-hour $BMCL_{05}$ in rats (DuPont , 1982)

SELECTED CHLOROFORMATES

Methyl Chloroformate (CAS Reg. No. 79-22-1)
Ethyl Chloroformate (CAS Reg. No. 541-41-3)
Propyl Chloroformate (CAS Reg. No. 109-61-5)
Isopropyl Chloroformate (CAS Reg. No. 108-23-6)
Allyl Chloroformate (CAS Reg. No. 2937-50-0)
n-Butyl Chloroformate (CAS Reg. No. 593-34-7)
Isobutyl Chloroformate (CAS Reg. No. 543-27-1)
sec-Butyl Chloroformate (CAS Reg. No. 17462-58-7)
Ethyl Chlorothioformate (CAS Reg. No. 2941-64-2)
Diphosgene (CAS Reg. No. 503-38-8)

Staff Scientist: Cheryl Bast, ORNL
Chemical Manager: Ernest Falke, U.S. EPA

Overview

Cheryl Bast thanked Dr. Roland Rossbacher, representing BASF, Germany, for providing unpublished industry data on the chloroformates. These data were used as key and supporting studies for many of the chloroformates. Cheryl then discussed the overall data set available for the chloroformates (Attachment 11). Although data sets for individual chloroformates are sparse, the total data set for all chloroformates helped increase confidence in the derived AEGL values. All of the title chloroformates are direct-acting contact irritants and are corrosive to the eyes, skin, gastrointestinal, and respiratory tracts. Therefore, when AEGL values were derived, uncertainty factors of 3 each were applied for inter- and intraspecies extrapolation (total UF = 10). Time scaling for all chloroformates was done using the default values of n =1 (shorter-to- longer time) or n =3 (longer-to-shorter time), because data were not sufficient to derive chemical-specific exponents. Summaries of AEGL development for the title chloroformates are provided below.

Methyl Chloroformate (CAS Reg. No. 79-22-1)

AEGL-1 values for methyl chloroformate were not recommended due to insufficient data. Proposed AEGL-2 values (2.8 ppm for 10-min, 2.8 ppm for 30-min, 2.2 ppm for 1-hr, 1.4 ppm for 4 -hr, and 0.70 ppm for 8-hr) were derived by dividing the AEGL-3 values by 3. This approach is justified based on a steep concentration-response curve. Proposed AEGL-3 values (8.5 ppm for 10-min, 8.5 ppm for 30-min, 6.7 ppm for 1-hr, 4.2 ppm for 4 -hr, and 2.1 ppm for 8-hr) were based on a 4-hr $BMCL_{05}$ in rats of 42.4 ppm (Hoechst, 1986). Uncertainty factor application and time scaling were applied as discussed above in the overview section. After discussion, a motion was made by Bob Benson and seconded by George Woodall to accept AEGL-3 values as proposed except to time scale to the 10-min value (10-min AEGL-3 = 12 ppm), rather than flat-lining the 30-min value. Time scaling from 4-hr to 10-min is justified for this chemical based on

a 1-hr LC_{50} study (Bio-Test, 1975); utilizing the $BMCL_{05}$ from this study yields a 10-min AEGL-3 value of 13 ppm, which supports the time-scaled value of 12 ppm calculated from Hoechst (1986). The motion carried (YES: 19; NO: 0; ABSTAIN: 0) (APPENDIX H). A motion was then made by Richard Thomas and seconded by Bob Benson to adopt AEGL-2 values based on ⅓ the AEGL-3 values. The motion carried (YES: 20; NO: 0; ABSTAIN: 0) (APPENDIX H). Finally, a motion was made by George Woodall and seconded by Bob Benson to not recommend AEGL-1 values due to insufficient data. The motion carried unanimously by a show of hands (APPENDIX H).

Summary of AEGL Values for Methyl Chloroformate						
Classification	**10-minute**	**30-minute**	**1-hour**	**4-hour**	**8-hour**	**Endpoint (Reference)**
AEGL–1	NR	NR	NR	NR	NR	Not recommended due to insufficient data
AEGL–2	4.0 ppm	2.8 ppm	2.2 ppm	1.4 ppm	0.70 ppm	1/3 the AEGL-3 values
AEGL-3	12 ppm	8.5 ppm	6.7 ppm	4.2 ppm	2.1 ppm	4-hr $BMCL_{05}$ in rats (Hoechst, 1986)

Ethyl Chloroformate (CAS Reg. No. 541-41-3)

AEGL-1 values for ethyl chloroformate were not recommended due to insufficient data. Proposed AEGL-2 values (2.9 ppm for 10-min, 2.0 ppm for 30-min, 1.6 ppm for 1-hr, 0.40 ppm for 4 -hr, and 0.20 ppm for 8-hr) were derived by dividing the AEGL-3 values by 3. This approach is justified based on a steep concentration-response curve. Proposed AEGL-3 values (8.8 ppm for 10-min, 6.1 ppm for 30-min, 4.8 ppm for 1-hr, 1.2 ppm for 4 -hr, and 0.60 ppm for 8-hr) were based on an estimated 1-hr lethality threshold in rats of 48 ppm (⅓ of the most conservative LC_{50}; 145 ppm x ⅓ = 48 ppm) (Vernot et al., 1977). Uncertainty factor application and time scaling were applied as discussed above in the overview section. After discussion, a motion was made by George Rodgers and seconded by Richard Niemier to accept AEGL-1, AEGL-2, and AEGL-3 values as proposed. The motion carried (YES: 20; NO: 0; ABSTAIN: 0) (APPENDIX I).

Summary of AEGL Values for Ethyl Chloroformate						
Classification	**10-minute**	**30-minute**	**1-hour**	**4-hour**	**8-hour**	**Endpoint (Reference)**
AEGL–1	NR	NR	NR	NR	NR	Not recommended due to insufficient data
AEGL–2	2.9 ppm	2.0 ppm	1.6 ppm	0.40 ppm	0.20 ppm	1/3 the AEGL-3 values
AEGL-3	8.8 ppm	6.1 ppm	4.8 ppm	1.2 ppm	0.60 ppm	Estimated 1-hr lethality threshold in rats (Vernot et al., 1977)

Propyl Chloroformate (CAS Reg. No. 109-61-5)

AEGL-1 values for propyl chloroformate were not recommended due to insufficient data. Proposed AEGL-2 values (4.3 ppm for 10-min, 3.0 ppm for 30-min, 2.4 ppm for 1-hr, 0.60 ppm for 4 -hr, and 0.30 ppm for 8-hr) were derived by dividing the AEGL-3 values by 3. This approach is justified based on a steep concentration-response curve. Proposed AEGL-3 values (13 ppm for 10-min, 9.1 ppm for 30-min, 7.2 ppm for 1-hr, 1.8 ppm for 4 -hr, and 0.90 ppm for 8-hr) were based on an estimated 1-hr $BMCL_{05}$ in rats of 216 ppm (Bio-Test, 1970). Uncertainty factor application and time scaling were applied as discussed above in the overview section. Additionally, a modifying factor of 3 was proposed because the key study reported nominal, rather than analytical concentrations and there were no confirmatory studies. After discussion, a motion was made by George Woodall and seconded by Marc Ruijten to accept AEGL-1, AEGL-2, and AEGL-3 values as proposed except that a MF of 2, rather than 3, be applied. The application of a MF of 2 yields AEGL values for propyl chloroformate that are more consistent with the overall chloroformate data base regarding relative toxicity. The motion carried (AEGL-1: YES: 20; NO: 0; ABSTAIN: 0) (AEGL-2: YES: 16; NO: 4; ABSTAIN: 0) (AEGL-3: YES: 16; NO: 4; ABSTAIN: 0) (APPENDIX J).

Summary of AEGL Values for Propyl Chloroformate						
Classification	10-minute	30-minute	1-hour	4-hour	8-hour	Endpoint (Reference)
AEGL–1	NR	NR	NR	NR	NR	Not recommended due to insufficient data
AEGL–2	6.7 ppm	4.7 ppm	3.7 ppm	0.90 ppm	0.47 ppm	1/3 the AEGL-3 values
AEGL-3	20 ppm	14 ppm	11 ppm	2.7 ppm	1.4 ppm	1-hr $BMCL_{05}$ in rats (Bio-Test, 1970)

Isopropyl Chloroformate (CAS Reg. No. 108-23-6)

AEGL-1 values for isopropyl chloroformate were not recommended due to insufficient data. Proposed AEGL-2 values (6.0 ppm for 10-min, 4.3 ppm for 30-min, 3.3 ppm for 1-hr, 0.83 ppm for 4 -hr, and 0.43 ppm for 8-hr) were derived by dividing the AEGL-3 values by 3. Proposed AEGL-3 values (18 ppm for 10-min, 13 ppm for 30-min, 10 ppm for 1-hr, 2.5 ppm for 4 -hr, and 1.3 ppm for 8-hr) were based on an estimated 1-hr lethality threshold in rats of 100 ppm (⅓ of the LC_{50}; 300 ppm x ⅓ = 100 ppm) (Bio-Test, 1970). Uncertainty factor application and time scaling were applied as discussed above in the overview section. After discussion, a motion was made by Richard Thomas and seconded by Marc Ruijten to accept AEGL-1, AEGL-2, and AEGL-3 values as proposed. The motion carried (AEGL-1: YES: 20; NO: 0; ABSTAIN: 1) (AEGL-2: YES: 19; NO: 1; ABSTAIN: 1) (AEGL-3: YES: 20; NO: 1; ABSTAIN: 1) (APPENDIX K).

Summary of AEGL Values for Isopropyl Chloroformate						
Classification	10-minute	30-minute	1-hour	4-hour	8-hour	Endpoint (Reference)
AEGL–1	NR	NR	NR	NR	NR	Not recommended due to insufficient data
AEGL–2	6.0 ppm	4.3 ppm	3.3 ppm	0.83 ppm	0.43 ppm	1/3 the AEGL-3 values
AEGL-3	18 ppm	13 ppm	10 ppm	2.5 ppm	1.3 ppm	Estimated 1-hr lethality threshold in rats (Bio-Test, 1970)

Allyl Chloroformate (CAS Reg. No. 2937-50-0)

AEGL-1 values for allyl chloroformate were not recommended due to insufficient data. Proposed AEGL-2 values (1.3 ppm for 10-min, 0.87 ppm for 30-min, 0.70 ppm for 1-hr, 0.18 ppm for 4 -hr, and 0.09 ppm for 8-hr) were derived by dividing the AEGL-3 values by 3. This approach is justified by the steep concentration-response curve. Proposed AEGL-3 values (3.8 ppm for 10-min, 2.6 ppm for 30-min, 2.1 ppm for 1-hr, 0.53 ppm for 4 -hr, and 0.26 ppm for 8-hr) were based on a 1-hour rat $BMCL_{05}$ of 21 ppm (Stillmeadow, 1987). Uncertainty factor application and time scaling were applied as discussed above in the overview section. After discussion, a motion was made by Marc Riujten and seconded by Steve Barbee to accept AEGL-1, AEGL-2, and AEGL-3 values as proposed. The motion carried (AEGL-1: YES: 19; NO: 0; ABSTAIN: 0) (AEGL-2: YES: 17; NO: 3; ABSTAIN: 1) (AEGL-3: YES: 17; NO: 3; ABSTAIN: 1) (APPENDIX L).

Summary of AEGL Values for Allyl Chloroformate						
Classification	**10-minute**	**30-minute**	**1-hour**	**4-hour**	**8-hour**	**Endpoint (Reference)**
AEGL–1	NR	NR	NR	NR	NR	Not recommended due to insufficient data
AEGL–2	1.3 ppm	0.87 ppm	0.70 ppm	0.18 ppm	0.09 ppm	1/3 the AEGL-3 values
AEGL-3	3.8 ppm	2.6 ppm	2.1 ppm	0.53 ppm	0.26 ppm	1-hr $BMCL_{05}$ in rats (Stillmeadow, 1987)

n-Butyl Chloroformate (CAS Reg. No. 593-34-7)

AEGL-1 values for n-butyl chloroformate were not recommended due to insufficient data. Proposed AEGL-2 values (4.0 ppm for 10-min, 2.8 ppm for 30-min, 2.2 ppm for 1-hr, 0.57 ppm for 4 -hr, and 0.28 ppm for 8-hr) were derived by dividing the AEGL-3 values by 3. Proposed AEGL-3 values (12 ppm for 10-min, 8.4 ppm for 30-min, 6.7 ppm for 1-hr, 1.7 ppm for 4 -hr, and 0.83 ppm for 8-hr) were based on an estimated 1-hr lethality threshold in rats of 66.7 ppm (⅓ of the concentration causing death in 4/10 rats; 200 ppm x ⅓ = 66.7 ppm) (BASF, 1970). Uncertainty factor application

and time scaling were applied as discussed above in the overview section. After discussion, a motion was made by Marc Ruijten and seconded by Bob Benson to accept AEGL-1, AEGL-2, and AEGL-3 values as proposed. The motion carried (YES: 20; NO: 0; ABSTAIN: 1) (APPENDIX M).

Summary of AEGL Values for n-Butyl Chloroformate						
Classification	10-minute	30-minute	1-hour	4-hour	8-hour	Endpoint (Reference)
AEGL–1	NR	NR	NR	NR	NR	Not recommended due to insufficient data
AEGL–2	4.0 ppm	2.8 ppm	2.2 ppm	0.57 ppm	0.28 ppm	1/3 the AEGL-3 values
AEGL-3	12 ppm	8.4 ppm	6.7 ppm	1.7 ppm	0.83 ppm	Estimated 1-hr lethality threshold in rats (BASF, 1970)

Isobutyl Chloroformate (CAS Reg. No. 543-27-1)
sec-Butyl Chloroformate (CAS Reg. No. 17462-58-7)

No AEGL-1, AEGL-2, or AEGL-3 values were proposed for isobutyl chloroformate or sec-butyl chloroformate due to insufficient data. However, these chloroformates are structural analogs of n-butyl chloroformate and mouse RD_{50} data (Carpenter, 1982) suggest that isobutyl chloroformate, and sec-butyl chloroformate are of similar toxicity to n-butyl chloroformate. Therefore, a motion was made by George Woodall and seconded by Richard Thomas to adopt the AEGL-1, AEGL-2, and AEGL-3 values for n-butyl chloroformate as surrogates for isobutyl- and sec-butyl chloroformate. The motion carried (YES: 19; NO: 2; ABSTAIN: 0) (APPENDICES N and O). The no-data chapters for isobutyl chloroformate and sec-butyl chloroformate will be removed from the chloroformate TSD and an explanation will be provided in the n-butyl chloroformate chapter stating that values for sec-butyl and isobutyl chloroformate were derived by analogy to n-butyl chloroformate.

Summary of AEGL Values for Isobutyl Chloroformate and sec-Butyl Chloroformate						
Classification	10-minute	30-minute	1-hour	4-hour	8-hour	Endpoint (Reference)
AEGL–1	NR	NR	NR	NR	NR	Not recommended due to insufficient data
AEGL–2	4.0 ppm	2.8 ppm	2.2 ppm	0.57 ppm	0.28 ppm	By analogy to n-butyl chloroformate
AEGL-3	12 ppm	8.4 ppm	6.7 ppm	1.7 ppm	0.83 ppm	By analogy to n-butyl chloroformate

Ethyl Chlorothioformate (CAS Reg. No. 2941-64-2)

AEGL-1 values for ethylchlorothioformate were not recommended due to insufficient data. Proposed AEGL-2 values (0.47 ppm for 10-min, 0.47 ppm for 30-min, 0.37 ppm for 1-hr, 0.23 ppm for 4 -hr, and 0.12 ppm for 8-hr) were derived by dividing the AEGL-3 values by 3. This approach is justified by the steep concentration-response curve. Proposed AEGL-3 values (1.4 ppm for 10-min, 1.4 ppm for 30-min, 1.1 ppm for 1-hr, 0.70 ppm for 4 -hr, and 0.35 ppm for 8-hr) were based on a 4-hour rat $BMCL_{05}$ of 21 ppm (Stauffer, 1983). Uncertainty factor application and time scaling were applied as discussed above in the overview section. An additional modifying factor of 3 was proposed to account for possible delayed effects of the thio moiety. Discussion focused on whether the calculated $BMCL_{05}$ was valid because of the absence of a zero response concentration in the key study. Another point of discussion was whether the intraspecies UF should be increased to 10 and the proposed MF of 3 should be removed. After discussion, a motion was made by George Woodall and seconded by Bob Benson to accept AEGL-1 values of NR, AEGL-2 values of ⅓ the AEGL-3 values, and AEGL-3 values based on a point-of-departure of ⅓ the 4-hr rat LC_{50} from the Stauffer (1983) study (45 ppm x ⅓ = 15). An interspecies uncertainty factor of 3 was applied, and an intraspecies UF of 10 was applied to account for systemic effects from the thio moiety. Time scaling used default values of n =1 or n = 3. The motion carried (AEGL-1: YES: 18; NO: 0; ABSTAIN: 0) (AEGL-2: YES: 17; NO: 1; ABSTAIN: 0) (AEGL-3: YES: 17; NO: 1; ABSTAIN: 0) (APPENDIX P).

Summary of AEGL Values for Ethylchlorothioformate						
Classification	10-minute	30-minute	1-hour	4-hour	8-hour	Endpoint (Reference)
AEGL–1	NR	NR	NR	NR	NR	Not recommended due to insufficient data
AEGL–2	0.33 ppm	0.33 ppm	0.26 ppm	0.17 ppm	0.083 ppm	1/3 the AEGL-3 values
AEGL-3	1.0 ppm	1.0 ppm	0.79 ppm	0.50 ppm	0.25 ppm	Estimated 4-hr lethality threshold in rats (Stauffer, 1983)

Diphosgene (CAS Reg. No. 503-38-8)

No AEGL-1, AEGL-2, or AEGL-3 values were proposed for diphosgene due to insufficient data. A motion was made by Bob Benson and seconded by John Hinz to not recommend AEGL-1, AEGL-2, or AEGL-3 values for diphosgene. The motion carried unanimously by a show of hands (APPENDIX Q). The diphosgene chapter will be removed from the chloroformate TSD and the chemical will be placed in "holding" status.

Summary of AEGL Values for Diphosgene						
Classification	10-minute	30-minute	1-hour	4-hour	8-hour	Endpoint (Reference)
AEGL–1	NR	NR	NR	NR	NR	Not recommended due to insufficient data
AEGL–2	NR	NR	NR	NR	NR	Not recommended due to insufficient data
AEGL-3	NR	NR	NR	NR	NR	Not recommended due to insufficient data

Summary: An analysis comparing the relative toxicity of the chloroformates vs. the derived AEGL values will be presented at NAC-40. Also, chapters for benzyl chloroformate, phenyl chloroformate, and 2-ethylhexyl chloroformate will be prepared and discussed at NAC-40.

ADMINISTRATIVE MATTERS

The site and time of future meetings is as follows:

NAC/AEGL-40: May 31, June 1-2, 2006, Washington DC
NAC/AEGL-41: September, 2006 (Exact dates and location to be determined)
NAC/AEGL-42: December 11-13, 2006, Washington DC

All items in the agenda were discussed as thoroughly as the time permitted. The meeting highlights were prepared by Cheryl Bast and Robert Young, Oak Ridge National Laboratory, and Robert Benson, U.S. EPA, with input from the respective staff scientists, chemical managers, and other contributors.

LIST OF ATTACHMENTS

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

Attachment 1. NAC/AEGL-39 Meeting Agenda
Attachment 2. NAC/AEGL-39 Attendee List
Attachment 3. Protections for Subjects in Human Research- Final Rule Summary
Attachment 4. AEGL Databases
Attachment 5. NAC Member Suggestions AEGL Databases
Attachment 6. Use of Occupational Standards and Recommendations in Setting AEGL Values
Attachment 7. Calculation Correction for cyclohexyl isocyanate
Attachment 8. Data analysis for silane
Attachment 9. Data analysis for trimethoxysilane and tetramethoxysilane
Attachment 10. Data analysis for sulfuryl chloride
Attachment 11. Data analysis for selected chloroformates

LIST OF APPENDICES

Appendix A. Ballot for NAC-38 meeting summary
Appendix B. Final NAC-38 Meeting Highlights
Appendix C. Ballot for Cyclohexyl Isocyanate
Appendix D. Ballot for Silane
Appendix E. Ballot for Trimethoxysilane
Appendix F. Ballot for Tetramethoxysilane
Appendix G. Ballot for Sulfuryl Chloride
Appendix H. Ballot for Methyl Chloroformate
Appendix I. Ballot for Ethyl Chloroformate
Appendix J. Ballot for Propyl Chloroformate
Appendix K. Ballot for Isopropyl Chloroformate
Appendix L. Ballot for Allyl Chloroformate
Appendix M. Ballot for n-butyl Chloroformate
Appendix N. Ballot for Isobutyl Chloroformate
Appendix O. Ballot for sec-Butyl Chloroformate
Appendix P. Ballot for Ethylchlorothioformate
Appendix Q. Ballot for Diphosgene
Appendix R. Committee chairman certification of minutes

ATTACHMENT 1

National Advisory Committee for Acute Exposure Guideline Levels for Hazardous Substances

NAC/AEGL-39
February 1-3, 2006

U.S. Department of Labor
Rooms C5515 1A and 1B
200 Constitution Ave., N.W.
Washington, DC 20210

Metro: Judiciary Square (Red Line)

AGENDA

Wednesday, February 1, 2006

10:00 a..m.	Introductory remarks and approval of NAC/AEGL-38 Highlights (George Rusch, Ernie Falke, and Paul Tobin)
10:30	Revisit of Cyclohexyl Isocyanate- Correction of $BMCL_{05}$ calculation (Marc Ruijten/Carol Wood)
10:45	AEGL Databases (Richard Williams)
12:00 p.m.	Lunch
1:00	Review of Silane, Tetramethoxy silane, and Trimethoxy silane (Bob Benson/Dana Glass)
3:15	Break
3:30	Review of Silane, Tetramethoxy silane, and Trimethoxy silane (continued)
5:30	Adjourn for the day

Thursday, February 2, 2006

8:30 a.m.	Review of Selected Chloroformates- Allyl chloroformate, Diphosgene, Ethyl Chloroformate, Ethyl chlorothioformate, Isobutyl chloroformate, Isopropyl chloroformate, Methyl chloroformate, n-Butyl chloroformate, Propyl chloroformate, sec-Butyl chloroformate (Ernie Falke/Cheryl Bast)
10:30	Break
10:45	Review of Selected Chloroformates (continued)
12:00 p.m.	Lunch
1:00	Occupational Standards (John Morawetz)
2:00	Break
2:15	Review of Sulfuryl Chloride (Steve Barbee/Bob Young)
5:30	Adjourn for the day

Friday, February 3, 2006

8:30 a.m.	Unresolved issues
10:00	Break
10:15	Unresolved issues
11:30	Administrative matters
12:00 noon	Adjourn meeting

NAC/AEGL Meeting 39: February 1-3, 2006

Chemical: Attendance List **CAS Reg. No.:**

Action: Proposed_____ **Interim**_____ **Other**___

ATTACHMENT 2

Chemical Manager: X = Present **Staff Scientist.**

NAC Member	AEGL1	AEGL2	AEGL3	LOA	NAC Member	AEGL1	AEGL 2	AEGL3	LOA
Steven Barbee	X				Nancy Kim	X			
Lynn Beasley	X				Glenn Leach	X			
Robert Benson	X				John Morawetz	X			
Jonathan Borak	X				Richard Niemeier	X			
William Bress	X				Marinelle Payton	X			
George Cushmac	X				Susan Ripple	X			
Ernest Falke	X				George Rodgers	X			
Alfred Feldt	X				Marc Ruijten	X			
John Hinz	X				George Rusch, Chair	X			
Jim Holler	X				Richard Thomas	X			
Tom Hornshaw	X				George Woodall	X			
Warren Jederberg	ABSENT								
					TALLY				
					PASS/ FAIL				

PPM, (mg/m^3)	10 Min	30 Min	1 Hr	4 Hr	8 Hr
AEGL 1	, ( )	, ( )	, ( )	, ( )	, ( )
AEGL 2	, ( )	, ( )	, ( )	, ( )	, ( )
AEGL 3	, ( )	, ( )	, ( )	, ( )	, ( )
LOA					
* = ≥10% LEL					
** = ≥ 50% LEL					
*** = ≥100% LEL					

*Safety considerations against the hazard(s) of explosion(s) must be taken into account.
** and ***Extreme safety considerations against the hazard(s) of explosion(s) must be taken into account.

NR= Not Recommended due to_____

AEGL 1 Motion by: _____ **Second by:** _____
AEGL 2 Motion by:_____ **Second by:** _____
AEGL 3 Motion by: _____ **Second by:** _____
LOA Motion by: _____ **Second by:** _____

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

ATTACHMENT 3

PROTECTIONS FOR SUBJECTS IN HUMAN RESEARCH

FINAL RULE

PARTS A THROUGH Q

Subpart A—Basic EPA Policy for Protection of Subjects in Human Research Conducted or Supported by EPA

-Adds subparts B-Q

Subpart B—Prohibition of Research Conducted or Supported by EPA Involving Intentional Exposure of Human Subjects who are Pregnant Women or Children

-Self explanatory. Child is under 18.

Subpart C—Observational Research: Additional Protections for Pregnant Women and Fetuses Involved as Subjects in Observational Research Conducted or Supported by EPA

-Essentially applies Common Rule provisions to these studies with additional EPA protections.

Subpart D—Observational Research: Additional Protections for Children Involved as Subjects in Observational Research Conducted or Supported by EPA

-Essentially applies Common Rule provisions to these studies with additional EPA protections.

Subpart E—[Reserved]
Subpart F—[Reserved]
Subpart G—[Reserved]
Subpart H—[Reserved]
Subpart I—[Reserved]
Subpart J—[Reserved]

Subpart K—Basic Ethical Requirements for Third-Party Human Research for Pesticides Involving Intentional Exposure of Nonpregnant Adults

Extends the basic protections of the **Common Rule** to subjects in certain research conducted or supported by third parties. It applies to **third-party** human research involving intentional exposure of **non-pregnant adult** subjects and that is **intended to be submitted to EPA under the pesticide laws**. In addition to the basic procedures and protections contained in the Common Rule, it also requires researchers who propose to conduct new research covered by the rule to **submit protocols** and other materials for **science and ethics review by both EPA and a newly created Human Studies Review Board (HSRB)**

Subpart L—Prohibition of Third-Party Research for Pesticides Involving Intentional Exposure of Human Subjects who are Pregnant Women or Children

Prohibition of new **third-party** human subjects research for pesticides involving intentional exposure of **pregnant women, fetuses, or children**. Subpart L applies to research conducted or supported by any person who **intends to provide** the results of the research to EPA **under FIFRA or the FFDCA**. The final rule retains the text from the proposal establishing how EPA will determine a person's intent for purposes of applying the prohibition.

Subpart M—Requirements for Submission of Information on the Ethical Conduct of Completed Human Research

Requires people who submit data from completed human research to EPA to accompany that submission with information documenting the ethical conduct of the research. It applies only to reports of completed human research submitted after the effective date of the final rule.

The requirement applies to reports on all types of human research submitted to the Agency for consideration under the pesticide laws, FIFRA and FFDCA. Recognizing that not all of the information specified by subpart M may be available to the data submitter in some cases -- for example, if the research were conducted in the past, or if the submitter did not conduct the study, the specified information should be provided "to the extent available" and asks the submitter to describe the efforts made to obtain information which he or she was unable to provide.

Subpart O—Administrative Actions for Noncompliance

Subpart O contains provisions, adapted from similar regulations issued by FDA, that describe the range of administrative actions EPA could take to address noncompliance by third parties with the requirements of part 26. These actions include: **Withdrawal or**

suspension of a research institution's **Federal wide assurance**, **disqualification** of an **institution or an IRB**; **debarment; and public censure**. This subpart describes procedures EPA would follow in reaching a decision to take any of these administrative actions. Other than the addition of a new section explaining the scope of research to which these actions could be applied, the final rule is unchanged from the proposal.

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Subpart P—Review of Proposed and Completed Human Research

EPA will **review all proposals** by **third parties** to conduct research covered by subpart K, i.e., all research involving the intentional exposure of human subjects, if the research is **intended for submission to EPA under the pesticide laws**.

The subpart also requires EPA to establish an independent group of experts, referred to as the Human Studies Review Board (HSRB), to assist EPA in evaluating such proposals.

In addition, the subpart requires that **EPA review reports** submitted by third parties on completed human research and, **if** EPA decides to rely on information from such research in an **action** under the **pesticide laws**, to submit the results of its assessment of the research to the **HSRB**. The HSRB would perform science and ethics reviews of proposals from third parties to conduct specified types of human research and of the results of specified types of human research if EPA intended to rely on the information in its decision-making under the pesticide laws. Further, when HSRB review is not required by the final rule, EPA would nonetheless retain discretion to ask the HSRB to review studies or to offer advice on other issues.

Under the final rule, the **HSRB will review** all research involving intentional exposure conducted **after the effective date** of the final rule, as well as all research involving intentional exposure performed **before the rule takes effect**, if the **purpose** of the research was to identify or measure a **toxic effect**. But the final rule grants to the Agency discretion to decide whether studies performed before the effective date of the final rule that do not measure toxicity should undergo HSRB review.

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Subpart Q—Ethical Standards for Assessing Whether to Rely on the Results of Human Research in EPA Actions

§ 26.1701 To what does this subpart apply?
This subpart applies to **EPA's decisions** whether to rely in its **actions** taken **under** the **Federal Insecticide, Fungicide, and Rodenticide Act** (7 U.S.C. 136 et seq.) or section 408 of the **Federal Food, Drug, and Cosmetic Act** (21 U.S.C. 346a) on scientifically valid and relevant data from research involving intentional exposure of human subjects.

§ 26.1703 Prohibition of reliance on research involving intentional exposure of human subjects who are pregnant women (and therefore their fetuses) or children.

§ 26.1704 Prohibition of reliance on unethical human research with nonpregnant adults conducted before [insert date 60 days after date of publication in the FEDERAL REGISTER].

Except as provided in § 26.1706, in actions within the scope of § 26.1701, EPA shall not rely on data from any research initiated before [insert date 60 days after date of publication in the Federal Register], if there is clear and convincing evidence that the conduct of the research was fundamentally unethical (e.g., the research was intended
to seriously harm participants or failed to obtain informed consent), or was significantly deficient relative to the ethical standards prevailing at the time the research was conducted. This prohibition is in addition to the prohibition in § 26.1703.

§ 26.1705 Prohibition of reliance on unethical human research with nonpregnant adults conducted after [insert date 60 days after date of publication in the FEDERAL REGISTER].

Except as provided in § 26.1706, in actions within the scope of § 26.1701, EPA shall not rely on data from any research initiated after [insert date 60 days after date of publication in the Federal Register], unless EPA has adequate information to determine that the research was conducted in substantial compliance with subparts A through L of this part, or if conducted in a foreign country, under procedures at least as protective as those in subparts A through L of this part. This prohibition is in addition to the prohibition in § 26.1703.

§ 26.1706 Criteria and procedure for decisions to protect public health by relying on otherwise unacceptable research.

Acute Exposure Guideline Levels Databases

Richard Williams IV
Environmental Careers Organization
2/1/06

Outline of Presentation

Introduction

- AEGL Database Projects
  - AEGL Expert System Database
    - A newly created database developed from a table of AEGL chemical data
  - AEGL Derivation Database
    - A synthesis and expansion of three preexisting AEGL databases into one functional database tool

AEGL Expert System Database

- Purpose
  - To examine AEGL chemicals using a chemical class approach
  - To compile a broad range of safety and emergency data (Federal and nongovernmental) for these chemicals

AEGL Expert System Database

- Applications
  - Quick reference in the event of an emergency
  - Increased awareness by chemists, chemical hygienists and chemical engineers of acutely toxic by inhalation chemicals
  - Facilitation of the development of detection devices and protective equipment by chemical class
  - Aid in harmonizing the various existing chemical emergency lists
  - And provide a guide to green chemistry opportunities based on chemical class

AEGL Expert System Database

Demonstration

AEGL Derivation Database

- Purpose
  - To store and categorize data pertaining to the development of AEGL values.
- Applications
  - Analysis of AEGL derivation methodology
  - Development of more standardized and consistent procedures for similar scenarios.

AEGL Derivation Database

Demonstration

Summary

- AEGL Expert System Database
  - has a wide range of safety and emergency applications involving AEGL chemical classes
  - approaches the universe of toxic by inhalation chemicals in a novel manner
- AEGL Derivation Database
  - developed as a tool for AEGL staff and NAC/AEGL committee members
  - provides a means for the detailed analysis of AEGL development

Database Usage

- AEGL Expert System Database
  - Will possibly be made accessible as a public resource
  - Has potential use as a training tool for risk managers and emergency responders
  - As part of the grant with the ISTC, will be potentially used by RIHTOP in the development of shared products

Database Usage

- AEGL Derivation Database
  - Will be utilized immediately by the AEGL staff members (and later the NAC committee) as an instrumental tool in the ongoing development of AEGLs

Acknowledgements

- AEGL Staff
  - Iris Camacho
  - Ernest Falke
  - Sharon Frazier
  - Marquea King
  - Paul Tobin
- ECO
- NAC
- RAD
- RIHTOP

ATTACHMENT 5

NAC-39 Meeting, February 1, 2006
Suggestions to improve AEGL databases

The following suggestions were made after Richard Williams gave his presentation:

a. AEGL Expert System database
- Add WEEL values
- Include occupational values from other countries
- Provide web link to refer user to ChemFinder for synonyms, tradenames, etc. of a particular chemical
- Include acute RfC's (Woodall is the contact person for this)
- Post database on the AEGL website
- Tables should have a note indicating that the values are either in ppm or mg/m3 besides the color coding that is currently present
- Add web link to information on flammability, reactivity, etc.
- Add LOA values
- Changes to database should be made by only one person
- Increase font to make database more readable
- Market database and AEGL program by publishing database, giving seminars, etc.
- Have records of past and current values to keep track of changes.
- Include LEL notations and carcinogenicity assessment

b. AEGL Derivation database
- Keep it for internal purposes. Distribute it to committee members and program staff
- Link database to supporting documents available in the bulletin board
- Allow database to search different toxicity endpoints
- Include category plots
- Separate multiple studies into independent entries when used to derive a particular AEGL level
- Add an introductory section about the AEGL program, AEGL definitions, etc. to avoid people misusing AEGL values
- Add a searchable box for irritation (e.g. mild, medium, severe irritation)
- Create a beta-version of the database and allow testing by committee members before the next NAC meeting

Use of Occupational Standards and Recommendations in setting AEGL values

Existing Occupational Standards and Recommendations

PEL – OSHA
legally enforceable

TLV – ACGIH

REL - NIOSH

Basic Application of Occupational Standards and Recommendations

8 hours per day
5 days per week
Working lifetime
Working population

Setting of Occupational Standards/Recommendations

PEL – OSHA Formal rule making
Economic and technological feasibility
Risk level

TLV – ACGIH Private organization

REL – NIOSH Best available evidence

Setting of Occupational Standards/Recommendations

Economic and technological factors
Occupational values may not be as low as the evidence demonstrates

Legal implications
No OSHA standards in last 5 years
Law suits against ACGIH TLV procedure

AEGLs and Occupational Standards/Recommendations

Working lifetime vs. rare exposure
Occupational values may be lower than AEGLs

Working population vs. public
Different populations
AEGLs may be lower than occupational values

Occupational Data

Most exposure is below legal limit

Analysis of 5 years of OSHA personal TWA data

Only 15 chemicals had at least 10% overexposures

Data does NOT support the premise that most workers are exposed at the recommended limit

OSHA Personal TWA samples

Substance	Percent overexposures
Silver metal	37.2
Coke Oven Emissions	31.1
Respirable Silica	28.5
Lead – inorganic	27.5
Wood dust	22.9
Carbon monoxide	21.4
Chromic acid and chromates	20.4

OSHA Personal TWA samples

Substance	Percent overexposures
Total dust	15.6
Beryllium	14.5
Coal tar pitch volatiles	13.9
Copper dusts and mists	12.9
Mercury	12.4
Welding fume particulate	11.2
Ethylene oxide	10.5
Arsenic	10.1

Occupational standards and AEGLs Does it pass the "laugh test" ?

AEGL-3 Highly unlikely exposure

AEGL-2 Inability to escape unlikely

Permanent damage ?

Healthy worker effect

AEGL-1 AEGL SOP

"scientifically credible concentration"

"signs and symptoms of toxicity"

Questions on using occupational recommended levels

- **Is there data that workers are exposed at recommended levels?**
- **Are there health studies of workers with matched exposure data?**
- **Was technical or economic feasibility a factor in setting recommended levels?**
- **Are there sub populations that might react differently than a working population?**

Bottom line

- **Recommended occupational values give no specific information that AEGL-1 symptoms will not be present at that exposure level to the public.**

Cyclohexyl Isocyanate (CAS No. 3173-53-3)

Correction of $BMCL_{05}$ calculation from NAC-38 (September 28-30, 2005)

Staff Scientist: Carol Wood, ORNL
Chemical Manager: Marc Ruijten, RIVM

POD: Calculated $BMCL_{05}$ (1.88 ppm) from a 6-hour rat study (Eastman Kodak, 1990, 1992).

Inter- and intraspecies UFs of 3 each (total = 10) were applied because cyclohexyl isocyanate is highly irritating.

A modifying factor of 3 was applied to account for the sparse data base.

Default time scaling values of n =1 or n = 3 were applied; the 30-min value was adopted as the 10-min value.

POD was calculated incorrectly at NAC-38. The correctly calculated $BMCL_{05}$ = 1.67 ppm, and corrected AEGL-3 values are presented below.

Summary of AEGL Values for Cyclohexyl Isocyanate						
Classification	**10-minute**	**30-minute**	**1-hour**	**4-hour**	**8-hour**	**Endpoint (Reference)**
AEGL–1	NR	NR	NR	NR	NR	Not recommended: Insufficient data
AEGL–2	NR	NR	NR	NR	NR	Not recommended: Insufficient data
AEGL–3	~~0.14 ppm~~ 0.13 ppm	~~0.14 ppm~~ 0.13 ppm	~~0.11 ppm~~ 0.10 ppm	~~0.072 ppm~~ 0.064 ppm	~~0.047 ppm~~ 0.042 ppm	6-hr $BMCL_{05}$ in rats (Eastman Kodak, 1990; 1992)

ACUTE EXPOSURE GUIDELINE LEVELS (AEGLs) FOR SILANE

NAC/AEGL-39
February 1-3, 2006
Washington D.C.

ORNL Staff Scientist- Dana F. Glass
Chemical Manager- Bob Benson
Chemical Reviewers- Marquea King and Richard Thomas

Silane- Background

- Currently used in industry in microelectronics
- Highly explosive, can react easily with air
- Colorless gas
- Repulsive odor
- Limited data available in laboratory animals or humans

AEGL-1 Values

AEGL-1 Values				
10 minute	30 minute	1 hour	4 hour	8 hour
30 ppm	30 ppm	30 ppm	30 ppm	30 ppm

- Key Reference: Omae et al. 1992
- Test species: Ten, male ICR mice
- Exposure: Inhalation: 0 or 1000 ppm for 1, 2, 4 and 8 hours and for 6 hrs/day, 5 days/week for 2 and 4 weeks
- Effect:
  - 1-8 hours: Only effect was increased face washing
  - 2 and 4 weeks: Mild irritation of nasal cavity in exposed mice (after 4 weeks)

AEGL-1 Values (cont'd.)

- Endpoint/Concentration/Rationale: 1000 ppm- no-effect level.
- Uncertainty Factors/Rationale: 30
  - Interspecies: 3, mouse most sensitive species
  - Intraspecies: 10, lack of human data
- Time Scaling: No time-scaling done because no change in effect with time for the 1-8 hours of exposure

AEGL-2 Values

AEGL-2 Values				
10 minute	30 minute	1 hour	4 hour	8 hour
170 ppm	170 ppm	130 ppm	80 ppm	42 ppm

- Key Reference:
  - Takebayashi 1993

- Test species: 12 male ICR mice

- Exposure: Inhalation: 0, 2500, 5000 or 10,000 ppm, 1 or 4 hours

- Effect:

  - 2500 ppm: ruffled fur, face washing
    - 2-day recovery (4 hr) - renal lesions
    - 2-week recovery (4 hr) - no renal lesions- appears reversible

  - 5000 ppm: ruffled fur, face washing
    - 2-day and 2-week recovery- renal lesions (non-reversible in 4 hr group)

AEGL-2 Values (cont'd)

  - 10,000 ppm: 6/8 mice exposed died within 24 hours post-exposure (those in 2-week recovery group)
    - 2-day and 2-week recovery- renal lesions
    - Statistically significant ($p<0.05$) increase in BUN, decrease in RBC's and hematocrit

- Endpoint/Concentration/Rationale: 2500 ppm- concentration resulting in reversible renal lesions

- Uncertainty Factors/Rationale: 30
  - Interspecies: 3, mouse most sensitive species
  - Intraspecies: 10, lack of human data

- Time Scaling: Extrapolation to time points was done:
  - n= 3 for 30 min., and 1 hr (30-min. value adopted as the 10-min.)
  - n=1 for 8 hr

Data

Table 2. Observations after inhalation of silane[a]			
Microscopic lesions after 2-day observation			
	Nasal Cavity	Kidney – ATN[b]	Lung
1-hour exposure			
Control	0/4	0/4	0/4
2500 ppm	0/4	0/4	0/4
5000 ppm	1/4	0/4	0/4
10,000 ppm	0/4	2/4	0/4
4-hour exposure			
Control	0/4	0/4	0/4
2500 ppm	0/4	1/4	0/4
5000 ppm	0/4	1/4	0/4
10,000 ppm	1/1	1/1	0/1
10,000 ppm (D)[c]	7/9	9/9	0/9
Microscopic lesions after 2-week observation			
	Nasal Cavity	Kidney- TIN[d]	Lung
30-minute exposure			
Control	0/5	0/5	0/5
2500 ppm	0/8	0/8	0/8
5000 ppm	0/8	0/8	0/8
7500 ppm	0/8	4/8	0/8
10,000 ppm	0/8	6/8	0/8
1-hour exposure			
Control	0/8	0/8	0/8
2500 ppm	0/7[e]	0/7	0/7
5000 ppm	0/8	1/8	0/8
10,000 ppm	1/8	7/8	0/8
4-hour exposure			
Control	0/8	0/8	0/8
2500 ppm	0/7	0/7	0/7
5000 ppm	0/8	2/8	0/8
10,000 ppm	0/2	1/2	0/2
10,000 ppm (D)	-	-	-

[a] Data from Takebayashi 1993.
[b] ATN = acute tubular necrosis
[c] 10,000 ppm (D)= dead mice exposed to 10,000 ppm silane
[d] TIN = tubular interstitial nephritis
[e] One insufficiently fixed organ was excluded from the exam

AEGL-3 Values

AEGL-3 Values				
10 minute	30 minute	1 hour	4 hour	8 hour
300 ppm	300 ppm	270 ppm	170 ppm	80 ppm

- Key Reference:
  - Takebayashi 1993
- Test species: 12 male ICR mice
- Exposure: Inhalation: 0, 2500, 5000 or 10,000 ppm, 1 or 4 hours
- Effect:
  - 2500 ppm: ruffled fur, face washing
    - with 2-day recovery- renal lesions
    - with 2-week recovery- no renal lesions (reversible)
  - 5000 ppm: ruffled fur, face washing
    - with 2-day recovery- renal lesions
    - with 2-week recovery- renal lesions (non-reversible)

AEGL-3 Values (cont'd)

— 10,000 ppm: 6/8 mice exposed for 4 hrs died within 24 hours post-exposure (those in 2-week recovery group)
  • with 2-day and 2-week recovery- renal lesions present
  • Statistically significant ($p<0.05$) increase in BUN, decrease in RBC's and hematocrit

- Endpoint/Concentration/Rationale: 5000 ppm- highest concentration that did not cause mortality and showed irreversible renal lesions

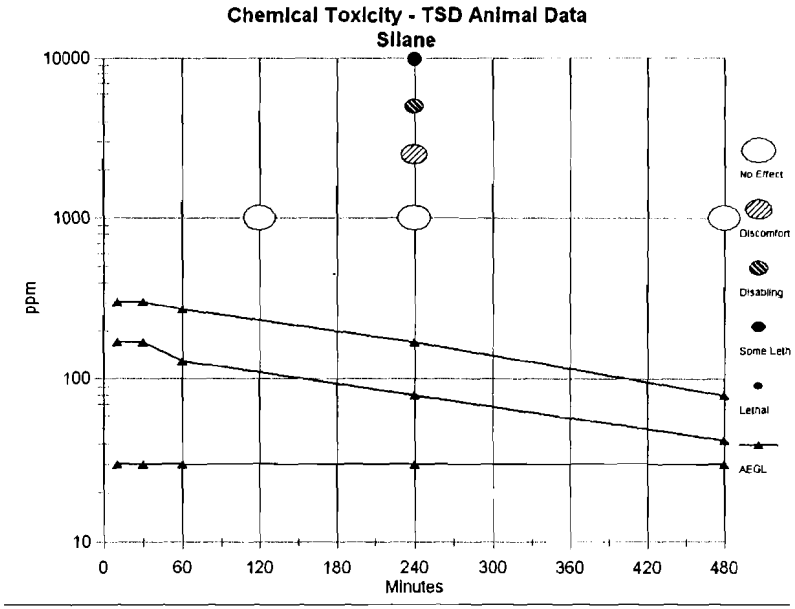
- Uncertainty Factors/Rationale: Total: 30
  — Interspecies: 3, mouse most sensitive species
  — Intraspecies: 10, lack of human data

- Time Scaling: Extrapolation to timepoints:
  — n= 3 for 30 min. and 1 hr (30-min. value adopted as the 10-min.)
  — n=1 for 8 hr

Exposure Guidelines

Extant Standards and Guidelines for Silane					
Guideline	Exposure Duration				
	10 min	30 min	1 hr	4 hr	8 hr
AEGL-1	30 ppm	30 ppm	30 ppm	30 ppm	30 ppm
AEGL-2	170 ppm	170 ppm	130 ppm	80 ppm	42 ppm
AEGL-3	300 ppm	300 ppm	270 ppm	170 ppm	80 ppm
REL-TWA (NIOSH)					5 ppm
TLV-TWA (ACGIH)					5 ppm

Time-Scaling



No effect= No effect or mild discomfort
Discomfort= Notable transient discomfort/irritation
Disabling= Irreversible/long lasting effects or impaired ability to escape
Some lethality= Some, but not all, exposed animals died
Lethal= All exposed animals died

ACUTE EXPOSURE GUIDELINE LEVELS (AEGLs) FOR TRIMETHOXYSILANE AND TETRAMETHOXYSILANE

NAC/AEGL-39
February 1-3, 2006
Washington D.C.

ORNL Staff Scientist- Dana F. Glass
Chemical Manager- Bob Benson
Chemical Reviewers- Marquea King and Richard Thomas

Trimethoxysilane and Tetramethosxysilane - Background

- Both are structural analogs
- Colorless liquids
- Ester-like odor
- Limited data available on laboratory animals or humans

AEGL-1 Values for Trimethoxysilane and Tetramethoxysilane

AEGL-1 Values				
10 minute	30 minute	1 hour	4 hour	8 hour
NR	NR	NR	NR	NR

- Limited data results in no AEGL-1 values recommended

AEGL-2 Values for Trimethoxysilane

AEGL-2 Values				
10 minute	30 minute	1 hour	4 hour	8 hour
1.2 ppm	0.83 ppm	0.67 ppm	0.24 ppm	0.12 ppm

- Key Reference:
  - Nachreiner and Dodd 1988

- Endpoint/Concentration/Rationale: 1/3 of AEGL-3 values taken due to steep dose response curve and lack of data

- Uncertainty Factors/Rationale: Total = 30

  - Interspecies: 3, data on rats, mice and hamsters show similar effects in an inhalation study (Dow Corning 1981)
  - Intraspecies: 10, lack of human data

AEGL-3 Values for Trimethoxysilane

AEGL-3 Values				
10 minute	30 minute	1 hour	4 hour	8 hour
3.6 ppm	2.5 ppm	2.0 ppm	0.73 ppm	0.37 ppm

- Key Reference:
  - Nachreiner and Dodd 1988

- Test species: 5 Sprague-Dawley rats/sex/dose

- Exposure: Inhalation: 19, 39, 71 or 166 ppm for 4 hours (LC_{50} = 60 ppm) and 68, 155, 342 or 643 ppm for 1 hour (LC_{50} = 154 ppm)

- Effects (4 hours): Lung lesions increased in severity with increased concentration

  - 19 ppm: No deaths
  - 39 ppm: 1/10 deaths
  - 71 ppm: 7/10 deaths
  - 166 ppm: 10/10 deaths

AEGL-3 Values for Trimethoxysilane (cont'd)

- Effects (1 hour): Similar increase in severity of lung lesions with increase in concentration

  - 68 ppm: No deaths
  - 155 ppm: 5/10 deaths
  - 342 and 643 ppm: 10/10 deaths

- Endpoint/Concentration/Rationale: U.S. EPA Benchmark Calculation Dose Software used to calculate $BMCL_{05}$ of 60 ppm for 1 hour (POD for 10 min, 30 min and 1 hr) and 22 ppm for 4 hours (POD for 4 and 8 hrs)

- Uncertainty Factors/Rationale: Total = 30

  - Interspecies: 3, data on rats, mice and hamsters show similar effects in an inhalation study (Dow Corning 1981)
  - Intraspecies: 10, lack of human data

AEGL-3 Values for Trimethoxysilane (cont'd)

- Time Scaling: Extrapolation to time points was done:
  - n= 3 for 10 min, 30 min., and 1 hr
  - n=1 for 8 hr

AEGL-2 Values for Tetramethoxysilane

AEGL-2 Values				
10 minute	30 minute	1 hour	4 hour	8 hour
0.57 ppm	0.57 ppm	0.47 ppm	0.30 ppm	0.14 ppm

- Key Reference:
  - Dow Corning Corp. 1992

- Endpoint/Concentration/Rationale: 1/3 of AEGL-3 values taken due to steep dose response curve and lack of data

- Uncertainty Factors/Rationale: Total = 30
  - Interspecies: 3, data on rats, mice and hamsters show similar effects in an inhalation study (Dow Corning 1981) using analog, trimethoxysilane
  - Intraspecies: 10, lack of human data

AEGL-3 Values for Tetramethoxysilane

AEGL-3 Values				
10 minute	30 minute	1 hour	4 hour	8 hour
1.7 ppm	1.7 ppm	1.4 ppm	0.87 ppm	0.43 ppm

- Key Reference:
  - Dow Corning Corp. 1992

- Test species: 10 male Sprague-Dawley rats/exposure level

- Exposure: Inhalation: 31, 50 or 88 ppm for 4 hours (LC_{50} = 63 ppm)

- Effect:

  - 31 ppm: No deaths, no clinical signs
  - 50 ppm: 3/10 deaths; gasping/coughing; evidence of lung damage on histopathological examination

AEGL-3 Values for Tetramethoxysilane (cont'd)

  - 88 ppm: 9/10 deaths; more severe gasping/coughing; more dispersed lung damage

- Endpoint/Concentration/Rationale: U.S. EPA Benchmark Calculation Dose Software used to calculate $BMCL_{05}$ of 26 ppm for 4 hours

- Uncertainty Factors/Rationale: Total = 30

  - Interspecies: 3, data on rats, mice and hamsters show similar effects
  - Intraspecies: 10, lack of human data

- Time Scaling: Extrapolation to time points was done:

  - n= 3 for 30 min. and 1 hr
  - n=1 for 8 hr
  - 30-minute AEGL-3 value also adopted as the 10-minute value.

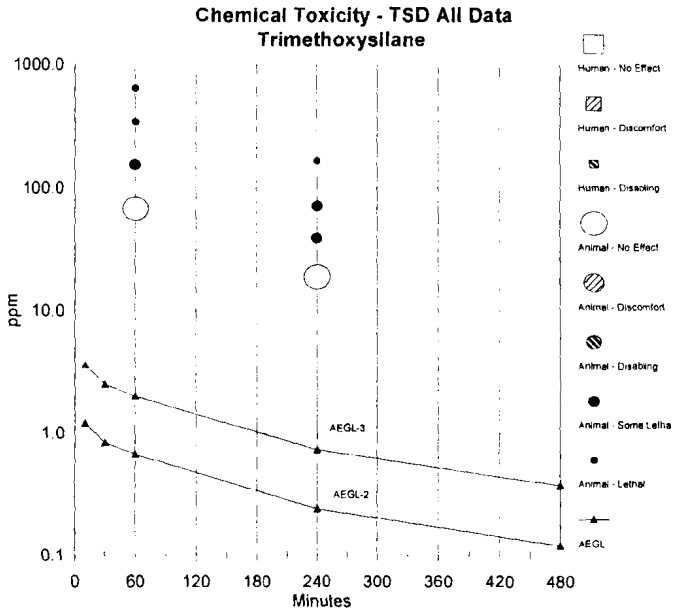
Exposure Guidelines

Extant Standards and Guidelines for Trimethoxysilane					
Guideline	**Exposure Duration**				
	10 min	**30 min**	**1 hr**	**4 hr**	**8 hr**
AEGL-1	NR	NR	NR	NR	NR
AEGL-2	1.2 ppm	0.83 ppm	0.67 ppm	0.24 ppm	0.12 ppm
AEGL-3	3.6 ppm	2.5 ppm	2.0 ppm	0.73 ppm	0.37 ppm
ERPG-1 (AHIA)			0.5 ppm		
ERPG-2 (AHIA)			2.0 ppm		
ERPG-3 (AHIA)			5.0 ppm		
WEEL-AIHA					0.05 ppm

Exposure Guidelines

Extant Standards and Guidelines for Tetramethoxysilane					
Guideline	**Exposure Duration**				
	10 min	**30 min**	**1 hr**	**4 hr**	**8 hr**
AEGL-1	NR	NR	NR	NR	NR
AEGL-2	0.57 ppm	0.57 ppm	0.47 ppm	0.30 ppm	0.14 ppm
AEGL-3	1.7 ppm	1.7 ppm	1.4 ppm	0.87 ppm	0.43 ppm
ERPG-1 (AHIA)			N/A		
ERPG-2 (AHIA)			10 ppm		
ERPG-3 (AHIA)			20 ppm		
REL-TWA (NIOSH)					1 ppm
TLV-TWA (ACGIH)					1 ppm
MAC (Dutch)					1 ppm

Time-Scaling



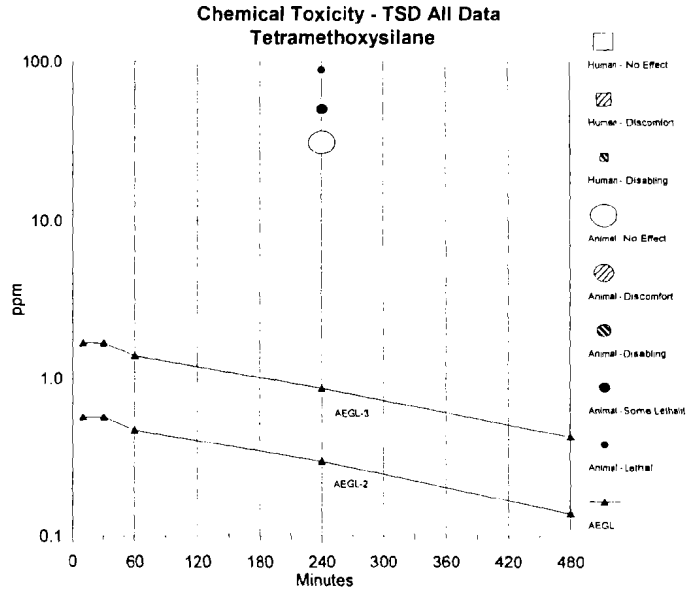
No effect= No effect or mild discomfort

Discomfort= Notable transient discomfort/irritation

Disabling= Irreversible/long lasting effects or impaired ability to escape

Some lethality= Some, but not all, exposed animals died

Lethal= All exposed animals died



No effect= No effect or mild discomfort

Discomfort= Notable transient discomfort/irritation

Disabling= Irreversible/long lasting effects or impaired ability to escape

Some lethality= Some, but not all, exposed animals died

Lethal= All exposed animals died

Trimethoxysilane and Tetramethoxysilane

Table 12. Summary of AEGL Values in ppm (mg/m^3)					
Classification	10-minute	30-minute	1-hour	4-hour	8-hour
Trimethoxysilane					
AEGL-1 (Nondisabling)	NR	NR	NR	NR	NR
AEGL-2 (Disabling)	1.2 (6)	0.83 (4.2)	0.67 (3.4)	0.24 (1.2)	0.12 (0.60)
AEGL-3 (Lethality)	3.6 (18)	2.5 (13)	2.0 (10)	0.73 (3.7)	0.37 (1.9)
Tetramethoxysilane					
AEGL-1 (Nondisabling)	NR	NR	NR	NR	NR
AEGL-2 (Disabling)	0.57 (3.6)	0.57 (3.6)	0.47 (2.9)	0.30 (1.9)	0.14 (.88)
AEGL-3 (Lethality)	1.7 (11)	1.7 (11)	1.4 (8.8)	0.87 (5.4)	0.43 (2.7)

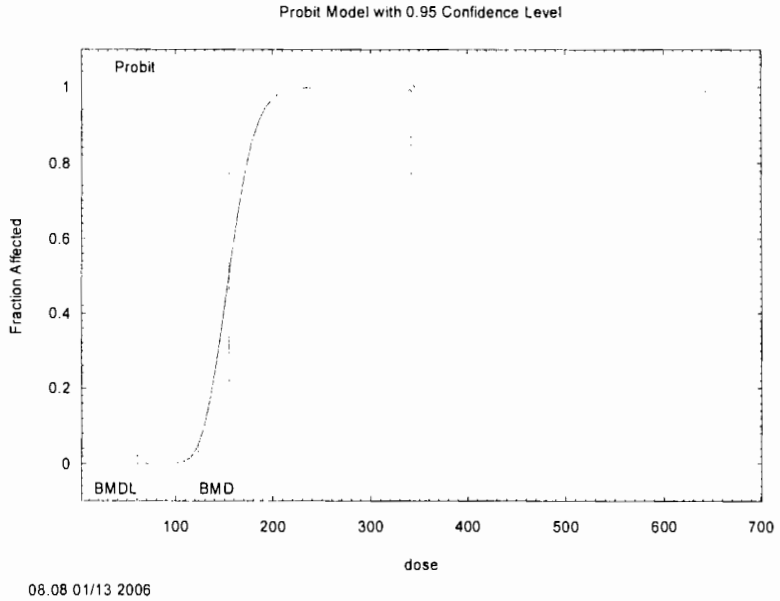
Data of multiple species exposure (Dow Corning 1981)

Exposed rats, mice, hamsters and rabbits to 0, 10, 25 or 50 ppm 7 hours/day for 5 days

Table 5. Clinical signs observed in trimethoxysilane exposure to different species[a]				
Exposure (ppm)	Rats	Mice	Hamsters	Rabbits
0	NS[b]	NS	NS	NS
10	depression + nasal discharge +	depression + nasal discharge +	depression + nasal discharge +	depression + nasal discharge ++
25	depression + nasal discharge + gasping -NS	depression + nasal discharge + gasping +	depression ++ nasal discharge + gasping +	depression ++ nasal discharge ++ gasping ++
50	depression + nasal discharge + gasping +	depression + nasal discharge + gasping +	depression ++ nasal discharge + gasping +	depression ++ nasal discharge +++ gasping +++

[a] Data from Dow Corning 1981
[b] NS = no signs observed

Trimethoxysilane- 1 hour data



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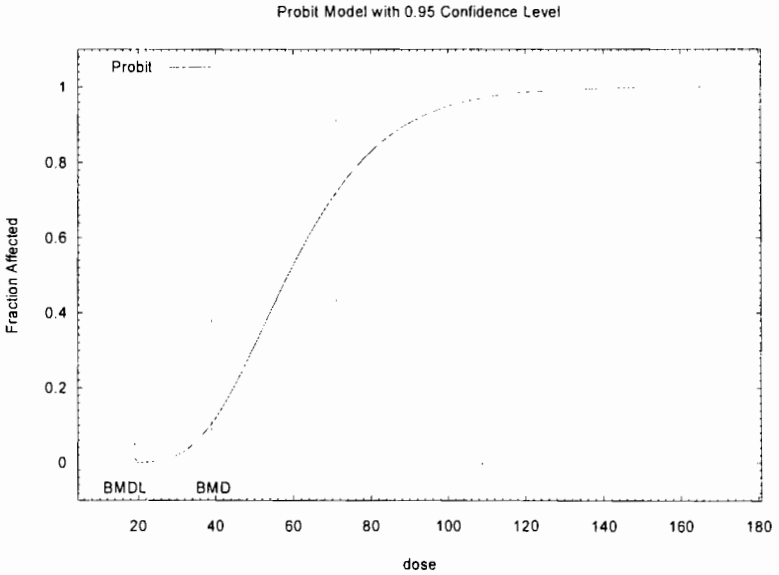
Trimethoxysilane- 4-hour data



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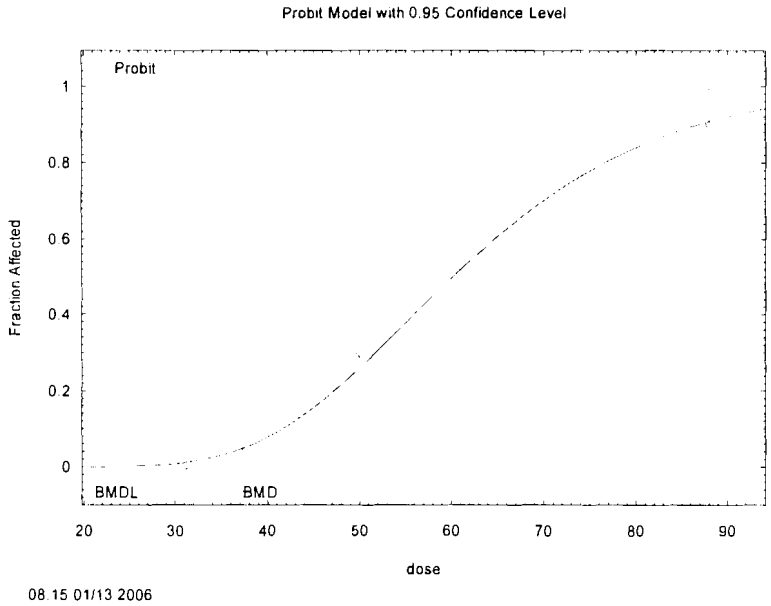
Tetramethoxysilane- 4 hour data



ATTACHMENT 10

ACUTE EXPOSURE GUIDELINE LEVELS

SULFURYL CHLORIDE

NAC/AEGL-39
February 1-3, 2006

ORNL Staff Scientist:
Robert Young

Chemical Manager:
Steven Barbee

Chemical Reviewers:
Marinelle Payton
George Cushmac

SULFURYL CHLORIDE - LETHAL TOXICITY

- No human data
- Animal data
  - data for rats only
  - 1-hr and 4-hr exposures
  - signs of toxicity consistent with exposure to an irritant (lacrimation, erythema around the eyes and ears, nasal discharge; salivation, dyspnea).
  - necropsy: necrosis and erythema in the nasal passages; pulmonary hemorrhage

SULFURYL CHLORIDE - NONLETHAL TOXICITY

- No human data
- Limited data from animal lethality studies - respiratory tract involvement

Nonlethal toxicity of sulfuryl chloride in rats		
Exposure (ppm)	Effect	Reference
84.4 (4 hrs)	Reddish exudate around the eyes and nostrils. Body weight loss for two days 14-day post exposure observation	Kelly and Stula, 1983
3.1*	concentration-related increase in blood urea nitrogen histopathologic evidence of respiratory tract damage	Kelly and Stula, 1983
9.9*	concentration-related increase in blood urea nitrogen histopathologic evidence of respiratory tract damage	Kelly and Stula, 1983

* 14-day exposure; 6 hour/day, 5 days/week

SULFURYL CHLORIDE - LETHAL TOXICITY

Lethal toxicity of sulfuryl chloride in rats 4-hour exposure		
Exposure	Mortality	Reference
84.4 ppm	0/10	Du Pont & Co., 1982
134 ppm	2/10 (1 during exposure and 1 within 24 hrs)	
155 ppm	8/10 (6 during exposure; 2 within 24 hrs)	
207 ppm	7/10 (all died during exposure)	
273 ppm	10/10 (all during exposure)	

Lethal toxicity of sulfuryl chloride in rats		
Exposure	Mortality	Reference
131 ppm	1-hr LC_{50} ♂	Bayer AG, 1993a; IUCLID, 2000
242 ppm	1-hr LC_{50} ♀	

Lethal toxicity of sulfuryl chloride in rats 1-hour exposure		
Exposure	Mortality	Reference
43 ppm	0/10	Stauffer Chemical Company, 1969
71 ppm	0/10 (1-18 hrs)	
108 ppm	8/10 (1-16 hrs)	
200 ppm	10/10 (1-10 hrs)	
252 ppm	10/10 (1-5 hrs)	
392 ppm	10/10 (1-5 hrs)	
31.3 ppm	0/10	Stauffer Chemical Company, 1970
62.3 ppm	6/10 (16-72 hrs)	
125.1 ppm	10/10 (8-12 hrs)	

SULFURYL CHLORIDE AEGL-1

- **Not recommended - insufficient data**

AEGL-1 Values for Sulfuryl Chloride				
10-min	30-min	1-hr	4-hr	8-hr
NR	NR	NR	NR	NR

NR: not recommended; insufficient data.

SULFURYL CHLORIDE AEGL-2

- **Data insufficient - derived by 1/3 of AEGL-3 following AEGL SOP guidance (NRC, 2001)**

AEGL-2 Values for Sulfuryl Chloride				
10-min	30-min	1-hr	4-hr	8-hr
4.7 ppm	4.7 ppm	3.7 ppm	2.3 ppm	1.2 ppm

SULFURYL CHLORIDE AEGL-3

- Inconsistencies between Du Pont/Haskell Laboratory data and Stauffer Chemical Co. (4-hr vs 1-hr lethality)
- 4-hr lethality data from Haskell Laboratory (Du Pont, 1982) used for AEGL-3 development

SULFURYL CHLORIDE AEGL-3

Critical effect/POD: **$BMCL_{05}$ of 70.1 ppm (4 hrs) used as estimated lethality threshold (Du Pont, 1982)**

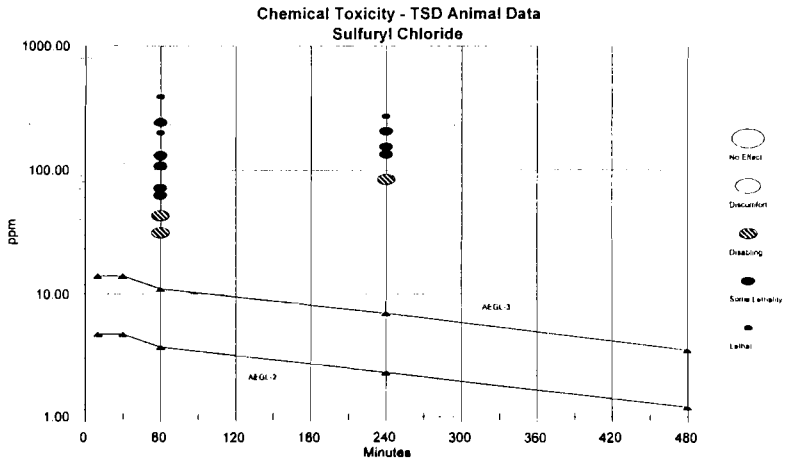
Uncertainty factors: **Total uncertainty adjustment of 10.**

Interspecies: UF = 3: contact tissue damage resulting from the degradation of sulfuryl chloride to sulfuric acid and hydrochloric acid

Intraspecies: UF=3: sufficient to account for individual variability in direct-contact toxic response to corrosive agents and for individuals with compromised respiratory function

Time scaling: **$n = 3$ when extrapolating to shorter time points and $n = 1$ when extrapolating to longer time points using the $C^n \times t = k$ equation (NRC, 2001). 10-min values equivalent to 30-min**

AEGL-3 Values for Sulfuryl Chloride				
10-min	30-min	1-hr	4-hr	8-hr
14 ppm	14 ppm	11 ppm	7.0 ppm	3.5 ppm



ATTACHMENT 11

ACUTE EXPOSURE GUIDELINE LEVELS (AEGLs) FOR SELECTED CHLOROFORMATES

NAC/AEGL-39
February 1-3, 2006

ORNL Staff Scientist: Cheryl Bast

Chemical Manager: Ernest Falke

Chemical Reviewers: Lynn Beasley and Paul Tobin

- Hydrolyze in water or moist air to produce the parent hydroxy compound, hydrogen chloride, carbon dioxide, and a carbonate.
- All title chloroformates are direct-acting contact irritants, and are corrosive to the eyes, skin, gastrointestinal and respiratory tracts.

  Ethyl chlorothioformate may cause both portal of entry and systemic effects. These systemic effects are likely due to the ability of the thio moiety to interact with other biomolecules.

  Myocardial degeneration, nephrosis, hepatic necrosis, adrenal necrosis, spleen and lymph node necrosis, and lymphoid cell depletion noted in rats
- Values derived for seven chloroformates
- In all cases the inter- and intra- species uncertainty factors were 3 and 3, respectively.
- In 2 cases a modifying factor was used:

  One for limited data

  One for the possibility of systemic effects.
- Where an AEGL-2 was calculated it was determined by dividing the AEGL-3 by 3.

  Justified by steep concentration-response curve (SOP Section 2.2.2.3)
- AEGL-1 values are Not Recommended for any chloroformates due to insufficient data

CHEMICAL	AEGL-2 POD	AEGL-3 POD	Rat LC_{50} Data Available *POD	COMMENTS
Methyl chloroformate	1/3 AEGL-3 (steep curve support)	$BMCL_{05}$ (Hoechst, 1986)	Analytical 1-hr Male- 88 ppm (Vernot et al., 1977) 1-hr Male- 92-123 ppm (Fisher et al., 1981) 1-hr Female- 103 ppm (Vernot et al., 1977) 1-hr Female- 100 ppm (Fisher et al., 1981) 4-hr Male- 51 ppm (Hoechst, 1986) 4-hr Female- 53 ppm (Hoechst, 1986) *($BMCL_{05}$ = 42.4 ppm) **4-hr Male- 13 ppm (BASF, 1980) **4-hr Female- 15 ppm (BASF, 1980) Nominal 1-hr 163 ppm (Bio-Test, 1975)	Proposed AEGL values supported by repeated-exposure studies. **BASF (1980) study appears to be outlier and is inconsistent with other available data. Study report suggests analytical difficulties. *Significant changes from Draft 1: New key study*
Ethyl chloroformate	1/3 AEGL-3 (steep curve support)	1/3 LC_{50} for males (Vernot et al., 1977)	Analytical 1-hr Male- 145 ppm (Vernot et al., 1977) *(145 ppm x ⅓ = 48 ppm) 1-hr Male- 189 ppm (Fisher et al., 1981) 1-hr Female- 170 ppm (Vernot et al., 1977) 1-hr Female- 200 ppm (Fisher et al., 1981)	*No* significant changes from Draft 1 except AEGL-1 values now NR.
Propyl chloroformate	1/3 AEGL-3 (steep curve support)	$BMCL_{05}$	Nominal 1-hr- 410 ppm (Bio-Test, 1970) *($BMCL_{05}$ = 216 ppm)	MF=3 for limited data *No* significant changes from Draft 1 except AEGL-1 values now NR.
Isopropyl chloroformate	1/3 AEGL-3	1/3 LC_{50}	Nominal 1-hr- 300 ppm (Bio-Test, 1970) *(300 ppm x ⅓ = 100 ppm)	No MF- support with repeat-exposure data *No* significant changes from Draft 1 except AEGL-1 values now NR.
Allyl chloroformate	1/3 AEGL-3 (steep curve support)	$BMCL_{05}$	Analytical 1-hr- 65.1 ppm (Stillmeadow, 1987) *($BMCL_{05}$ = 21 ppm)	No MF- analytical concentration *No* significant changes from Draft 1 except AEGL-1 values now NR.
n-Butyl chloroformate	1/3 AEGL-3	1/3 Conc. where 4/10 rats died	4/10 rats dead- 200 ppm, 1-hr (BASF, 1970) *(200 ppm x ⅓ = 66.7 ppm)	Proposed AEGL values supported by repeated-exposure data *Significant changes from Draft 1.*
Isobutyl chloroformate	NR	NR		*No* significant changes from Draft 1.
sec-Butyl chloroformate	NR	NR		*No* significant changes from Draft 1.
Ethyl chlorothioformate	1/3 AEGL-3	$BMCL_{05}$	Analytical 4-hr Male- 51 ppm (Stauffer, 1983) 4-hr Female- 41 ppm (Stauffer, 1983) *($BMCL_{05}$ = 21 ppm)	MF=3 for systemic effects of thio moiety *No* significant changes from Draft 1.
Diphosgene	NR	NR		*No* significant changes from Draft 1.

AEGL-1 VALUES: METHYL CHLOROFORMATE				
10 minute	30 minute	1 hour	4 hour	8 hour
NR	NR	NR	NR	NR

Not Recommended due to insufficient data.

AEGL-2 VALUES: METHYL CHLOROFORMATE				
10 minute	30 minute	1 hour	4 hour	8 hour
2.8 ppm	2.8 ppm	2.2 ppm	1.4 ppm	0.70 ppm

Endpoint: ⅓ The AEGL-3 values

Endpoint is justified based on the steep concentration-response curve:

Rat 4-hr exposure (Hoechst, 1986):
0% Mortality at 45 ppm
LC_{50} = 51-53 ppm
80% mortality at 57 ppm

1-hr rat LC_{50} is approximately 100 ppm
Rats exposed to 26 ppm for 1-hr were clinically-normal (Fisher et al., 1981)

Support: Values are considered protective because rats showed no deaths and only nasal turbinate histopathology and laryngeal lesions when repeatedly exposed to 3.1 ppm for 6 hours/day, 5 days/week for 4 weeks (BASF, 1993).

AEGL-3 VALUES: METHYL CHLOROFORMATE				
10 minute	30 minute	1 hour	4 hour	8 hour
8.5 ppm	8.5 ppm	6.7 ppm	4.2 ppm	2.1 ppm

Species: Rat (5 sex/group)
Concentration: 42.4 ppm
Time: 4-hours
Endpoint: Estimated lethality threshold: $BMCL_{05}$, male and female combined
Reference: Hoechst, 1986

Time Scaling: $C^n \times t = k$, where $n = 3$ for the 30-minute and 1-hour time periods, and $n = 1$ for the 8-hour time period, to provide AEGL values that would be protective of human health (NRC, 2001).

Uncertainty Factors:

Interspecies = 3 Intraspecies = 3

Highly reactive and clinical signs are likely caused by a direct chemical effect on the tissues; this type of portal-of-entry effect is not expected to vary greatly between species or among individuals.

Support: POD supported by the fact that no deaths were observed in rats exposed to 45 ppm for 4-hours (Hoechst, 1986).

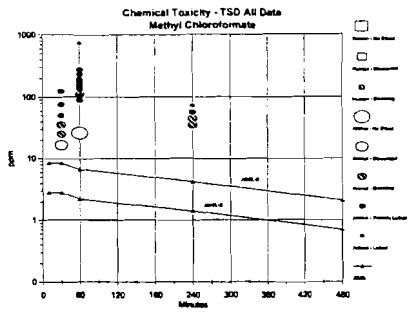
Derived values are considered protective because:

Rats showed no deaths when repeatedly exposed to 7.8 ppm for 6 hours/day, 5 days/week for 4 weeks (BASF, 1999)

Rats had no deaths until week 4 when repeatedly exposed to 8.8 ppm for 6 hours/day, 5 days/week for 4 weeks (BASF, 1993)

THERE ARE NO OTHER EXTANT STANDARDS AND GUIDELINES FOR METHYL CHLOROFORMATE!

Summary of Proposed AEGL Values for Methyl Chloroformate					
Guideline	Exposure Duration				
	10-minutes	30-minutes	1-hour	4-hours	8-hours
AEGL-1	NR	NR	NR	NR	NR
AEGL-2	2.8 ppm	2.8 ppm	2.2 ppm	1.4 ppm	0.70 ppm
AEGL-3	8.5 ppm	8.5 ppm	6.7 ppm	4.2 ppm	2.1 ppm



AEGL-1 VALUES: ETHYL CHLOROFORMATE				
10 minute	30 minute	1 hour	4 hour	8 hour
NR	NR	NR	NR	NR

Not Recommended due to insufficient data.

AEGL-2 VALUES: ETHYL CHLOROFORMATE				
10 minute	30 minute	1 hour	4 hour	8 hour
2.9 ppm	2.0 ppm	1.6 ppm	0.40 ppm	0.20 ppm

Endpoint: ⅓ The AEGL-3 values

Endpoint is justified based on the steep concentration-response curve:

1-hr rat LC_{50} is 189-200 ppm
Rats exposed to 47 ppm for 1-hr were clinically-normal
(Fisher et al., 1981)

AEGL-3 VALUES: ETHYL CHLOROFORMATE				
10 minute	30 minute	1 hour	4 hour	8 hour
8.8 ppm	6.1 ppm	4.8 ppm	1.2 ppm	0.60 ppm

Species: Rat (10 males/group)
Concentration: 48 ppm
Time: 1-hour
Endpoint: Estimated lethality threshold: ⅓ of the most conservati
1-hr LC_{50} value in rats (145 ppm x ⅓ =48 ppm)
Reference: Vernot et al., 1977

Time Scaling: $C^n \times t = k$, where n= 3 for the 10- and 30-minute time periods, and n= 1 for the 4- and 8-hour time periods, to provide AEGL values that would be protective of huma health (NRC, 2001).

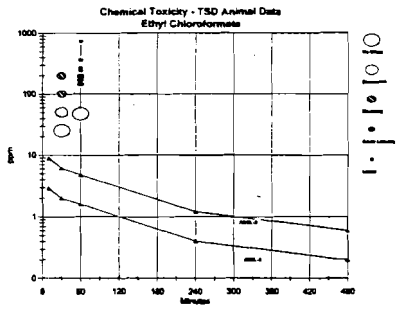
Uncertainty Factors:

Interspecies = 3 Intraspecies = 3

Highly reactive and clinical signs are likely caused by a direct chemical effect on the tissues; this type of portal-of-entry effect is not expected to vary greatl between species or among individuals.

Support: POD supported by the fact that no deaths were observe in rats exposed to 47 ppm for 1 hour (Fisher et al., 1981

Summary of Proposed AEGL Values for Ethyl Chloroformate					
Guideline	Exposure Duration				
	10-minutes	30-minutes	1-hour	4-hours	8-hours
AEGL-1	NR	NR	NR	NR	NR
AEGL-2	2.9 ppm	2.0 ppm	1.6 ppm	0.40 ppm	0.20 ppm
AEGL-3	8.8 ppm	6.1 ppm	4.8 ppm	1.2 ppm	0.60 ppm
Dutch MAC					1 ppm



AEGL-1 VALUES: PROPYL CHLOROFORMATE				
10 minute	30 minute	1 hour	4 hour	8 hour
NR	NR	NR	NR	NR

Not Recommended due to insufficient data.

AEGL-2 VALUES: PROPYL CHLOROFORMATE				
10 minute	30 minute	1 hour	4 hour	8 hour
4.3 ppm	3.0 ppm	2.4 ppm	0.6 ppm	0.30 ppm

Endpoint: **⅓ The AEGL-3 values**

Endpoint is justified based on the steep concentration-response curve:

1-hr exposures(Bio-Test, 1970)

0/10 dead at 249 ppm

2/10 dead at 333 ppm

10/10 dead at 1000 ppm

AEGL-3 VALUES: PROPYL CHLOROFORMATE				
10 minute	30 minute	1 hour	4 hour	8 hour
13 ppm	9.1 ppm	7.2 ppm	1.8 ppm	0.90 ppm

Species: Rat (5/sex/group)
Concentration: 216 ppm
Time: 1-hour
Endpoint: Estimated lethality threshold: $BMCL_{05}$
Reference: Bio-Test, 1970

Time Scaling: $C^n \times t = k$, where $n = 3$ for the 10- and 30-minute time periods, and $n = 1$ for the 4- and 8-hour time periods, to provide AEGL values that would be protective of human health (NRC, 2001).

Uncertainty Factors:

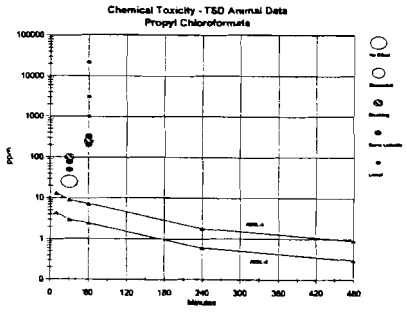
Interspecies = 3 Intraspecies = 3

Highly reactive and clinical signs are likely caused by a direct chemical effect on the tissues; this type of portal-of-entry effect is not expected to vary greatly between species or among individuals.

Modifying Factor = 3

Key study reported nominal, not analytical, concentrations

No other confirmatory studies



THERE ARE NO OTHER EXTANT STANDARDS AND GUIDELINES FOR PROPYL CHLOROFORMATE!

Summary of Proposed AEGL Values for Propyl Chloroformate					
Guideline	Exposure Duration				
	10-minutes	30-minutes	1-hour	4-hours	8-hours
AEGL-1	NR	NR	NR	NR	NR
AEGL-2	4.3 ppm	3.0 ppm	2.4 ppm	0.6 ppm	0.30 ppm
AEGL-3	13 ppm	9.1 ppm	7.2 ppm	1.8 ppm	0.90 ppm

AEGL-1 VALUES: ISOPROPYL CHLOROFORMATE				
10 minute	30 minute	1 hour	4 hour	8 hour
NR	NR	NR	NR	NR

Not Recommended due to insufficient data.

AEGL-2 VALUES: ISOPROPYL CHLOROFORMATE				
10 minute	30 minute	1 hour	4 hour	8 hour
6.0 ppm	4.3 ppm	3.3 ppm	0.83 ppm	0.43 ppm

Endpoint: ⅓ The AEGL-3 values

Support: Values are considered protective because rats showed only nasal irritation when exposed to 20 ppm repeatedly (6 hours/day for 20 days) (Gage, 1970)

AEGL-3 VALUES: ISOPROPYL CHLOROFORMATE				
10 minute	30 minute	1 hour	4 hour	8 hour
18 ppm	13 ppm	10 ppm	2.5 ppm	1.3 ppm

Species: Rat (5/sex/group)
Concentration: 100 ppm
Time: 1-hour
Endpoint: Estimated lethality threshold: ⅓ x LC50: ⅓ x 300 ppm = 100 ppm
Reference: Bio-Test, 1970

POD supported by the fact that no deaths were observed in rats exposed to approximately 200 ppm for 1 hour (BASF, 1968a).

Time Scaling: $C^n \times t = k$, where $n = 3$ for the 10- and 30-minute time periods, and $n = 1$ for the 4- and 8-hour time periods, to provide AEGL values that would be protective of human health (NRC, 2001).

Uncertainty Factors:

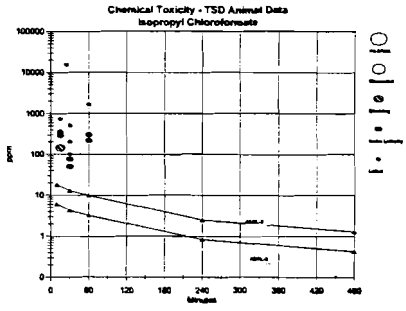
Interspecies = 3 Intraspecies = 3

Highly reactive and clinical signs are likely caused by a direct chemical effect on the tissues; this type of portal-of-entry effect is not expected to vary greatly between species or among individuals.

Support:

Values considered protective because no deaths were noted in rats exposed to 42 ppm isopropyl chloroformate 6 hours/day for 5 days (Collins and Proctor, 1984).

Extant Standards and Guidelines for Isopropyl Chloroformate					
Guideline	Exposure Duration				
	10 minutes	30 minutes	1 hour	4 hours	8 hours
AEGL-1	NR	NR	NR	NR	NR
AEGL-2	6.0 ppm	4.3 ppm	3.3 ppm	0.83 ppm	0.43 ppm
AEGL-3	18 ppm	13 ppm	10 ppm	2.5 ppm	1.3 ppm
ERPG-1[a]	Insufficient Data				
ERPG-2[a]	5 ppm				
ERPG-3[a]	20 ppm				
Dutch MAC[b]					1 ppm



AEGL-1 VALUES: ALLYL CHLOROFORMATE				
10 minute	30 minute	1 hour	4 hour	8 hour
NR	NR	NR	NR	NR

Not Recommended due to insufficient data.

AEGL-2 VALUES: ALLYL CHLOROFORMATE				
10 minute	30 minute	1 hour	4 hour	8 hour
1.3 ppm	0.87 ppm	0.70 ppm	0.18 ppm	0.09 ppm

Endpoint: ⅓ the AEGL-3 values

Endpoint is justified based on the steep concentration-response curve:

1-hr rat exposures (Stillmeadow, 1987)

0/10 dead at 33.7 ppm

6/10 dead at 65 ppm

10/10 dead at 175.7 ppm

AEGL-3 VALUES: ALLYL CHLOROFORMATE				
10 minute	30 minute	1 hour	4 hour	8 hour
3.8 ppm	2.6 ppm	2.1 ppm	0.53 ppm	0.26 ppm

Species: Rat (5/sex/group)
Concentration: 21 ppm
Time: 1-hour
Endpoint: Estimated lethality threshold: $BMCL_{05}$
Reference: Stillmeadow, 1987

Time Scaling: $C^n \times t = k$, where $n = 3$ for the 10- and 30-minute time periods, and $n = 1$ for the 4- and 8-hour time periods, to provide AEGL values that would be protective of human health (NRC, 2001).

Uncertainty Factors:

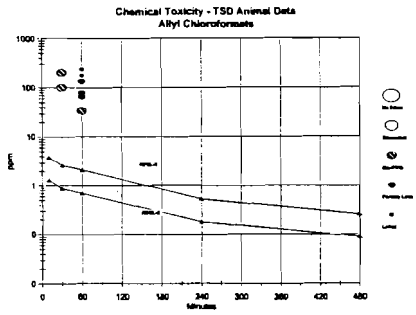
Interspecies = 3 Intraspecies = 3

Highly reactive and clinical signs are likely caused by a direct chemical effect on the tissues; this type of portal-of-entry effect is not expected to vary greatly between species or among individuals.

THERE ARE NO OTHER EXTANT STANDARDS AND GUIDELINES FOR ALLYL CHLOROFORMATE!

Summary of Proposed AEGL Values for Allyl Chloroformate					
Guideline	Exposure Duration				
	10-minutes	30-minutes	1-hour	4-hours	8-hours
AEGL-1	NR	NR	NR	NR	NR
AEGL-2	1.3 ppm	0.87 ppm	0.70 ppm	0.18 ppm	0.09 ppm
AEGL-3	3.8 ppm	2.6 ppm	2.1 ppm	0.53 ppm	0.26 ppm

AEGL-1 VALUES: n-BUTYL CHLOROFORMATE				
10 minute	30 minute	1 hour	4 hour	8 hour
NR	NR	NR	NR	NR



Not recommended due to insufficient data.

AEGL-2 VALUES: n-BUTYL CHLOROFORMATE				
10 minute	30 minute	1 hour	4 hour	8 hour
4.0 ppm	2.8 ppm	2.2 ppm	0.57 ppm	0.28 ppm

Endpoint: ⅓ the AEGL-3 values

Support:

Values considered protective because no effects were noted in rats exposed to 1.8 ppm n-butyl chloroformate for 6 hours/day, 5 days/week for 4 weeks or to 2.9 ppm, 6 hours/day for 5 days (HRC, 1990).

AEGL-3 VALUES: n-BUTYL CHLOROFORMATE				
10 minute	30 minute	1 hour	4 hour	8 hour
12 ppm	8.4 ppm	6.7 ppm	1.7 ppm	0.83 ppm

Species: Rat (10/group)
Concentration: 66.7 ppm
Time: 1-hour
Endpoint: Estimated lethality threshold: 1/3 the concentration where 4/10 rats died
Reference: BASF, 1970

Time Scaling: $C^n \times t = k$, where $n = 3$ for the 10- and 30-minute time periods, and $n = 1$ for the 4- and 8-hour time periods, to provide AEGL values that would be protective of huma health (NRC, 2001).

Uncertainty Factors:

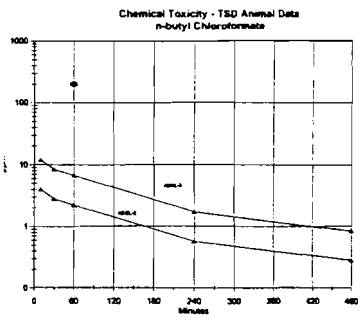
Interspecies = 3 Intraspecies = 3

Highly reactive and clinical signs are likely caused by a direct chemical effect on the tissues; this type of portal-of-entry effect is not expected to vary greatl between species or among individuals.

Support:

Values considered protective because no deaths were noted in rats exposed t 5.1 ppm n-butyl chloroformate for 6 hours/day, 5 days/week for 4 weeks or t 28.4 ppm, 6 hours/day for 5 days (HRC, 1990).

Extant Standards and Guidelines for n-Butyl Chloroformate					
Guideline	Exposure Duration				
	10 minutes	30 minutes	1 hour	4 hours	8 hours
AEGL-1	NR	NR	NR	NR	NR
AEGL-2	4.0 ppm	2.8 ppm	2.2 ppm	0.57 ppm	0.28 ppm
AEGL-3	12 ppm	8.4 ppm	6.7 ppm	1.7 ppm	0.83 ppm
TLV (Australia and UK)					1 ppm
Dutch MAC					1 ppm



Summary of AEGL Values For Isobutyl Chloroformate						
Classification	10-Minute	30-Minute	1-Hour	4-Hour	8-Hour	Endpoint (Reference)
AEGL-1 (Nondisabling)	NR	NR	NR	NR	NR	Insufficient data
AEGL-2 (Disabling)	NR	NR	NR	NR	NR	Insufficient data
AEGL-3 (Lethality)	NR	NR	NR	NR	NR	Insufficient data

Summary of AEGL Values For sec-Butyl Chloroformate						
Classification	10-Minute	30-Minute	1-Hour	4-Hour	8-Hour	Endpoint (Reference
AEGL-1 (Nondisabling)	NR	NR	NR	NR	NR	Insufficient data
AEGL-2 (Disabling)	NR	NR	NR	NR	NR	Insufficient data
AEGL-3 (Lethality)	NR	NR	NR	NR	NR	Insufficient data

AEGL-1 VALUES: ETHYL CHLOROTHIOFORMATE				
10 minute	30 minute	1 hour	4 hour	8 hour
NR	NR	NR	NR	NR

Not Recommended due to insufficient data.

AEGL-2 VALUES: ETHYL CHLOROTHIOFORMATE				
10 minute	30 minute	1 hour	4 hour	8 hour
0.47 ppm	0.47 ppm	0.37 ppm	0.23 ppm	0.12 ppm

Endpoint: ⅓ the AEGL-3 values

Endpoint is justified based on the steep concentration-response curve:

4-hr rat exposures (Stauffer, 1983)

4/20 dead at 33 ppm

14/20 dead at 59 ppm

20/20 dead at 65 ppm

AEGL-3 VALUES: ETHYL CHLOROTHIOFORMATE				
10 minute	30 minute	1 hour	4 hour	8 hour
1.4 ppm	1.4 ppm	1.1 ppm	0.70 ppm	0.35 ppm

Species: Rat (10/sex/group)
Concentration: 21 ppm
Time: 4-hour
Endpoint: Estimated lethality threshold: $BMCL_{05}$
Reference: Stauffer, 1983

Time Scaling: $C^n \times t = k$, where $n = 3$ for the 30-minute and 1-hour time periods, and $n = 1$ for the 8-hour time period, to provide AEGL values that would be protective of human health (NRC, 2001). The 30-minute value was adopted as the 10-minute value.

Uncertainty Factors:

Interspecies = 3 Intraspecies = 3

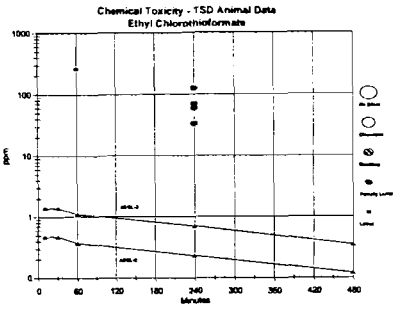
Highly reactive and clinical signs are likely caused by a direct chemical effect on the tissues; this type of portal-of-entry effect is not expected to vary greatly between species or among individuals.

Modifying Factor: 3

To protect against potential delayed systemic effects from the thio moitey.

THERE ARE NO OTHER EXTANT STANDARDS AND GUIDELINES FOR ETHYL CHLOROTHIOFORMATE!

Summary of AEGL Values for Ethyl Chlorothioformate					
Classification	10-minute	30-minute	1-hour	4-hour	8-hour
AEGL-1 (Nondisabling)	NR	NR	NR	NR	NR
AEGL-2 (Disabling)	0.47 ppm	0.47 ppm	0.37 ppm	0.23 ppm	0.12 ppm
AEGL-3 (Lethal)	1.4 ppm	1.4 ppm	1.1 ppm	0.70 ppm	0.35 ppm



Summary of AEGL Values For Diphosgene						
Classification	10-Minute	30-Minute	1-Hour	4-Hour	8-Hour	Endpoint (Referenc
AEGL-1 (Nondisabling)	NR	NR	NR	NR	NR	Insufficient data
AEGL-2 (Disabling)	NR	NR	NR	NR	NR	Insufficient data
AEGL-3 (Lethality)	NR	NR	NR	NR	NR	Insufficient data

NAC/AEGL Meeting 39: February 1-3, 2006

Chemical: * MINUTES from NAC-38 **CAS Reg. No.:** Appendix A

Action: Proposed_____ **Interim**_____ **Other**_____

Chemical Manager: **Staff Scientist:**

NAC Member	AEGL1	AEGL2	AEGL3	LOA	NAC Member	AEGL1	AEGL 2	AEGL3	LOA
Steven Barbee					Nancy Kim				
Lynn Beasley					Glenn Leach				
Robert Benson					John Morawetz				
Jonathan Borak					Richard Niemeier				
William Bress					Marinelle Payton				
George Cushmac					Susan Ripple				
Ernest Falke					George Rodgers				
Alfred Feldt					Marc Ruijten				
John Hinz					George Rusch, Chair				
Jim Holler					Richard Thomas				
Tom Hornshaw					George Woodall				
Warren Jederberg									
					TALLY				
					PASS/ FAIL				

PPM, (mg/m^3)	10 Min	30 Min	1 Hr	4 Hr	8 Hr
AEGL 1	, ( )	, ( )	, ( )	, ( )	, ( )
AEGL 2	, ( )	, ( )	, ( )	, ( )	, ( )
AEGL 3	, ( )	, ( )	, ( )	, ( )	, ( )
LOA					
* = ≥10% LEL					
** = ≥ 50% LEL					
*** = ≥100% LEL					

*Safety considerations against the hazard(s) of explosion(s) must be taken into account.
** and ***Extreme safety considerations against the hazard(s) of explosion(s) must be taken into account.

* passes unanimous

NR= Not Recommended due to_____

AEGL 1 **Motion by:** Rodgers **Second by:** Kim
AEGL 2 **Motion by:**_____ **Second by:**_____
AEGL 3 **Motion by:**_____ **Second by:**_____
LOA **Motion by:**_____ **Second by:**_____

Approved by Chair: _____ **DFO:** Paul Stern **Date:** 2/1/06

National Advisory Committee (NAC)
for Acute Exposure Guideline Levels (AEGLs) for Hazardous Substances

September 28-30, 2005

Final Meeting-38 Highlights

U.S. Department of Labor
Rooms 3437 A, B, & C
200 Constitution Ave., N.W.
Washington, DC 20210

INTRODUCTION

Chairman George Rusch welcomed the committee, and encouraged chemical managers to take notes on the staff scientists' presentations.

The draft NAC/AEGL-37 meeting highlights were not discussed because of the current issue on intentional dosing human data.

Richard Niemier discussed a practical use of AEGL values; AEGL-1 values were used for re-entry after a recent styrene release in Cincinnati, OH.

The highlights of the NAC/AEGL-38 meeting are summarized below along with the Meeting Agenda (Attachment 1) and the Attendee List (Attachment 2). The subject categories of the highlights do not necessarily follow the order listed in the NAC/AEGL-38 Agenda.

SUMMARY OF COT SUBCOMMITTEE MEETING

George Rusch led a discussion of the most recent COT subcommittee meeting (NAS-16; Aug. 31, Sept. 1-2, Woods Hole, MA). Major discussion points were as follows:

1. LOA (Level of Odor Awareness) paper needs to be published so that we can finalize the many TSDs where an LOA is calculated. Marc Ruijten stated that the paper is currently in the RIVM internal review process.

2. The COT subcommittee emphasized the need to track TSD revisions (red-line/cross out). This should also be used for revised TSDs discussed at NAC meetings.

3. The COT subcommittee showed an interest in the use of human data issue.

4. After incorporation of formal comments from the COT subcommittee, the PBPK white paper may be finalized and will become an addendum to the SOP.

5. The "Adjustment Factor" concept was discussed, and the consensus of the COT subcommittee appeared to be in conflict with discussions at previous COT subcommittee meetings. At NAS-15 (January, 2005), the suggestion was to apply an additional factor to obtain AEGL values consistent with available data. At NAS-16, subcommittee members seemed to think it was more appropriate to adjust the final AEGL values, and not to apply an additional "adjustment factor" to the derivation or to adjust the uncertainty factors. As this issue needs to be resolved, the NAC/AEGL staff will present options and request clear direction from COT subcommittee members at NAS-17.

6. Fifteen chemicals were presented at NAS-16, and ten of these were provisionally approved as "final."

7. The COT subcommittee was concerned about the use of animal developmental toxicity endpoints for derivation of AEGL-2 values, specifically, if reduced fetal body weight is the result of a single exposure or is a cumulative effect.

HUMAN STUDIES ISSUES

Iris Camacho presented information on the FY 2006 EPA Appropriations Act language and Proposed Rule, published on September 12, 2005, (Attachment 3) and on how this may impact the AEGL program. The appropriations act language prohibits use of 3rd party, intentional human dosing data for pesticides until a Final Rule on the topic is published. The Agency has interpreted this law to include both pesticides and industrial chemicals. Impacts on the AEGL program include: no discussion of chemicals/TSDs containing intentional human dosing data at NAC meetings (until publication of the final rule); a "hold" on the Federal Register package (FR09); and cancellation of the December meeting. The proposed rule has been published in the Federal Register and is open for public comment until December 12, 2005.

UNCERTAINTY FACTOR DATA BASE

Richard Williams, intern with the AEGL program, provided information and a demonstration of the Uncertainty Factor data base (Attachment 4). The data base is designed to store and categorize AEGL uncertainty factor application data and rationales. The data base should allow for the analysis of trends in UF application, evaluation of processes and rationales, and consistency in UF application. The data base was well received by the NAC members. Suggestions for improvement included addition of toxicity endpoints other that irritation,

identification of human or animal data used to adjust UFs, tracking dates when UFs were proposed, inclusion of chemical class information, addition of synonyms/CAS numbers, and inclusion of the value and source of the time scaling exponent 'n'.

RD_{50} METHODOLOGY

Peter Bos discussed the RD_{50} assay and relevance for setting AEGLs (Attachment 5). Discussion focused on whether or not the RD_{50} is an appropriate endpoint as a point-of-departure for AEGL value derivation, whether the RD_{50} may be an AEGL-1 or AEGL-2 endpoint, and how to handle scaling across time. The ASTM (2004) standard methodology was also discussed, as was the necessity of evaluating the raw data set used in calculating RD_{50} values. It was pointed out that use of the RD_{50} may amplify the uncertainty associated with scaling across time, and that in some cases, the RD_{50} methodology necessitates extrapolation over three orders of magnitude, also amplifying the uncertainty. A further challenge involves equating respiratory depression in animals with an equivalent effect in humans and distinguishing between stimulation of the olfactory versus trigeminal nerve. There was also a discussion about including a statement regarding use of the RD_{50} in the revised SOP; a suggestion was made that the RD_{50} could be used cautiously, acknowledging the limitations inherent in the method. A white paper regarding the relevance of the RD_{50} methodology for setting AEGL values will be drafted and included as an addendum to the SOP.

REVIEW AND RESOLUTION OF COT/AEGL COMMENTS ON INTERIM AEGL VALUES

Boron Trifluoride (CAS No. 7637-07-2)

Chemical Manager: George Rusch, Honeywell
Staff Scientist: Claudia Troxel, CMTox

George Rusch pointed out that Honeywell is the largest producer of boron trifluoride, and that he was responsible for all modern toxicology studies conducted with boron trifluoride. Dr. Rusch was chemical manager for this compound due to his familiarity with its' toxicology. He abstained from all votes, and presented the review of this chemical because the staff scientist, Claudia Troxel, was unable to attend the meeting. The AEGL values developed in the TSD and the presentation overheads were developed by Dr. Troxel. George Rusch then discussed the data set and COT/AEGL's comments (Attachment 6). The COT/AEGL suggested that the AEGL-1 and AEGL-2 derivations be revised, because these values were based on repeated-exposure studies. The COT/AEGL also suggested that the interspecies UF of 10, applied in the AEGL-3 derivation, be reduced. Dr. Rusch explained that the Honeywell Corporation conducted a 4-hour inhalation toxicity study in rats (Bowden et al., 2005) in response to the COT subcommittee comments. Proposed AEGL-1 values (2.5 mg/m^3 for all time points) were based on histological signs of

irritation noted in rats exposed to 74.4 mg/m^3 for 4 hours (Bowden et al., 2005). This was considered a NOAEL for notable irritation because there were no overt clinical signs of irritation. An interspecies UF of 10 (default) was applied, and intraspecies UF of 3 was applied because irritation is not expected to vary greatly within species. Values were held constant at all time points. Proposed AEGL-3 values (48 mg/m^3 for 10-min, 48 mg/m^3 for 30-min, 38 mg/m^3 for 1-hr, 24 mg/m^3 for 4-hr, and 12 mg/m^3 for 8-hr) were based on a 4-hour $BMCL_{05}$ in rats (Rusch et al., 1986). An interspecies UF of 10 was proposed because species differences exist in sensitivity to boron trifluoride, with the guinea pig being most sensitive. An intraspecies UF of 3 was applied due to the steep concentration-response curve and irritation endpoint. Time scaling was accomplished using default values of n=1 or n=3. The 30-min value was adopted as the 10-min value. Proposed AEGL-2 values (16 mg/m^3 for 10-min, 16 mg/m^3 for 30-min, 13 mg/m^3 for 1-hr, 8 mg/m^3 for 4-hr, and 4 mg/m^3 for 8-hr) were derived by dividing the proposed AEGL-3 values by 3; this approach was justified by the steep concentration-response curve. After discussion, a motion was made by Bob Benson and seconded by Nancy Kim to adopt AEGL-3 values of 140 mg/m^3 for 10-min, 140 mg/m^3 for 30-min, 110 mg/m^3 for 1-hr, 72 mg/m^3 for 4-hr, and 36 mg/m^3 for 8-hr. The values used the point-of-departure, intraspecies UF and time scaling as proposed. An interspecies UF of 3 was applied, because boron trifluoride is a highly-reactive, corrosive irritant. The motion carried (YES: 15; NO: 0; ABSTAIN: 1) (APPENDIX A). A motion was then made by Steve Barbee and seconded by Richard Thomas to derive AEGL-2 values (47 mg/m^3 for 10-min, 47 mg/m^3 for 30-min, 37 mg/m^3 for 1-hr, 24 mg/m^3 for 4-hr, and 12 mg/m^3 for 8-hr) by dividing the AEGL-3 values by 3. The motion carried (YES: 15; NO: 0; ABSTAIN: 1) (APPENDIX A). A motion was then made by Marc Ruijten and seconded by Richard Niemier to adopt an AEGL-1 value of 2.5 mg/m^3 at all time points based on the NOEL of 24.6 mg/m^3 in rats exposed for 4 hours. Uncertainty factors of 3 each were applied for inter- and intraspecies extrapolation. The motion carried (YES: 15; NO: 0; ABSTAIN: 1) (APPENDIX A).

Summary of AEGL Values for Boron Trifluoride						
Classification	**10-minute**	**30-minute**	**1-hour**	**4-hour**	**8-hour**	**Endpoint (Reference)**
AEGL–1	2.5 mg/m^3	2.5 mg/m^3	2.5 mg/m^3	2.5 mg/m^3	2.5 mg/m^3	NOEL in rats (Bowden et al., 2005)
AEGL–2	47 mg/m^3	47 mg/m^3	37 mg/m^3	24 mg/m^3	12 mg/m^3	1/3 the AEGL-3 values
AEGL-3	140 mg/m^3	140 mg/m^3	110 mg/m^3	72 mg/m^3	36 mg/m^3	4- hr. $BMCL_{05}$ in rats (Rusch et al., 1986)

JP-8 (Jet Fuel) (CAS No. 8008-20-6)

Chemical Manager: John Hinz, U.S. Air Force
Staff Scientist: Sylvia Talmage, ORNL

Sylvia Talmage and John Hinz discussed the data set and COT/AEGL's comments (Attachment 7). The COT/AEGL's main concerns were as follows: 1) Delete JP-4 discussions from the TSD; 2)

Improve the justification of the interspecies UF of 1; 3) Explain the Alaris 10-fold reduction factor; 4) Clarify the discussion of immune response to JP-8 with regard to vapors and aerosols; and 5) Discuss PBPK models and the lack of time scaling for AEGL-2 values. Much of the NAC discussion focused on the use of the RD_{50}. Sylvia explained that the AEGL values were based on a weight-of-evidence approach and that the values derived from the RD_{50} were supported by a lack of histopathology in other studies. The AEGL values will not change; however, the TSD will be revised so that the presentation of the RD_{50} data in the JP-8 TSD is not in conflict with the RD_{50}/SOP presentation (Attachment 5).

REVIEW of PRIORITY CHEMICALS

Ketene (CAS No. 463-51-4)

Staff Scientist: Peter Bos, RIVM
Chemical Manager: Jim Holler, ATSDR

Peter Bos reviewed the available data (Attachment 8). Proposed AEGL-1 values (0.24 ppm for 10-min, 0.24 ppm for 30-min, 0.19 ppm for 1-hour, 0.12 ppm for 4-hours, and 0.088 ppm for 8-hours) were based on no effects in mice exposed to 1 ppm for 7 hours (Treon et al., 1949). An interspecies UF of 3 was proposed because the mouse is the most sensitive species, and an intraspecies UF was also proposed because ketene acts directly at the port of entry. Time scaling was accomplished using the default values of n =1 or n = 3. The 30-min AEGL-1 was adopted as the 10-min AEGL-1. Proposed AEGL-2 values (0.83 ppm for 10-min, 0.83 ppm for 30-min, 0.66 ppm for 1-hour, 0.42 ppm for 4-hours, and 0.23 ppm for 8-hours) were based on one-third of the AEGL-3 values; this approach is supported by the steep concentration-response curve. Proposed AEGL-3 values (2.5 ppm for 10-min, 2.5 ppm for 30-min, 2.0 ppm for 1-hour, 1.2 ppm for 4-hours, and 0.68 ppm for 8-hours) were based on no mortality in mice exposed to 12 ppm for 4 hours (Treon et al., 1949). Uncertainty factor application and time scaling were proposed similar to AEGL-1. After discussion, a motion was made by Bob Benson and seconded by Marc Ruijten to accept AEGL values as proposed except that the point-of-departure for AEGL-2 will be the 12 ppm, 7 hour exposure of mice divided by three to estimate a NOAEL for effects defined by AEGL-2 (12 ppm ÷ 3 = 4 ppm). Time scaling and UF application are the same as for AEGL-1 and AEGL-3. (It is noted that the resulting AEGL-2 values are the same as proposed, but the rationale is different. The motion carried The motion carried (AEGL-1: YES: 12; NO: 1; ABSTAIN: 3) (AEGL-2: YES: 10; NO: 1; ABSTAIN: 6) (AEGL-3: YES: 10; NO: 1; ABSTAIN: 6) (APPENDIX B).

Summary of AEGL Values for Ketene						
Classification	**10-minute**	**30-minute**	**1-hour**	**4-hour**	**8-hour**	**Endpoint (Reference)**
AEGL–1	0.24 ppm	0.24 ppm	0.19 ppm	0.12 ppm	0.088 ppm	NOEL in mice (Treon et al., 1949)
AEGL–2	0.83 ppm	0.83 ppm	0.66 ppm	0.42 ppm	0.23 ppm	Estimated NOAEL for AEGL-2 effects in mice (Treon et al., 1949)
AEGL–3	2.5 ppm	2.5 ppm	2.0 ppm	1.2 ppm	0.68 ppm	4-hr NOEL for death in mice (Treon et al., 1949)

SELECTED CHLOROFORMATES

Methyl Chloroformate (CAS Reg. No. 79-22-1)
Ethyl Chloroformate (CAS Reg. No. 541-41-3)
Propyl Chloroformate (CAS Reg. No. 109-61-5)
Isopropyl Chloroformate (CAS Reg. No. 108-23-6)
Allyl Chloroformate (CAS Reg. No. 2937-50-0)
n-Butyl Chloroformate (CAS Reg. No. 593-34-7)
Isobutyl Chloroformate (CAS Reg. No. 543-27-1)
sec-Butyl Chloroformate (CAS Reg. No. 17462-58-7)
Ethyl Chlorothioformate (CAS Reg. No. 2941-64-2)
Diphosgene (CAS Reg. No. 503-38-8)

Staff Scientist: Cheryl Bast, ORNL
Chemical Manager: Ernest Falke, U.S. EPA

Cheryl Bast reviewed the sparse data set available in the published literature (Attachment 9). Dr. Roland Rossbacher, representing BASF, Germany, was in attendance and informed the NAC that there are new, unpublished chloroformate data developed by BASF Germany on many of the title chemicals. These data had not previously been available to the NAC. Dr. Rossbacher offered to submit these data to the NAC. These data will be included in a revised TSD which will be reviewed at NAC-39.

ARSENIC TRIOXIDE (CAS No. 1327-53-3)

Staff Scientist: Johan Schefferlie, RIVM
Chemical Manager: Richard Thomas, INTERCET, Ltd.

Johan Schefferlie reviewed the data set for arsenic trioxide (Attachment 10). AEGL-1 values were not proposed because of insufficient data. Proposed AEGL-2 values (2.5 mg/m^3 for 10-min, 2.5 mg/m^3 for 30-min, 2.0 mg/m^3 for 1-hr, 1.3 mg/m^3 for 4-hr, and 1.0 mg/m^3 for 8-hr) were based on 8-hour occupational exposures up to 1.0 mg/m^3. No UF was proposed because no acute AEGL-2 effects were expected at these concentration. The default value of n = 3 was used for time scaling. The proposed AEGL-3 values (11 mg/m^3 for 10-min, 11 mg/m^3 for 30-min, 9.1 mg/m^3 for 1-hr, 5.7 mg/m^3 for 4-hr, and 3.7 mg/m^3 for 8-hr) were based on a NOEL for lethality in rats exposed to 50 mg/m^3 for 6 hours (Holson et al., 1999). Uncertainty factors of 3 each were proposed for inter- and intraspecies extrapolation (total 10) because a larger total UF would yield AEGL-3 values within the range of some occupational exposure concentrations. Default time scaling (n = 1 or n = 3) was applied. After discussion, a motion was made by Marc Ruijten and seconded by Bob Benson to adopt AEGL-3 values as proposed. The motion carried (YES: 18; NO: 0; ABSTAIN: 0) (APPENDIX C). A motion was then made by Marc Ruijten and seconded by Richard Niemier to adopt AEGL-2 values of (3.7 mg/m^3 for 10-min, 3.7 mg/m^3 for 30-min, 3.0 mg/m^3 for 1-hr, 1.9 mg/m^3 for 4-hr, and 1.2 mg/m^3 for 8-hr) derived by dividing the AEGL-3 values by 3. This approach is supported because of the steep concentration-response curve (0/10 rats dead at 50 mg/m^3 and 10/10 rats dead at 100 mg/m^3). The motion carried (YES: 16; NO: 0; ABSTAIN: 0) (APPENDIX C). A motion was then made by Bob Benson and seconded by Marc Ruijten to not recommend AEGL-1 values because of insufficient data. The motion carried (YES: 16; NO: 0; ABSTAIN: 0) (APPENDIX C). A statement regarding use/non-use of the cancer values will be added to the TSD.

Summary of AEGL Values for Arsenic Trioxide

Classification	10-minute	30-minute	1-hour	4-hour	8-hour	Endpoint (Reference)
AEGL–1	NR	NR	NR	NR	NR	Not recommended due to insufficient data
AEGL–2	3.7 mg/m^3	3.7 mg/m^3	3.0 mg/m^3	1.9 mg/m^3	1.2 mg/m^3	1/3 the AEGL-3 values
AEGL-3	11 mg/m^3	11 mg/m^3	9.1 mg/m^3	5.7 mg/m^3	3.7 mg/m^3	6- hr. NOEL for lethality in rats (Holson et al., 1999)

CYCLOHEXYL ISOCYANATE (CAS No. 3173-53-3)

Staff Scientist: Carol Wood, ORNL
Chemical Manager: Marc Ruijten, RIVM

Marc Ruijten discussed the sparse data base for cyclohexyl isocyanate and proposed that no AEGL values be derived because of insufficient data. (Attachment 17). After discussion, a motion was made by Bob Benson and seconded by George Rodgers to adopt AEGL-3 values (0.14 ppm for 10-min, 0.14 ppm for 30-min, 0.11 ppm for 1-hour, 0.072 ppm for 4-hours, and 0.047 ppm for 8-hours) based on a calculated $BMCL_{05}$ (1.88 ppm) from a 6-hour rat study (Eastman Kodak, 1990, 1992). Inter- and intraspecies UFs of 3 each (total = 10) were applied because cyclohexyl isocyanate is highly irritating. A modifying factor of 3 was applied to account for the sparse data base. Default time scaling values of n =1 or n = 3 were applied; the 30-min value was adopted as the 10-min value. The motion carried (YES: 15; NO: 0; ABSTAIN: 2) (APPENDIX D). A motion was then made by Richard Niemier and seconded by George Woodall to derive AEGL-2 values by dividing the AEGL-3 values by 3. This motion did not carry (YES: 3; NO: 11; ABSTAIN: 4) (APPENDIX D). A motion was then made by Richard Niemier and Seconded by George Woodall to not recommend AEGL-1 or AEGL-2 values due to insufficient data. This motion carried (AEGL-1: YES: 15; NO: 0; ABSTAIN: 2) (AEGL-2: YES: 13; NO: 2; ABSTAIN: 1) (APPENDIX D).

The methyl isocyanate lethality should be included in the TSD for comparison. Mehyl isocyanate is more toxic than cyclohexyl isocyanate, so the derived cyclohexyl isocyanate values are protective. This TSD will be revisited if a SIDS is published and contains additional relevant data.

Summary of AEGL Values for Cyclohexyl Isocyanate

Classification	10-minute	30-minute	1-hour	4-hour	8-hour	Endpoint (Reference)
AEGL–1	NR	NR	NR	NR	NR	Not recommended: Insufficient data
AEGL–2	NR	NR	NR	NR	NR	Not recommended: Insufficient data
AEGL–3	0.14 ppm	0.14 ppm	0.11 ppm	0.072 ppm	0.047 ppm	6-hr $BMCL_{05}$ in rats (Eastman Kodak, 1990; 1992)

ADMINISTRATIVE MATTERS

The site and time of future meetings is as follows:

NAC/AEGL-39: February 1-3, 2006, Washington DC

All items in the agenda were discussed as thoroughly as the time permitted. The meeting highlights were prepared by Cheryl Bast and Sylvia Talmage, Oak Ridge National Laboratory, with input from the respective staff scientists, chemical managers, and other contributors.

LIST OF ATTACHMENTS

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

Attachment 1. NAC/AEGL-38 Meeting Agenda
Attachment 2. NAC/AEGL-38 Attendee List
Attachment 3. FY 2006 EPA Appropriations Act
Attachment 4. Uncertainty Factor Database
Attachment 5. RD_{50}: Relevance for Setting AEGLs
Attachment 6. Response to COT comments for Boron Trifluoride
Attachment 7. Response to COT comments for JP-8
Attachment 8. Data analysis for ketene
Attachment 9. Data analysis for selected chloroformates
Attachment 10. Data analysis for arsenic trioxide
Attachment 11. Data analysis for cyclohexyl isocyanate

LIST OF APPENDICES

Appendix A. Ballot for Boron Trifluoride
Appendix B. Ballot for Ketene
Appendix C. Ballot for Arsenic Trioxide
Appendix D. Ballot for Cyclohexyl Isocyanate
Appendix E. Committee chairman certification of minutes

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Appendix C

Chemical: CYCLOHEXYL ISOCYANATE **CAS Reg. No.:**

Action: Proposed_____ **Interim**_____ **Other** Update based on Calculation

Chemical Manager: RUIJTEN **Staff Scientist:** WOOD

NAC Member	AEGL1	AEGL2	AEGL3	LOA	NAC Member	AEGL1	AEGL 2	AEGL3	LOA
Steven Barbee			Y		Nancy Kim			Y	
Lynn Beasley			A		Glenn Leach			Y	
Robert Benson			Y		John Morawetz			Y	
Jonathan Borak			Y		Richard Niemeier			Y	
William Bress			Y		Marinelle Payton			Y	
George Cushmac			Y		Susan Ripple			Y	
Ernest Falke			Y		George Rodgers			Y	
Alfred Feldt			Y		Marc Ruijten			Y	
John Hinz			Y		George Rusch, Chair			Y	
Jim Holler			Y		Richard Thomas			Y	
Tom Hornshaw			Y		George Woodall			Y	
Warren Jederberg									
					TALLY				
					PASS/ FAIL				

PPM, (mg/m^3)	10 Min	30 Min	1 Hr	4 Hr	8 Hr
AEGL 1	,( )	,( )	,( )	,( )	,( )
AEGL 2	,( )	,( )	,( )	,( )	,( )
AEGL 3	,(.13)	,(.13)	,(.10)	,(.064)	,(.042)
LOA					
* = ≥10% LEL					
** = ≥ 50% LEL					
*** = ≥100% LEL					

*Safety considerations against the hazard(s) of explosion(s) must be taken into account.

** and ***Extreme safety considerations against the hazard(s) of explosion(s) must be taken into account.

NR= Not Recommended due to_____

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

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

AEGL 3 Motion by: Niemeier **Second by:** Woodall

LOA Motion by: _____ **Second by:** _____

Approved by Chair: [signature] **DFO:** Paul S. Tobin **Date:** 2/1/06

NAC/AEGL Meeting 39: February 1-3, 2006

Chemical: SILANE **CAS Reg. No.:** 7803-62-5

Action: Proposed ✓ **Interim** _____ **Other** _____

Chemical Manager: BENSON **Staff Scientist:** GLASS

NAC Member	AEGL1	AEGL2	AEGL3	LOA	NAC Member	AEGL1	AEGL 2	AEGL3	LOA
Steven Barbee	Y	Y	P		Nancy Kim	N	Y	Y	
Lynn Beasley	Y	Y	Y		Glenn Leach	P	Y	Y	
Robert Benson	Y	Y	Y		John Morawetz	N	Y	Y	
Jonathan Borak	Y	Y	Y		Richard Niemeier	Y	Y	P	
William Bress	Y	Y	Y		Marinelle Payton	Y	Y	Y	
George Cushmac	Y	Y	Y		Susan Ripple	Y	Y	Y	
Ernest Falke	P	Y	Y		George Rodgers	N	Y	Y	
Alfred Feldt	Y	Y	Y		Marc Ruijten	Y	P	P	
John Hinz	P	Y	Y		George Rusch, Chair	P	Y	Y	
Jim Holler	Y	Y	Y		Richard Thomas	Y	Y	Y	
Tom Hornshaw	P	Y	Y		George Woodall	P	Y	Y	
Warren Jederberg									
					TALLY				
					PASS/ FAIL	13/17	21/21	19/19	

PPM, (mg/m³)	10 Min	30 Min	1 Hr	4 Hr	8 Hr
AEGL 1	,(100)	,(100)	,(100)	,(NR)	,(NR)
AEGL 2	,(170)	,(170)	,(130)	,(80)	,(42)
AEGL 3	,(300)	,(300)	,(270)	,(170)	,(80)
LOA					
* = ≥10% LEL					
** = ≥ 50% LEL					
*** = ≥100% LEL					

*Safety considerations against the hazard(s) of explosion(s) must be taken into account.

** and ***Extreme safety considerations against the hazard(s) of explosion(s) must be taken into account.

NR = Not recommended due to overlap w. AEGL-2

NR= Not Recommended due to _____

AEGL 1 Motion by: Rodgers Ruijten **Second by:** Barbee

AEGL 2 Motion by: Benson **Second by:** Thomas

AEGL 3 Motion by: Benson **Second by:** Falke

LOA Motion by: _____ **Second by:** _____

Approved by Chair: _____ **DFO:** Paul S. Tobin **Date:** 2/1/06

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Appendix E

Chemical: TRIMETHOXYSILANE **CAS Reg. No.:** 2487-90-3

Action: Proposed ✓ **Interim**_____ **Other**_____

Chemical Manager: BENSON **Staff Scientist:** GLASS

NAC Member	AEGL1	AEGL2	AEGL3	LOA
Steven Barbee	Y	Y	Y	
Lynn Beasley	Y	Y	Y	
Robert Benson	Y	Y	Y	
Jonathan Borak	P	Y	Y	
William Bress	Y	Y	Y	
George Cushmac	Y	Y	Y	
Ernest Falke	Y	Y	Y	
Alfred Feldt	Y	Y	Y	
John Hinz	Y	Y	Y	
Jim Holler	Y	Y	Y	
Tom Hornshaw	Y	Y	Y	
Warren Jederberg				

NAC Member	AEGL1	AEGL 2	AEGL3	LOA
Nancy Kim	Y	Y	Y	
Glenn Leach	Y	Y	Y	
John Morawetz	Y	Y	Y	
Richard Niemeier	P	Y	N	
Marinelle Payton	A	Y	A	
Susan Ripple	Y	Y	P	
George Rodgers	Y	Y	Y	
Marc Ruijten	N	N	N	
George Rusch, Chair	Y	Y	Y	
Richard Thomas	Y	Y	Y	
George Woodall	Y	Y	Y	
TALLY				
PASS/ FAIL	18/18	21/22	18/20	

PPM, (mg/m^3)	10 Min	30 Min	1 Hr	4 Hr	8 Hr
AEGL 1	,(NR)	,(NR)	,(NR)	,(NR)	,(NR)
AEGL 2	,(3.9)	,(1.4)	0,83 ,(~~0.83~~)	0,33 ,(~~0.33~~)	0,20 ,(~~0.20~~)
AEGL 3	,(8,8)	,(4.1)	,(2.5)	,(0,98)	,(0,61)
LOA					
* = ≥10% LEL					
** = ≥ 50% LEL					
*** = ≥100% LEL					

*Safety considerations against the hazard(s) of explosion(s) must be taken into account.
** and ***Extreme safety considerations against the hazard(s) of explosion(s) must be taken into account.

NR= Not Recommended due to_____

AEGL 1 Motion by: Benson **Second by:** Thomas
AEGL 2 Motion by: Benson **Second by:** Falke
AEGL 3 Motion by: Falke **Second by:** Thomas
LOA Motion by: _____ **Second by:** _____

Approved by Chair: [signature] **DFO:** Paul Miller **Date:** 2/1/06

NAC/AEGL Meeting 39: February 1-3, 2006

Chemical: TETRAMETHOXYSILANE **CAS Reg. No.:** 681-84-5

Action: Proposed ✓ **Interim**_____ **Other**_____

Chemical Manager: BENSON **Staff Scientist:** CLASS

NAC Member	AEGL1	AEGL2	AEGL3	LOA
Steven Barbee	Y	P	Y	
Lynn Beasley	Y	Y	Y	
Robert Benson	Y	Y	Y	
Jonathan Borak	A	P	Y	
William Bress	Y	Y	Y	
George Cushmac	Y	Y	Y	
Ernest Falke	Y	Y	Y	
Alfred Feldt	A	Y	Y	
John Hinz	A	P	Y	
Jim Holler	Y	Y	Y	
Tom Hornshaw	Y	Y	Y	
Warren Jederberg	A			

NAC Member	AEGL1	AEGL 2	AEGL3	LOA
Nancy Kim	Y	Y	Y	
Glenn Leach	Y	Y	Y	
John Morawetz	P	Y	Y	
Richard Niemeier	A	P	Y	
Marinelle Payton	A	Y	P	
Susan Ripple	A	P	Y	
George Rodgers	Y	Y	Y	
Marc Ruijten	Y	N	N	
George Rusch, Chair	Y	Y	Y	
Richard Thomas	Y	N	Y	
George Woodall	A	P	Y	
TALLY				
PASS/ FAIL	14/14	14/16	20/21	

PPM, (mg/m^3)	10 Min	30 Min	1 Hr	4 Hr	8 Hr
AEGL 1	,(NR)	,(NR)	,(NR)	,(NR)	,(NR)
AEGL 2	,(1.1)	,(1.1)	,(0.91)	,(0.57)	,(0.38)
AEGL 3	,(1.7)	,(1.7)	,(1.4)	,(0.87)	,(0.43)
LOA					
* = ≥10% LEL					
** = ≥ 50% LEL					
*** = ≥100% LEL					

*Safety considerations against the hazard(s) of explosion(s) must be taken into account.
** and ***Extreme safety considerations against the hazard(s) of explosion(s) must be taken into account.

NR= Not Recommended due to_____

AEGL 1 **Motion by:** Benson **Second by:** Bress
AEGL 2 **Motion by:** Benson **Second by:** Falke
AEGL 3 **Motion by:** Benson **Second by:** Kim
LOA **Motion by:**_____ **Second by:**_____

Approved by Chair: [signature] **DFO:** [signature] **Date:** 2/1/06

FALKE ←→ 2/2/06 AEGL-1

NAC/AEGL Meeting 39: February 1-3, 2006

Chemical: SULFURYL CHLORIDE **CAS Reg. No.:** 7791-25-5

Action: Proposed ✓ **Interim** _____ **Other** _____

Chemical Manager: BARBEE **Staff Scientist:** YOUNG

NAC Member	AEGL1	AEGL2	AEGL3	LOA
Steven Barbee		Y	Y	
Lynn Beasley		A	A	
Robert Benson		Y	Y	
Jonathan Borak		A	A	
William Bress		Y	Y	
George Cushmac		Y	Y	
Ernest Falke		Y	Y	
Alfred Feldt		Y	Y	
John Hinz		N	A	
Jim Holler		Y	Y	
Tom Hornshaw		Y	Y	
Warren Jederberg				

NAC Member	AEGL1	AEGL 2	AEGL3	LOA
Nancy Kim		N	N	
Glenn Leach		A	A	
John Morawetz		A	A	
Richard Niemeier		Y	Y	
Marinelle Payton		N	Y	
Susan Ripple		Y	Y	
George Rodgers		N	P	
Marc Ruijten		Y	Y	
George Rusch, Chair		Y	Y	
Richard Thomas		Y	Y	
George Woodall		Y	Y	
TALLY				
PASS/ FAIL		14/15	15/15	

PPM, (mg/m³)	10 Min	30 Min	1 Hr	4 Hr	8 Hr
AEGL 1	NR, ( )	NR, ( )	NR, ( )	NR, ( )	NR, ( )
AEGL 2	, (4.7)	, (4.7)	, (3.7)	, (2.3)	, (1.2)
AEGL 3	, (14)	, (14)	, (11)	, (7.0)	, (3.5)
LOA					
* = ≥10% LEL					
** = ≥ 50% LEL					
*** = ≥100% LEL					

*Safety considerations against the hazard(s) of explosion(s) must be taken into account.
** and ***Extreme safety considerations against the hazard(s) of explosion(s) must be taken into account.

† VINDICUS

NR= Not Recommended due to _____

AEGL 1 Motion by: Benson **Second by:** Benson Falke
AEGL 2 Motion by: Woodall **Second by:** Benson
AEGL 3 Motion by: RUIJTEN **Second by:** NIEMEIER
LOA Motion by: _____ **Second by:** _____

Approved by Chair: _____ **DFO:** Paul S. Tobin **Date:** 2/1/06

NAC/AEGL Meeting 39: February 1-3, 2006

Chemical: ~~METHYL~~ METHYL CHLOROFORMATE **CAS Reg. No.:** ~~2937-50-0~~ 79-22-1

Action: Proposed ✓ **Interim**_____ **Other**_____

Chemical Manager: FALKE **Staff Scientist:** BAST

NAC Member	AEGL1	AEGL2	AEGL3	LOA
Steven Barbee	*	Y	Y	
Lynn Beasley		Y	Y	
Robert Benson		Y	Y	
Jonathan Borak		A	A	
William Bress		Y	A	
George Cushmac		Y	Y	
Ernest Falke		Y	Y	
Alfred Feldt		Y	Y	
John Hinz		A	A	
Jim Holler		Y	Y	
Tom Hornshaw		Y	Y	
Warren Jederberg				

NAC Member	AEGL1	AEGL 2	AEGL3	LOA
Nancy Kim		Y	Y	
Glenn Leach		Y	Y	
John Morawetz		Y	Y	
Richard Niemeier		Y	Y	
Marinelle Payton		Y	Y	
Susan Ripple		Y	Y	
George Rodgers		Y	Y	
Marc Ruijten		Y	Y	
George Rusch, Chair		Y	Y	
Richard Thomas		Y	Y	
George Woodall		Y	Y	
TALLY				
PASS/ FAIL		20/20	19/19	

PPM, (mg/m^3)	10 Min	30 Min	1 Hr	4 Hr	8 Hr
AEGL 1	,(NR)	,(NR)	,(NR)	,(NR)	,(NR)
AEGL 2	,(4.0)	,(2.8)	,(2.2)	,(1.4)	,(0.70)
AEGL 3	,(12)	,(8.5)	,(6.7)	,(4.2)	,(2.1)
LOA					
* = ≥10% LEL					
** = ≥ 50% LEL					
*** = ≥100% LEL					

*Safety considerations against the hazard(s) of explosion(s) must be taken into account.

** and ***Extreme safety considerations against the hazard(s) of explosion(s) must be taken into account.

* UNANIMOUS NR = NOT RECOMMENDED DUE TO LACK OF DATA

NR= Not Recommended due to_____

AEGL 1 Motion by: Woodall **Second by:** Benson
AEGL 2 Motion by: Thomas **Second by:** Benson
AEGL 3 Motion by: Benson **Second by:** Woodall
LOA Motion by:_____ **Second by:**_____

Approved by Chair: [signature] **DFO:** Paul S. Tobin **Date:** 2/2/06

NAC/AEGL Meeting 39: February 1-3, 2006

Chemical: ETHYL CHLOROFORMATE **CAS Reg. No.:** 541-41-3

Action: Proposed ✓ **Interim**_____ **Other**_____

Chemical Manager: FALKE **Staff Scientist:** GLASS

NAC Member	AEGL1	AEGL2	AEGL3	LOA	NAC Member	AEGL1	AEGL 2	AEGL3	LOA
Steven Barbee	Y	Y	Y		Nancy Kim	Y	Y	Y	
Lynn Beasley	Y	Y	Y		Glenn Leach	Y	Y	Y	
Robert Benson	Y	Y	Y		John Morawetz	Y	Y	Y	
Jonathan Borak	A	A	A		Richard Niemeier	Y	Y	Y	
William Bress	Y	Y	Y		Marinelle Payton	Y	Y	Y	
George Cushmac	Y	Y	Y		Susan Ripple	Y	Y	Y	
Ernest Falke	Y	Y	Y		George Rodgers	Y	Y	Y	
Alfred Feldt	Y	Y	Y		Marc Ruijten	Y	Y	Y	
John Hinz	A	A	A		George Rusch, Chair	Y	Y	Y	
Jim Holler	Y	Y	Y		Richard Thomas	Y	Y	Y	
Tom Hornshaw	Y	Y	Y		George Woodall	Y	Y	Y	
Warren Jederberg									
					TALLY				
					PASS/ FAIL	20/20	20/20	20/20	

PPM, (mg/m^3)	10 Min	30 Min	1 Hr	4 Hr	8 Hr
AEGL 1	,(NR)	,(NR)	,(NR)	,(NR)	,(NR)
AEGL 2	,(2.9)	,(2.0)	,(1.6)	,(0.40)	,(0.20)
AEGL 3	,(8.8)	,(6.1)	,(4.8)	,(1.2)	,(0.60)
LOA					
* = ≥10% LEL					
** = ≥ 50% LEL					
*** = ≥100% LEL					

*Safety considerations against the hazard(s) of explosion(s) must be taken into account.

** and ***Extreme safety considerations against the hazard(s) of explosion(s) must be taken into account.

NR = Not recommended due to lack of data.

NR= Not Recommended due to_____

AEGL 1 Motion by: Rodgers **Second by:** Niemeier

AEGL 2 Motion by: Rodgers **Second by:** Niemeier

AEGL 3 Motion by: Rodgers **Second by:** Niemeier

LOA Motion by:_____ **Second by:**_____

Approved by Chair: [signature] **DFO:** Paul S. Tobin **Date:** 2/2/06

NAC/AEGL Meeting 39: February 1-3, 2006

Appendix J

Chemical: PROPYL CHLOROFORMATE **CAS Reg. No.:** 109-61-5

Action: Proposed ✓ **Interim** _____ **Other** _____

Chemical Manager: FALKE **Staff Scientist:** BAST

NAC Member	AEGL1	AEGL2	AEGL3	LOA	NAC Member	AEGL1	AEGL 2	AEGL3	LOA
Steven Barbee	Y	Y	Y		Nancy Kim	Y	N	N	
Lynn Beasley	Y	Y	Y		Glenn Leach	Y	Y	Y	
Robert Benson	Y	Y	Y		John Morawetz	Y	N	N	
Jonathan Borak	A	A	A		Richard Niemeier	Y	Y	Y	
William Bress	Y	Y	Y		Marinelle Payton	Y	Y	Y	
George Cushmac	Y	Y	Y		Susan Ripple	Y	Y	Y	
Ernest Falke	Y	Y	Y		George Rodgers	Y	N	N	
Alfred Feldt	Y	Y	Y		Marc Ruijten	Y	Y	Y	
John Hinz	A	A	A		George Rusch, Chair	Y	Y	Y	
Jim Holler	Y	Y	Y		Richard Thomas	Y	Y	Y	
Tom Hornshaw	Y	N	N		George Woodall	Y	Y	Y	
Warren Jederberg									
					TALLY				
					PASS/ FAIL	20/20	16/20	16/20	

PPM, (mg/m^3)	10 Min	30 Min	1 Hr	4 Hr	8 Hr
AEGL 1	,(NR)	,(NR)	,(NR)	,(NR)	,(NR)
AEGL 2	,(6.7)	,(4.7)	,(3.7)	,(0.90)	,(0.47)
AEGL 3	,(20)	,(14)	,(11)	,(2.7)	,(1.4)
LOA					
* = ≥10% LEL					
** = ≥ 50% LEL					
*** = ≥100% LEL					

*Safety considerations against the hazard(s) of explosion(s) must be taken into account.
** and ***Extreme safety considerations against the hazard(s) of explosion(s) must be taken into account.

NR= Not Recommended due to LACK OF DATA

AEGL 1 Motion by: Woodall **Second by:** Ruijten
AEGL 2 Motion by: _____ **Second by:** _____
AEGL 3 Motion by: _____ **Second by:** _____
LOA Motion by: _____ **Second by:** _____

Approved by Chair: _____ **DFO:** Paul S. Tobin **Date:** 2/2/06

NAC/AEGL Meeting 39: February 1-3, 2006

Appendix K

Chemical: ISOPROPYL CHLOROFORMATE **CAS Reg. No.:** 108-23-6

Action: Proposed ✓ **Interim** _____ **Other** _____

Chemical Manager: FALKE **Staff Scientist:** BAST

NAC Member	AEGL1	AEGL2	AEGL3	LOA
Steven Barbee	Y	Y	Y	
Lynn Beasley	Y	Y	Y	
Robert Benson	Y	Y	Y	
Jonathan Borak	A	A	A	
William Bress	Y	Y	Y	
George Cushmac	Y	Y	Y	
Ernest Falke	Y	Y	Y	
Alfred Feldt	Y	Y	Y	
John Hinz	Y	Y	Y	
Jim Holler	Y	Y	Y	
Tom Hornshaw	Y	Y	Y	
Warren Jederberg				

NAC Member	AEGL1	AEGL 2	AEGL3	LOA
Nancy Kim	Y	Y	Y	
Glenn Leach	Y	Y	Y	
John Morawetz	Y	N	N	
Richard Niemeier	Y	Y	Y	
Marinelle Payton	Y	Y	Y	
Susan Ripple	Y	Y	Y	
George Rodgers	Y	Y	Y	
Marc Ruijten	Y	Y	Y	
George Rusch, Chair	Y	Y	Y	
Richard Thomas	Y	Y	Y	
George Woodall	Y	Y	Y	
TALLY				
PASS/ FAIL	20/20	19/20	19/20	

PPM, (mg/m³)	10 Min	30 Min	1 Hr	4 Hr	8 Hr
AEGL 1	,(NR)	,(NR)	,(NR)	,(NR)	,(NR)
AEGL 2	,(6.0)	,(4.3)	,(3.3)	,(0.83)	,(0.43)
AEGL 3	,(18)	,(13)	,(10)	,(2.5)	,(1.3)
LOA					
* = ≥10% LEL					
** = ≥ 50% LEL					
*** = ≥100% LEL					

*Safety considerations against the hazard(s) of explosion(s) must be taken into account.
** and ***Extreme safety considerations against the hazard(s) of explosion(s) must be taken into account.

NR= Not Recommended due to LACK OF DATA

AEGL 1 Motion by: Thomas **Second by:** Ruijten
AEGL 2 Motion by: ↓ **Second by:** ↓
AEGL 3 Motion by: ↓ **Second by:** ↓
LOA Motion by: _____ **Second by:** _____

Approved by Chair: [signature] **DEO:** Paul S. Tobin **Date:** 2/3/06

NAC/AEGL Meeting 39: February 1-3, 2006

Appendix L

Chemical: ~~[redacted]~~ ALLYL CHLORO FORMATE **CAS Reg. No.:** ~~[redacted]~~ 2937-50-0

Action: Proposed ✓ **Interim** _____ **Other** _____

Chemical Manager: FALKE **Staff Scientist:** BAST

NAC Member	AEGL1	AEGL2	AEGL3	LOA	NAC Member	AEGL1	AEGL 2	AEGL3	LOA
Steven Barbee	Y	Y	Y		Nancy Kim	Y	N	N	
Lynn Beasley	Y	Y	Y		Glenn Leach	Y	Y	Y	
Robert Benson	Y	Y	Y		John Morawetz	Y	N	N	
Jonathan Borak	A	A	A		Richard Niemeier	Y	Y	Y	
William Bress	Y	Y	Y		Marinelle Payton	Y	Y	Y	
George Cushmac	Y	Y	Y		Susan Ripple	Y	Y	Y	
Ernest Falke	Y	Y	Y		George Rodgers	Y	N	N	
Alfred Feldt	Y	Y	Y		Marc Ruijten	Y	Y	Y	
John Hinz	Y	Y	Y		George Rusch, Chair	Y	P	P	
Jim Holler	Y	Y	Y		Richard Thomas	Y	Y	Y	
Tom Hornshaw	Y	Y	Y		George Woodall	Y	Y	Y	
Warren Jederberg									
					TALLY				
					PASS/ FAIL	19/19	17/19	17/19	

PPM, (mg/m³)	10 Min	30 Min	1 Hr	4 Hr	8 Hr
AEGL 1	,(NR)	,(NR)	,(NR)	;(NR)	,(NR)
AEGL 2	,(1.3)	,(0.87)	,(0.70)	,(0.18)	,(0.09)
AEGL 3	,(3.8)	,(2.6)	,(2.1)	,(0.53)	,(0.26)
LOA					
* = ≥10% LEL					
** = ≥ 50% LEL					
*** = ≥100% LEL					

*Safety considerations against the hazard(s) of explosion(s) must be taken into account.
** and ***Extreme safety considerations against the hazard(s) of explosion(s) must be taken into account.

NR= Not Recommended due to Lack of data

AEGL 1 Motion by: Ruijten **Second by:** Barbee
AEGL 2 Motion by: ↓ **Second by:** ↓
AEGL 3 Motion by: ↓ **Second by:** ↓
LOA Motion by: _____ **Second by:** _____

Approved by Chair: _____ **DFO:** Paul S. Tobin **Date:** 2/2/06

NAC/AEGL Meeting 39: February 1-3, 2006

Appendix M

Chemical: N-BUTYL CHLOROFORMATE **CAS Reg. No.:** 593-34-7

Action: Proposed ✓ **Interim**_____ **Other**_____

Chemical Manager: FALKE **Staff Scientist:** BAST

NAC Member	AEGL1	AEGL2	AEGL3	LOA
Steven Barbee	Y	Y	Y	
Lynn Beasley	Y	Y	Y	
Robert Benson	Y	Y	Y	
Jonathan Borak	A	A	A	
William Bress	Y	Y	Y	
George Cushmac	Y	Y	Y	
Ernest Falke	Y	Y	Y	
Alfred Feldt	Y	Y	Y	
John Hinz	Y	Y	Y	
Jim Holler	Y	Y	Y	
Tom Hornshaw	Y	Y	Y	
Warren Jederberg				

NAC Member	AEGL1	AEGL 2	AEGL3	LOA
Nancy Kim	Y	Y	Y	
Glenn Leach	Y	Y	Y	
John Morawetz	Y	Y	Y	
Richard Niemeier	Y	Y	Y	
Marinelle Payton	Y	Y	Y	
Susan Ripple	Y	Y	Y	
George Rodgers	Y	Y	Y	
Marc Ruijten	Y	Y	X	
George Rusch, Chair	Y	Y	Y	
Richard Thomas	Y	Y	Y	
George Woodall	Y	Y	Y	
TALLY				
PASS/ FAIL	20/20	20/20	20/20	

PPM, (mg/m³)	10 Min	30 Min	1 Hr	4 Hr	8 Hr
AEGL 1	,(NR)	,(NR)	,(NR)	,(NR)	,(NR)
AEGL 2	,(4.0)	,(2.8)	,(2.2)	,(0.57)	,(0.28)
AEGL 3	,(12)	,(8.4)	,(6.7)	,(1.7)	,(0.83)
LOA					
* = ≥10% LEL					
** = ≥ 50% LEL					
*** = ≥100% LEL					

*Safety considerations against the hazard(s) of explosion(s) must be taken into account.
** and ***Extreme safety considerations against the hazard(s) of explosion(s) must be taken into account.

NR= Not Recommended due to Lack of data.

AEGL 1 Motion by: Ruijten **Second by:** Benson
AEGL 2 Motion by: ↓ **Second by:** ↓
AEGL 3 Motion by: ↓ **Second by:** ↓
LOA Motion by: _____ **Second by:** _____

Approved by Chair: [signature] **DFO:** Paul S. Tobin **Date:** 2/2/06

NAC/AEGL Meeting 39: February 1-3, 2006

Appendix N

Chemical: ISOBUTYL CHLOROFORMATE **CAS Reg. No.:** 543-27-1

Action: Proposed ✓ **Interim** _____ **Other** _____

Chemical Manager: FALKE **Staff Scientist:** BAST

NAC Member	AEGL1	AEGL2	AEGL3	LOA	NAC Member	AEGL1	AEGL 2	AEGL3	LOA
Steven Barbee	Y	Y	Y		Nancy Kim	Y	Y	Y	
Lynn Beasley	Y	Y	Y		Glenn Leach	Y	Y	Y	
Robert Benson	Y	Y	Y		John Morawetz	N	N	N	
Jonathan Borak			A		Richard Niemeier	Y	Y	Y	
William Bress			Y		Marinelle Payton	Y	Y	Y	
George Cushmac			Y		Susan Ripple	Y	Y	Y	
Ernest Falke			Y		George Rodgers	Y	Y	Y	
Alfred Feldt			Y		Marc Ruijten	Y	Y	Y	
John Hinz	N	N	N		George Rusch, Chair	Y	Y	Y	
Jim Holler	Y	Y	Y		Richard Thomas	Y	Y	Y	
Tom Hornshaw	Y	Y	Y		George Woodall	Y	Y	Y	
Warren Jederberg									
					TALLY				
					PASS/ FAIL				

PPM, (mg/m^3)	10 Min	30 Min	1 Hr	4 Hr	8 Hr
AEGL 1	, (NR)	, (NR)	, (NR)	, (NR)	, (NR)
AEGL 2	, (4.0)	, (2.8)	, (2.2)	, (0.57)	, (0.28)
AEGL 3	, (12)	, (8.4)	, (6.7)	, (1.7)	, (0.83)
LOA					
* = ≥10% LEL					
** = ≥ 50% LEL					
*** = ≥100% LEL					

*Safety considerations against the hazard(s) of explosion(s) must be taken into account.
** and ***Extreme safety considerations against the hazard(s) of explosion(s) must be taken into account.

NR= Not Recommended due to Lack of data.

AEGL 1 Motion by: Woodall **Second by:** Thomas
AEGL 2 Motion by: ↓ **Second by:** ↓
AEGL 3 Motion by: ↓ **Second by:** ↓
LOA Motion by: _____ **Second by:** _____

Approved by Chair: _____ **DFO:** _____ **Date:** 2/2/06

NAC/AEGL Meeting 39: February 1-3, 2006

Chemical: sec-Butyl chloroformate **CAS Reg. No.:** 17462-58-7

Action: Proposed ✓ **Interim**_____ **Other**_____

Appendix O

Chemical Manager: FALKE **Staff Scientist:** BAST

NAC Member	AEGL1	AEGL2	AEGL3	LOA	NAC Member	AEGL1	AEGL 2	AEGL3	LOA
Steven Barbee					Nancy Kim				
Lynn Beasley					Glenn Leach				
Robert Benson					John Morawetz				
Jonathan Borak					Richard Niemeier				
William Bress					Marinelle Payton				
George Cushmac					Susan Ripple				
Ernest Falke					George Rodgers				
Alfred Feldt					Marc Ruijten				
John Hinz					George Rusch, Chair				
Jim Holler					Richard Thomas				
Tom Hornshaw	Y	Y	Y		George Woodall				
Warren Jederberg									
					TALLY				
					PASS/ FAIL				

PPM, (mg/m^3)	10 Min	30 Min	1 Hr	4 Hr	8 Hr
AEGL 1	,(NR)	,(NR)	,(NR)	,(NR)	,(NR)
AEGL 2	,(4.0)	,(2.8)	,(2.2)	,(0.57)	,(0.28)
AEGL 3	,(12)	,(8.4)	,(6.7)	,(1.7)	,(0.83)
LOA					
* = ≥10% LEL					
** = ≥ 50% LEL					
*** = ≥100% LEL					

*Safety considerations against the hazard(s) of explosion(s) must be taken into account.
** and ***Extreme safety considerations against the hazard(s) of explosion(s) must be taken into account.

NR= Not Recommended due to Lack of data.

AEGL 1 Motion by: Woodall **Second by:** Romo
AEGL 2 Motion by: ↓ **Second by:** ↓
AEGL 3 Motion by: ↓ **Second by:** ↓
LOA Motion by: _____ **Second by:** _____

Approved by Chair: [signature] **DFO:** [signature] **Date:** 2/2/06

NAC/AEGL Meeting 39: February 1-3, 2006

Chemical: ETHYLCHLOROTHIOFORMATE **CAS Reg. No.:** 2941-64-2

Action: Proposed ✓ **Interim**_____ **Other**_____

Chemical Manager: **Staff Scientist:**

NAC Member	AEGL1	AEGL2	AEGL3	LOA
Steven Barbee	Y	N	N	
Lynn Beasley	Y	Y	Y	
Robert Benson	Y	Y	Y	
Jonathan Borak	A	A	A	
William Bress	Y	Y	Y	
George Cushmac	Y	Y	Y	
Ernest Falke	Y	Y	Y	
Alfred Feldt	Y	Y	Y	
John Hinz	Y	Y	Y	
Jim Holler	A	A	A	
Tom Hornshaw	A	A	A	
Warren Jederberg				

NAC Member	AEGL1	AEGL 2	AEGL3	LOA
Nancy Kim	Y	Y	Y	
Glenn Leach	Y	Y	Y	
John Morawetz	Y	Y	Y	
Richard Niemeier	Y	Y	Y	
Marinelle Payton	Y	Y	Y	
Susan Ripple	Y	Y	Y	
George Rodgers	A	A	A	
Marc Ruijten	Y	Y	Y	
George Rusch, Chair	Y	Y	Y	
Richard Thomas	Y	Y	Y	
George Woodall	Y	Y	Y	
TALLY				
PASS/ FAIL				

PPM, (mg/m^3)	10 Min	30 Min	1 Hr	4 Hr	8 Hr
AEGL 1	, (NR)	, ( )	, ( )	, ( )	, ( )
AEGL 2	, (0.33)	, (0.33)	, (0.26)	, (0.17)	, (0.083)
AEGL 3	, (1.0)	, (1.0)	, (0.79)	, (0.50)	, (0.25)
LOA					
* = ≥10% LEL					
** = ≥ 50% LEL					
*** = ≥100% LEL					

*Safety considerations against the hazard(s) of explosion(s) must be taken into account.
** and ***Extreme safety considerations against the hazard(s) of explosion(s) must be taken into account.

NR= Not Recommended due to Lack of data

AEGL 1 Motion by: Woodall **Second by:** Benson
AEGL 2 Motion by:_____ **Second by:**_____
AEGL 3 Motion by:_____ **Second by:**_____
LOA Motion by:_____ **Second by:**_____

Approved by Chair: _____ **DFO:** Carl S. Plaisance **Date:** 2/2/06

NAC/AEGL Meeting 39: February 1-3, 2006

Appendix Q

Chemical: DIPHOSGENE **CAS Reg. No.:** 503-38-8

Action: Proposed ✓ **Interim**_____ **Other**_____

Chemical Manager: FALKE **Staff Scientist:** BAST

NAC Member	AEGL1	AEGL2	AEGL3	LOA	NAC Member	AEGL1	AEGL 2	AEGL3	LOA
Steven Barbee	*	*	*		Nancy Kim				
Lynn Beasley					Glenn Leach				
Robert Benson					John Morawetz				
Jonathan Borak					Richard Niemeier				
William Bress					Marinelle Payton				
George Cushmac					Susan Ripple				
Ernest Falke					George Rodgers				
Alfred Feldt					Marc Ruijten				
John Hinz					George Rusch, Chair				
Jim Holler					Richard Thomas				
Tom Hornshaw					George Woodall				
Warren Jederberg									
					TALLY				
					PASS/ FAIL				

PPM, (mg/m^3)	10 Min	30 Min	1 Hr	4 Hr	8 Hr
AEGL 1	*,(NR)	,(NR)	,(NR)	,(NR)	,(NR)
AEGL 2	,(NR)	,(NR)	,(NR)	,(NR)	,(NR)
AEGL 3	,(NR)	,(NR)	,(NR)	,(NR)	,(NR)
LOA					
* = ≥10% LEL					
** = ≥ 50% LEL					
*** = ≥100% LEL					

*Safety considerations against the hazard(s) of explosion(s) must be taken into account.
** and ***Extreme safety considerations against the hazard(s) of explosion(s) must be taken into account.

NR= Not Recommended due to * Lack of data. (HOLP 1/06)

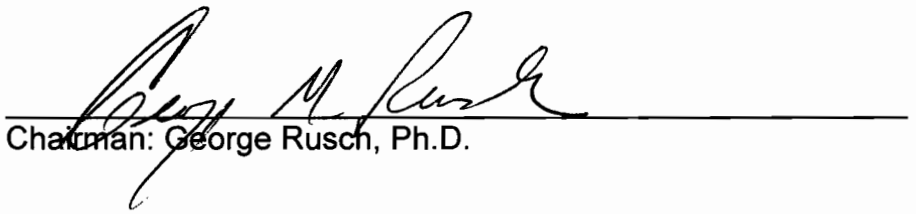
AEGL 1 Motion by: Benson **Second by:** Hinz
AEGL 2 Motion by: ↓ **Second by:** ↓
AEGL 3 Motion by: ↓ **Second by:** ↓
LOA Motion by:_____ **Second by:**_____

Approved by Chair: [signature] **DFO:** Paul S. Tobin **Date:** 2/2/06

AEGL Committee Chairman Certification of Minutes

National Advisory Committee for February 1-3, 2006 Meeting

I, Dr. George Rusch, certify that these Minutes for the February 1-3, 2006 meeting of the National Advisory Committee for the Development of Acute Exposure Guideline Levels represent a true and accurate representation of the conduct of the meeting.



Chairman: George Rusch, Ph.D.