National Advisory Committee (NAC)
for Acute Exposure Guideline Levels (AEGLs) for Hazardous Substances
Final Meeting 17 Highlights
Environmental & Occupational Health Sciences Institute
Rutgers University
Piscataway, New Jersey
April 26-28, 2000

INTRODUCTION

Dr. Robert Snyder, meeting host, welcomed the NAC/AEGL on behalf of the Environmental and Occupational Health Sciences Institute (EOSHI).

Dr. George Rusch (NAC Chairperson) opened the meeting with comments regarding the application of AEGLs in fire codes (National Institute for Fire Prevention) and that upon approval by the National Research Council the AEGLs will be considered as lead values for emergency programs. It was also stated that the New Jersey on-scene coordinator for training and emergency response expressed an interest in using AEGLs.

The highlights of the meeting are noted below, and the meeting agenda (Attachment 1) and an attendee list (Attachment 2) are attached. Highlights of the NAC Meeting 16 (December 6-8, 1999) were reviewed (with a brief discussion and minor correction) and were approved (Appendix A).

GENERAL INTEREST ITEMS

Paul Tobin provided brief comments about the second list of priority chemicals (186 chemicals), noting that production volumes and emergency release data (Reportable Quantity release data) were focal points.

Ernest Falke provided brief status remarks of the most recent revision SOPs.

RESPONSE TO COMMENTS ON THE *FEDERAL REGISTER* NOTICE

Discussions were held regarding comments (Attachment 3) on the *Federal Register* notice for eight chemicals: HFC-134a, 1,1,1-trichloroethane, Agent HD (sulfur mustard), 1,2-dichloroethylenes (*cis* and *trans*), Otto Fuel, HCFC-141b, hydrogen fluoride, and hydrogen sulfide. The dispositions of these comments are summarized in the following sections.

<u>HFC-134a</u>
In response to comments received from three sources on the *Federal Register* notice, there was discussion regarding the overall data set and its support of the proposed AEGL values. One submitter (Michigan Air Quality Division) indicated concurrence with the AEGLs. For AEGL-1, these discussions revolved around the appropriateness of an uncertainty factor of 1 from a study of 8 young health adults. A motion (moved by Loren Koller; seconded by John Hinz) passed [YES: 16; NO: 3; ABSTAIN: 0 (Appendix B)] to accept the original AEGL-1 value of 8,000 ppm for all time points as an Interim AEGL-1. Similarly, there was discussion focusing on the available data and their support of the previously proposed AEGL-2

and AEGL-3 values. Specifically, the discussion focused on the use of cardiac sensitization as a predictor for adverse effects. A motion (moved by John Morawetz and seconded by Mark McClanahan) passed unanimously [YES: 19; NO: 0; ABSTAIN: 0] (Appendix B) to accept the AEGL-2 and AEGL-3 values as Interim and respond accordingly to the *Federal Register* comments.

INTERIM AEGL VALUES FOR HFC-134a					
Classification	**10-Minute**	**30-Minute**	**1-Hour**	**4-Hour**	**8-Hour**
AEGL-1	8,000 ppm	8,000 ppm	8,000 ppm	8,000 ppm	8,000 ppm
AEGL-2	13,000 ppm	13,000 ppm	13,000 ppm	13,000 ppm	13,000 ppm
AEGL-3	27,000 ppm	27,000 ppm	27,000 ppm	27,000 ppm	27,000 ppm

1,1,1-Trichloroethane

Two submissions were received. The Michigan Air Quality Division expressed concurrence with the AEGLs. The International Chemical Workers Union Council contended that the proposed AEGL values were too high and that this contention is supported by monitoring data from reconstruction of a fatility. Following discussions, a motion to accept the originally proposed values as Interim AEGLs was made by Robert Snyder (seconded by Steve Barbee). The motion passed [YES: 13; NO: 6; ABSTAIN: 0] (Appendix C). For the AEGL-3 values, it was also decided to remove the modifying factor (3-fold adjustment to achieve a reasonable concentration at which humans might experience life-threatening effects) and change the interspecies uncertainty factor from 3 to 1. This results in a total uncertainty factor of 3 (rather than 3.3) based on differences in sensitivity among humans. The reduction of the interspecies uncertainty factor to 1 is based on the 2-fold difference in uptake between the rat and humans. This change in rationale altered the 10- and 30-minute, and 1-, 4-, and 8-hour values from 4800, 4800, 3800, 2400, and 1900 ppm, respectively, to 4200, 4200, 4200, 2700, and 2100 ppm.

INTERIM AEGL VALUES FOR 1,1,1-TRICHLOROETHANE					
Classification	**10-Minute**	**30-Minute**	**1-Hour**	**4-Hour**	**8-Hour**
AEGL-1	230 ppm	230 ppm	230 ppm	230 ppm	230 ppm
AEGL-2	930 ppm	670 ppm	600 ppm	380 ppm	310 ppm
AEGL-3[a]	4,200 ppm	4,200 ppm	4,200 ppm	2,700 ppm	2,100 ppm

[a] The 10- and 30-minute AEGL-3 values were flatlined to the 1-hour value so as not to exceed the threshold of 5,000 ppm for cardiac sensitization observed in dogs.

Agent HD (Sulfur Mustard)

The only comment submitted in response to the *Federal Register* notice was in support of the proposed values for sulfur mustard. A motion (Mark McClanahan, seconded by Richard Niemeier) to change the proposed AEGLs for Agent HD to Interim status passed unanimously (Appendix D).

INTERIM AEGL VALUES FOR SULFUR MUSTARD (AGENT HD)					
Classification	**10-Minute**	**30-Minute**	**1-Hour**	**4-Hour**	**8-Hour**
AEGL-1	0.060 ppm	0.020 ppm	0.010 ppm	0.0026 ppm	0.0012 ppm
AEGL-2	0.090 ppm	0.030 ppm	0.015 ppm	0.0038 ppm	0.0020 ppm
AEGL-3	0.92 ppm	0.63 ppm	0.32 ppm	0.080 ppm	0.041 ppm

1,2-Dichloroethylene

Comments from the Michigan Air Quality Division, PPG Industries, and Pinnacle West Capital Corp. were received in response to the *Federal Register* notice. The cis-values presented in the document were derived by a modification of the trans- values. Comments were received suggesting that cis-data be used for deriving cis-values. However, after deliberations, the NAC decided that data for the cis- isomer were sparse and it was appropriate to retain the modified trans-isomer values as cis-isomer values. Comments were also received concerning the selection of key studies. A human study from 1936 was used for derivation of all AEGL-1 values and AEGL-2 and AEGL-3 values for 10-min, 30-min, and 1-hr. The comments suggested the use of more recent controlled animal studies in place of the less robust human data. After much deliberation the NAC decided that the human data, could not be ignored and voted to elevate the values to interim status. In response to other comments, the introduction was changed to correctly summarize current uses and production methods; the previous introduction contained historical information. Summary information from genotoxicity studies were added. These data suggest that the trans-isomer is negative in both in vivo and in vitro tests and that the cis-isomer is negative in in vivo tests and equivocal in in vitro tests. A motion was made by Mark McClanahan (seconded by David Belluck) that the proposed AEGLs for this chemical be elevated to interim status and that the NAC/AEGL is satisfied with the explanations provided by Cheryl Bast and Ernie Falke in response to the *Federal Register* comments and that most of the issue had been addressed during the previous deliberations. The motion passed unanimously (Appendix E).

INTERIM AEGL VALUES FOR *trans-cis* 1,2-DICHLOROETHYLENE					
Classification	**10-Minute**	**30-Minute**	**1-Hour**	**4-Hour**	**8-Hour**
AEGL-1	280 ppm	280 ppm	280 ppm	280 ppm	280 ppm
AEGL-2	1,000 ppm	1,000 ppm	1,000 ppm	690 ppm	450 ppm
AEGL-3	1,700 ppm	1,700 ppm	1,700 ppm	1,200 ppm	620 ppm

INTERIM AEGL VALUES FOR *cis* 1,2-DICHLOROETHYLENE

Classification	10-Minute	30-Minute	1-Hour	4-Hour	8-Hour
AEGL-1	140 ppm	140 ppm	140 ppm	140 ppm	140 ppm
AEGL-2	500 ppm	500 ppm	500 ppm	340 ppm	230 ppm
AEGL-3	850 ppm	850 ppm	850 ppm	620 ppm	310 ppm

Otto Fuel

A comment from the International Chemical Workers Union Council to the *Federal Register* notice indicated that the 10-minute AEGL-2 value may be too high. This was based upon the contention that data in humans demonstrated severe headaches following a 3.5-hour exposure to 1.5 ppm and that this effect was too severe to be discounted. A motion was made by Robert Benson and seconded by Richard Niemeier to flatline the 30-minute and 10-minute AEGL-2 at 2 ppm and the 10- and 30-minute AEGL-3 at 16 ppm. The motion passed unanimously (Appendix F). The 10-minute AEGL-3 was flatlined from the 30-minute values because the key study utilized a 6-hour exposure duration. All of the AEGLs for Otto fuel were elevated to interim status.

INTERIM AEGL VALUES FOR OTTO FUEL					
Classification	**10-Minute**	**30-Minute**	**1-Hour**	**4-Hour**	**8-Hour**
AEGL-1	0.33 ppm	0.33 ppm	0.17 ppm	0.05 ppm	0.03 ppm
AEGL-2	2.0 ppm	2.0 ppm	1.0 ppm	0.25 ppm	0.13 ppm
AEGL-3	16 ppm	16 ppm	13 ppm	8.0 ppm	5.3 ppm

HCFC-141b

In response to a comment submitted by the International Chemical Workers Union Council to the *Federal Register* notice, initial discussion focused on the data set used to develop AEGL1- values. Specifically, an issue was raised regarding the reliability of an uncertainty factor of 1 from 8 young healthy adults. In response to this issue, it was explained that the subjects experienced no evidence of nasal irritation, and no specific unpleasant odor. Additionally, blood concentrations reach equilibrium very quickly and, therefore, development of effects at notably later time points is not likely. A motion was submitted by Mark McClanahan (seconded by Bob Benson) that the originally proposed AEGL-1 values be elevated to interim status. The motion passed [YES: 17; NO: 2; ABSTAIN: 0] (Appendix G). Mark McClanahan moved that the AEGL-2 and AEGL-3 values be elevated to interim status. The motion was seconded by Bob Benson and approved by the NAC/AEGL: [YES: 17; NO: 2; ABSTAIN: 0] (Appendix G).

INTERIM AEGL VALUES FOR HFC-141b					
Classification	**10-Minute**	**30-Minute**	**1-Hour**	**4-Hour**	**8-Hour**
AEGL-1	1,000 ppm	1,000 ppm	1,000 ppm	1,000 ppm	1,000 ppm
AEGL-2	1,700 ppm	1,700 ppm	1,700 ppm	1,700 ppm	1,700 ppm
AEGL-3	3,000 ppm	3,000 ppm	3,000 ppm	3,000 ppm	3,000 ppm

Hydrogen fluoride

Comments from the American Petroleum Institute, and BP Amoco on the *Federal Register* notice indicated concern regarding consistency between the endpoints used for AEGL development and the AEGL definitions. There was also concern regarding the use of data from the Rosenholtz et al. (1963) study in dogs as opposed to using the PERF (Dalbey, 1996) study for development of 30- and 60-minute AEGL-2 values. The Michigan Air Quality Division indicated that interspecies and intraspecies uncertainty factors for AEGL-2 and AEGL-3 values should be increased 3-fold. Discussion ensued regarding the AEGLs proposed by those submitting comments (BP Amoco, EM/API, State of Michigan, API). The comments/concerns from BPA and Michigan were addressed and comments from API and the recently available study by Lund et al. (1999) will be discussed at the next meeting.

Hydrogen sulfide

Comments were received from six organizations (American Petroleum Institute, Michigan Air Quality Division, American Forest and Paper Association, IBP, Inc., and the Chemical Manufacturers Association). Cheryl Bast summarized the comments and provided background information regarding the development of the proposed AEGLs. Comments on the hydrogen sulfide AEGLs were basically partitioned between AEGL-1, -2 and -3. For AEGL-1, many of the comments suggested the use of a study in asthmatics or withdrawal of the AEGLs. Following discussions, it was decided to retain the AEGL-1 values but to strengthen the rationale and justifications. A motion to retain the AEGL-1 values and elevate them to interim status was made by Dave Belluck (seconded by Ernest Falke) was voted upon and passed unanimously (Appendix H). For AEGL-2 and -3, the NAC/AEGL addressed several comments, including the use of endpoints with higher exposure concentrations, the use of a default *n* value for time scaling rather than the empirically derived *n* of 4.5, and the incorporation of a CIIT developmental neurotoxicity study recommended by the American Petroleum Institute. Following detailed discussions of each responder's comments, a motion was made by Bob Benson (seconded by Ernest Falke) to retain the AEGL-2 and -3 values and elevate them to interim status. AEGL-2 was also passed unanimously (Appendix H) and AEGL-3 was also passed [YES: 16; NO: 1; ABSTAIN: 0] (Appendix H).

INTERIM AEGL VALUES FOR HYDROGEN SULFIDE					
Classification	**10-Minute**	**30-Minute**	**1-Hour**	**4-Hour**	**8-Hour**
AEGL-1	0.03 ppm	0.03 ppm	0.03 ppm	0.03 ppm	0.03 ppm
AEGL-2	42 ppm	32 ppm	28 ppm	20 ppm	17 ppm
AEGL-3	76 ppm	60 ppm	50 ppm	37 ppm	31 ppm

Hydrogen cyanide

George Rodgers summarized the *Federal Register* comments. It was suggested that the AEGL-1 values be flatlined based upon a cross-sectional study of cyanide salt workers by Lesser et al. (1990). Following discussions on the comments pertaining to AEGL-1, a motion was made by George Rodgers (seconded by Tom Hornshaw) that the comments were adequately addressed and to elevate to interim status the AEGL-1 value of 1 ppm for all time points (10 minutes, 30 minutes, 1-, 4-, and 8 hours). Later, the motion was withdrawn and the discussion was tabled pending receipt of studies. For AEGL-2 and -3, discussion focused on the appropriate endpoints and exposure concentrations. It was the consensus of the NAC/AEGL that the comments were adequately addressed but that the TSD be revised to show that both a probit analysis and benchmark dose analysis provided similar values. A motion to elevate the AEGL-2 and AEGL-3 values to interim status was made by Ernest Falke (seconded by Bob Benson). The motions passed [YES: 21; NO: 1; ABSTAIN: 0] (Appendix I).

INTERIM AEGL VALUES FOR HYDROGEN CYANIDE					
Classification	**10-Minute**	**30-Minute**	**1-Hour**	**4-Hour**	**8-Hour**
AEGL-1	–	–	–	–	–
AEGL-2	17 ppm	10 ppm	7.1 ppm	3.5 ppm	2.5 ppm
AEGL-3	27 ppm	21 ppm	15 ppm	8.6 ppm	6.6 ppm

DEVELOPMENT OF 10-MINUTE AEGLS

In response to the need for 10-minute AEGLs, TSDs were revised to incorporate the development of 10-minute AEGLs. These values were developed by assessing data available for time periods less than 30 minutes, by temporal extrapolation from exposure with durations of 4 hours or less, or by flatlining from the previously established 30-minute AEGL. In the course of the discussions, it was agreed that extrapolation to 10-minute values would be limited to exposure data of less than 4 hours duration. If the AEGLs were developed using a key exposure of 4 hours or greater and no shorter duration data were available, the 10-minute AEGL would be flatlined from the 30-minute value. The 10-minute AEGLs and their rationales were presented by ORNL staff scientists or the chemical manager. Discussions were focused primarily on the newly derived 10-minute values and their relational consistency with the previously derived AEGLS.

Crotonaldehyde

Sylvia Milanez provided an overview of the available data pertinent to development of 10-minute AEGL values (Attachment 4). For AEGL-1, the same value was flatlined for 30 minutes to 8 hours was used for 10 minutes. AEGL-2 and AEGL-3 values were both based on studies that encompassed ≤10-minute exposures. Therefore, the 10-minute values were extrapolated using the *n* values previously used to derive 30 minute–8 hour values (Attachment 4). The NAC/AEGL approved development of the values as motioned by George Rogers and seconded by John Hinz (Appendix J). The resulting AEGLS for crotonaldehyde are shown below.

PROPOSED AEGL VALUES FOR CROTONALDEHYDE					
Classification	**10-Minute**	**30-Minute**	**1-Hour**	**4-Hour**	**8-Hour**
AEGL-1	0.19 ppm	0.19 ppm	0.19 ppm	0.19 ppm	0.19 ppm
AEGL-2	27 ppm	8.9 ppm	4.4 ppm	1.1 ppm	0.56 ppm
AEGL-3	44 ppm	27 ppm	14 ppm	2.6 ppm	1.5 ppm

Allylamine

Pertinent data and development of AEGLS were reviewed by Sylvia Milanez (Attachment 5). Specifically, the AEGL-1 values were developed based upon the Shell Oil Co. (1992) study of occupational exposures that showed an 8-hour exposure to 0.20 ppm was nonirritating. The AEGL-1 was flatlined at 0.20 ppm.

A slight modification of previously accepted AEGL-2 was made using a newly calculated value of $n = 1.71$ based upon the endpoint of cardiotoxicity. These revised values and the newly developed 10-minute values were accepted and are shown below. For AEGL-1, the motion was made by Mark McClanahan and seconded by Loren Koller. For AEGL-2 and -3, the motion was made by Loren Koller and seconded by John Hinz (Appendix K). The 10-minute values for AEGL-2 were flatlined from the 30-minute numbers.

PROPOSED AEGL VALUES FOR ALLYLAMINE					
Classification	**10-Minute**	**30-Minute**	**1-Hour**	**4-Hour**	**8-Hour**
AEGL-1	0.20 ppm	0.20 ppm	0.20 ppm	0.20 ppm	0.20 ppm
AEGL-2	4.2 ppm	4.2 ppm	2.8 ppm	1.2 ppm	0.83 ppm
AEGL-3	140 ppm	40 ppm	18 ppm	3.5 ppm	2.3 ppm

Ethylenediamine

The data and rationale pertinent to development of 10-minute AEGLS were summarized by Sylvia Milanez (Attachment 6). These values and a revision of the AEGL-2 and AEGL-3 values were discussed. AEGL-1 values were not recommended due to insufficient data. The AEGL-2 values were based upon an 8-hour animal exposure to approximately 484ppm. Due of the 8-hour duration, the 10-minute values were flatlined from the 30-minute value. Because the AEGL values were based on 8-hour exposures, the

10-minute AEGL-3 values were flatlined from the 30-minute value. Both the AEGL-2 and AEGL-3 values are supported by a multiple-exposure rat study. The accepted values are shown below (Appendix L). For AEGL-1, the motion was made by Bob Benson and seconded by Bob Snyder. For AEGL-2 and -3, the motion was made by Zarena Post and seconded by George Rodgers.

PROPOSED AEGL VALUES FOR ETHYLENEDIAMINE					
Classification	**10-Minute**	**30-Minute**	**1-Hour**	**4-Hour**	**8-Hour**
AEGL-1	NR	NR	NR	NR	NR
AEGL-2	12 ppm	12 ppm	9.7 ppm	6.1 ppm	4.8 ppm
AEGL-3	25 ppm	25 ppm	20 ppm	13 ppm	10 ppm

Cyclohexylamine

The rationale for development of 10-minute AEGLS was presented by Sylvia Milanez (Attachment 7). The AEGL-1 values were flatlined at 1.8 ppm. The AEGL-2 values were calculated based upon a well-defined study. The 10-minute values for AEGL-2 and AEGL-3 were flatlined from the 30-minute values. The values as presented below were accepted by the NAC/AEGL. A motion was made by George Rodgers and seconded by John Hinz to accept the proposed 10-minute AEGLS. The voting records for AEGL-1 through -3 are: AEGL-1: [YES: 18; NO: 3; ABSTAIN: 0]; AEGL-2: [YES: 19; NO: 2; ABSTAIN: 0]; for AEGL-3: [YES: 19; NO: 2; ABSTAIN: 0], respectively (Appendix M).

PROPOSED AEGL VALUES FOR CYCLOHEXYLAMINE					
Classification	**10-Minute**	**30-Minute**	**1-Hour**	**4-Hour**	**8-Hour**
AEGL-1	1.8 ppm	1.8 ppm	1.8 ppm	1.8 ppm	1.8 ppm
AEGL-2	11 ppm	11 ppm	8.6 ppm	5.4 ppm	2.7 ppm
AEGL-3	38 ppm	38 ppm	30 ppm	19 ppm	9.4 ppm

2,4- and 2,6-Toluene diisocyanate

The AEGL values for these chemicals were revised based upon an *n* of 1 (longer time periods) or 3 (shorter time periods) for time scaling rather than the previously applied *n* of 2. For AEGL-3 the 10-minute AEGL was set equivalent to the 30-minute value due to the use of a 4-hour exposure duration for the AEGL determinant. The 10-minute AEGLS were approved unanimously by the NAC/AEGL (motion made by Steve Barbee and seconded by Robert Niemeier) (Appendix N). The accepted values are shown below.

PROPOSED AEGL VALUES FOR 2,4, AND 2,6-TOLUENE DIISOCYANATE					
Classification	**10-Minute**	**30-Minute**	**1-Hour**	**4-Hour**	**8-Hour**

AEGL-1	0.02 ppm	0.02 ppm	0.02 ppm	0.02 ppm	0.02 ppm
AEGL-2	0.24 ppm	0.17 ppm	0.083 ppm	0.021 ppm	0.021 ppm
AEGL-3	0.65 ppm	0.65 ppm	0.51 ppm	0.32 ppm	0.16 ppm

Iron pentacarbonyl

Robert Young presented a review of the iron pentacarbonyl AEGLS explaining the need for minor adjustments in the previously accepted values (Attachment 8). The development of the 10-minute values was also presented. Because data consistent with a 10-minute exposure period were unavailable, 10-minute values were derived using an *n* of 1 which was based upon analysis of the available data. AEGL-1 values were not developed due to the steep exposure-response relationship and the apparently narrow margin between exposures causing no observable effects and those resulting in lethal responses. The 8-hour AEGLS, as previously decided, were not developed due to the rapid decomposition of the chemical under ambient conditions. A motion was made by George Rodgers and seconded by David Belluck to adopt the 10-minute AEGLS. The voting records (Appendix O) for AEGL-1 and AEGL-3 were unanimously approved; AEGL-2: [YES: 19; NO: 3, ABSTAIN: 0], respectively (Appendix O). The resulting accepted values are shown below.

PROPOSED AEGL VALUES FOR IRON PENTACARBONYL					
Classification	**10-Minute**	**30-Minute**	**1-Hour**	**4-Hour**	**8-Hour**
AEGL-1	NA	NA	NA	NA	NA
AEGL-2	1.2 ppm	0.40 ppm	0.19 ppm	0.050 ppm	NA
AEGL-3	3.5 ppm	1.2 ppm	0.58 ppm	0.15 ppm	NA

Nickel carbonyl

Robert Young presented a review of the nickel carbonyl AEGLS explaining the need for minor adjustments due to the use of default *n* values of 1 and 3 rather than the previously applied *n* of 2 (Attachment 8). The 10-minute values were developed by time scaling. Values for 8 hours, as determined at initial NAC/AEGL deliberations, were not developed because the chemical would not likely persist for that time under ambient conditions. The accepted values are presented in the following table. A motion was made by George Rogers and seconded by David Belluck. The motion passed unanimously [YES: 22; NO: 0; ABSTAIN: 0] (Appendix P).

PROPOSED AEGL VALUES FOR NICKEL CARBONYL					
Classification	**10-Minute**	**30-Minute**	**1-Hour**	**4-Hour**	**8-Hour**
AEGL-1	NA	NA	NA	NA	NA
AEGL-2	0.096 ppm	0.042 ppm	0.021 ppm	0.005 ppm	NA
AEGL-3	0.46 ppm	0.32 ppm	0.16 ppm	0.040 ppm	NA

Phosphorus oxychloride

As explained by Robert Young (Attachment 8), the previously proposed AEGLS were adjusted due to the use of default *n* values of 1 and 3 rather than the previously applied *n* of 2. Only AEGL-3 values were developed for this chemical due to the lack of data. Consistent with the procedure previously adopted by the NAC/AEGL, the 10-minute AEGL-3 was flatlined with the 30-minute AEGL-3 due to the use of data from a 4-hour exposure period. A motion was made by Zarena Post and seconded by David Belluck to adopt the proposed value. It was approved unanimously [YES: 18; NO: 0; ABSTAIN: 0] (Appendix Q). The proposed values are presented below.

PROPOSED AEGL VALUES FOR PHOSPHORUS OXYCHLORIDE					
Classification	**10-Minute**	**30-Minute**	**1-Hour**	**4-Hour**	**8-Hour**
AEGL-1	NR	NR	NR	NR	NR
AEGL-2	NR	NR	NR	NR	NR
AEGL-3	1.1 ppm	1.1 ppm	0.85 ppm	0.54 ppm	0.27 ppm

Phosphorus trichloride

The previously proposed AEGLS were adjusted due to the use of default *n* values of 1 and 3 rather than the formerly applied *n* of 2. Only AEGL-3 values had been developed for this chemical due to the lack of data. Consistent with the procedure previously adopted by the NAC/AEGL (Attachment 8), the 10-minute AEGL-3 was flatlined with the 30-minute AEGL-3 due to the use of data from a 4-hour exposure period. The proposed values are presented below. During the deliberations it was stated that an industry study was available that might be useful in the development of the AEGL-1 and/or AEGL-2 values. This will be pursued and the development of AEGLs for this chemical revisited if necessary. A motion was introduced by Ernie Falke and seconded by Mark McClanahan to adopt the 10-minute AEGL-3 value. It was passed unanimously [YES: 20; NO: 0; ABSTAIN: 0] (Appendix R).

PROPOSED AEGL VALUES FOR PHOSPHORUS TRICHLORIDE					
Classification	**10-Minute**	**30-Minute**	**1-Hour**	**4-Hour**	**8-Hour**
AEGL-1	NR	NR	NR	NR	NR
AEGL-2	NR	NR	NR	NR	NR
AEGL-3	1.1 ppm	1.1 ppm	0.88 ppm	0.56 ppm	0.28 ppm

Hydrogen chloride

Cheryl Bast provided an overview of the hydrogen chloride AEGLS (Attachment 9) and the derivation 10-minute values. For AEGL-1, the 10-minute values was flatlined with the AEGLS for other time points at 1.8 ppm. The NAC/AEGL briefly reviewed the available key data sets for this chemical. AEGL-1 values are based on a NOAEL in exercising human asthmatics. AEGL-2 levels for 30 minutes to 8 hours are based on nasal and lung histopathology in rats. The 10-minute AEGL-2 value is based on a modification of the mouse RD_{50} to obtain a concentration corresponding to irritation. AEGL-3 values are based on an estimated NOEL for death in rats. A motion was made by Mark McClanahan and seconded by John Hinz to adopt the proposed 10-minute AEGL values. In summary, AEGL-1 passed unanimously [YES: 20; NO: 0; ABSTAIN: 0]; AEGL-2: [YES: 16; NO: 3, ABSTAIN: 0]; AEGL-3: [YES: 18; NO: 2; ABSTAIN: 0], respectively (Appendix S). The 10-minute AEGLS presented in the following table were accepted.

PROPOSED AEGL VALUES FOR HYDROGEN CHLORIDE					
Classification	**10-Minute**	**30-Minute**	**1-Hour**	**4-Hour**	**8-Hour**
AEGL-1	1.8 ppm	1.8 ppm	1.8 ppm	1.8 ppm	1.8 ppm
AEGL-2	100 ppm	43 ppm	22 ppm	5.4 ppm	2.7 ppm
AEGL-3	620 ppm	210 ppm	100 ppm	26 ppm	13 ppm

Methyltrichlorosilane

Cheryl Bast presented an overview for the derivation of 10-minute AEGLS for methyltrichlorosilane (Attachment 10). The accepted values are shown in the table below. The 10-minute values for AEGL-2 and -3 were developed by extrapolation from the 1-hour key study. Motion was made by Loren Koller and seconded by Richard Niemeier. AEGL-1 was approved unanimously; AEGL-2: [YES: 16; NO: 4; ABSTAIN: 0]; AEGL-3: [YES: 18; NO: 2; ABSTAIN: 0], respectively (Appendix T).

PROPOSED AEGL VALUES FOR METHYLTRICHLOROSILANE					
Classification	**10-Minute**	**30-Minute**	**1-Hour**	**4-Hour**	**8-Hour**
AEGL-1	0.60 ppm	0.60 ppm	0.60 ppm	0.60 ppm	0.60 ppm
AEGL-2	37 ppm	12 ppm	6.2 ppm	1.6 ppm	0.78 ppm
AEGL-3	170 ppm	56 ppm	28 ppm	7.0 ppm	3.5 ppm

Dimethyldichlorosilane

Cheryl Bast presented an overview for the derivation of 10-minute AEGLS for dimethyldichlorosilane (Attachment 11). For the AEGL-1, the values were flatlined at 0.90 ppm for all time periods. The 10-minute values for AEGL-2 and -3 were developed by extrapolation from the 1-hour key study. A motion was made by Bob Benson and seconded by Mark McClanahan to accept the following AEGL values: AEGL-1: unanimously accepted; AEGL-2: [YES: 15; NO: 5; ABSTAIN: 0]; AEGL-3: [YES: 18; NO: 2; ABSTAIN: 0] (Appendix U).

PROPOSED AEGL VALUES FOR DIMETHYLDICHLOROSILANE					
Classification	**10-Minute**	**30-Minute**	**1-Hour**	**4-Hour**	**8-Hour**
AEGL-1	0.90 ppm	0.90 ppm	0.90 ppm	0.90 ppm	0.90 ppm
AEGL-2	78 ppm	26 ppm	13 ppm	3.3 ppm	1.6 ppm
AEGL-3	320 ppm	110 ppm	53 ppm	13 ppm	6.6 ppm

Methyl isocyanate

Ten-minute AEGLS for this chemical were based upon time scaling using an empirically-derived *n* value of 1 which is based upon exposures with durations as low as 7 minutes. The 10-minute AEGLS were approved as shown in the following table. No AEGL-1 values were developed because the exposures resulting in irritation would exceed AEGL-2 levels. A motion was made by Bob Benson and seconded by Loren Koller and all proposed 10-minute AEGL values were approved unanimously (Appendix V).

PROPOSED AEGL VALUES FOR METHYL ISOCYANATE					
Classification	**10-Minute**	**30-Minute**	**1-Hour**	**4-Hour**	**8-Hour**
AEGL-1	NA	NA	NA	NA	NA
AEGL-2	0.40 ppm	0.13 ppm	0.067 ppm	0.017 ppm	0.008 ppm
AEGL-3	1.2 ppm	0.40 ppm	0.20 ppm	0.05 ppm	0.25 ppm

AEGL PRIORITY CHEMICALS

Deliberations (other than development and approval of 10-minute values) took place for two additional priority chemicals. In both instances, the discussions were a revisit of chemicals that were, to varying extent, addressed at prior meetings.

Bromine, CAS Reg. No. 7726-95-6

Chemical Manager: Zarena Post, Texas NRCC
Staff Scientist: Sylvia Talmage, ORNL

Bromine was first reviewed in 1998 and no AEGLS were developed pending data development. Zarena Post presented an overview of the pertinent data on bromine. Following discussion of the data (especially that by Henschler [Attachment 12]) and uncertainty factor applications, a motion was made by Mark McClanahan (seconded by Bob Benson) to use a 0.1 ppm exposure for 30 minutes as an estimate of the threshold for ocular and nasopharyngeal irritation. The AEGL-1 values were derived using an uncertainty factor of 3 and extrapolation using an *n* value of 2.2 from a lethality study. The motion passed to accept AEGL-1 values of 0.055, 0.033, 0.024, 0.013, and 0.009 ppm, respectively for 10-minutes, 30-minutes, and 1-, 4-, and 8 hours [YES: 15; NO: 5; ABSTAIN: 0] (Appendix V). There was discussion of Henschler's interpretation of data and the exposure that would be considered a threshold for AEGL-2 effects. The determinant of AEGL-2 was a 30-minute exposure of human subjects to 1 ppm that resulted in severe sensory irritation of the eyes, nose, and throat, which was considered by the NAC/AEGL as appropriate AEGL-2 effects. An interspecies uncertainty factor of 3 was applied and time scaling performed using $n = 2.2$ to obtain the AEGL-2 values. A motion to accept the AEGL-2 values of 0.55, 0.33, 0.24, 0.13, and 0.095 ppm was made by Larry Gephart and seconded by Richard Niemeier. The motion passed [YES: 16: NO: 4; ABSTAIN: 0] (Appendix W). For AEGL-3, there was discussion regarding the relative toxicity of bromine and chlorine and the issue of bromination. Following the discussions, there was a motion made by Zarena Post and seconded by Larry Gephart to accept the following AEGL-3 values based on a lethality study with the mouse, time scaling using $n = 2.2$: 19, 12, 8.5, 4.5, and 3.2 ppm. The motion passed [YES: 18; NO: 1: ABSTAIN: 1] (Appendix W).

SUMMARY OF PROPOSED AEGL VALUES FOR BROMINE

Classification	10-Minute	30-Minute	1-Hour	4-Hour	8-Hour	Endpoint
AEGL-1	0.055 ppm	0.033 ppm	0.024 ppm	0.013 ppm	0.0095 ppm	Threshold for ocular and nasopharyngeal irritation in humans (Rupp and Henschler,1967)
AEGL-2	0.55 ppm	0.33 ppm	0.24 ppm	0.13 ppm	0.095 ppm	Threshold for irreversible effects in humans (Rupp and Henschler,1967)
AEGL-3	19 ppm	12 ppm	8.5 ppm	4.5 ppm	3.2 ppm	Mouse LC_{01} (Schlagbauer and Henschler, 1967)

Phosphine, CAS Reg. No. 7803-51-2

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

Cheryl Bast explained that comments from the NAS/COT Subcommittee on Acute Exposure Guideline Levels necessitated revisions/reconsideration of the phosphine AEGLS (Attachment 13). These comments included: (1) reconsideration of key study selection of AEGL-2 (i.e., no repeat exposures); (2) justification for an uncertainty factor of 3 for AEGL-2, and (3) development of AEGL-1 values. Following a review of available data and discussions, the NAC/AEGL unanimously decided that there were insufficient data with which to develop AEGL-1 values (motion made by Bob Benson; seconded by David Belluck). For AEGL-2 issues, discussion focused on data describing AEGL-2 type endpoints and the effects of the exponent, *n,* on the time scaling. The AEGL-2 values were based upon a NOAEL for histopathologic changes in mice following exposure to 5 ppm, 6 hrs/day for 4 days (a single 6-hour exposure was assumed for AEGL development). The AEGL-2 values were developed using an uncertainty factor of 30 (3 for interspecies and 10 for intraspecies) and time scaling performed using an *n* of 1 or 3. A motion to accept the resulting AEGL-2 values was made by Steve Barbee and seconded by Richard Niemeier. The motion passed [YES: 17; NO: 1; ABSTAIN: 0] (Appendix X). For AEGL-3 values, a 6-hour exposure of rats to 18 ppm was considered a NOAEL for lethality. The AEGL-3 values were developed using this endpoint, uncertainty factors of 3 for interspecies variability and 10 for intraspecies variability, and an *n* of 1 or 3 (the *n* of 1 as suggested by the COT Subcommittee was not used because the experimental data were from a time to death study which may not have revealed the actual mortality). A motion was made by Richard Niemeier and seconded by Bob Benson that the AEGL-3 values derived by the aforementioned process be accepted. The motion passed [YES: 19; NO: 1; ABSTAIN: 0] (Appendix X).

SUMMARY OF PROPOSED AEGL VALUES FOR PHOSPHINE						
Classification	**10-Minute**	**30-Minute**	**1-Hour**	**4-Hour**	**8-Hour**	**Endpoint**
AEGL-1	NA	NA	NA	NA	NA	Not applicable; insufficient data
AEGL-2	0.38 ppm	0.38 ppm	0.30 ppm	0.19 ppm	0.13 ppm	NOAEL for histopathologic changes
AEGL-3	1.4 ppm	1.4 ppm	1.1 ppm	0.69 ppm	0.45 ppm	Estimated lethality threshold.

ADMINISTRATIVE ISSUES

Plans for future NAC/AEGL meeting dates were discussed. The next proposed meeting date is

July 26-28, 2000 Washington, D.C.

There was also some discussion regarding the possibility of holding a meeting in San Antonio, Texas. John Hinz is working on preliminary investigations regarding feasibility. A possible date for this meeting is the first week in December.

Submitted by Bob Young and Po-Yung Lu
Oak Ridge National Laboratory

LIST OF ATTACHMENTS

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

1. NAC/AEGL Meeting No. 17 Agenda
2. NAC/AEGL Meeting No. 17 Attendee List
3. Public comments from *Federal Register* Notice
4. Data Analysis for Crotonaldehyde - Sylvia Milanez
5. Data Analysis for Allylamine - Sylvia Milanez
6. Data Analysis for Ethylenediamine - Sylvia Milanez
7. Data Analysis for Cyclohexamine - Sylvia Milanez
8. Data Analysis for Iron Pentacarbonyl, Nickel Carbonyl, Phosphorus Oxychloride, and Phosphorus Trichloride - Bob Young
9. Data Analysis for Hydrogen Chloride - Cheryl Bast
10. Data Analysis for Methyltrichlorosilane - Cheryl Bast
11. Data Analysis for Dimethyldichlorosilane - Cheryl Bast
12. Data Analysis for Bromine from Henschler publication
13. Data Analysis for Phosphine - Cheryl Bast

LIST OF APPENDICES

A. Approved NAC/AEGL-16 Meeting Highlights
B. Ballot for HFC-134a
C. Ballot for 1,1,1-Trichloroethane
D. Ballot for Agent HD
E. Ballot for 1,2-Dichloroethylene
F. Ballot for Otto Fuel
G. Ballot for HCFC-141b
H. Ballot for Hydrogen Sulfide
I. Ballot for Hydrogen Cyanide
J. Ballot for Crotonaldehyde
K. Ballot for Allylamine
L. Ballot for Ethylenediamine
M. Ballot for Cyclohexylamine
N. Ballot for 2,4- and 2,6-Toluene Diisocyanate
O. Ballot for Iron Pentacarbonyl
P. Ballot for Nickel Carbonyl
Q. Ballot for Phosphorus Oxychloride
R. Ballot for Phosphorus Trichloride
S. Ballot for Hydrogen Chloride
T. Ballot for Methyltrichlorosilane
U. Ballot for Dimethyldichlorosilane
V. Ballot for Methyl Isocyanate
W. Ballot for Bromine
X. Ballot for Phosphine

10:15	Status of the SOP manual and the TSDs for NAS publication (Roger Garrett/Ernie Falke)
10:30	Review and Discussions of Proposed AEGLs from F R Notice (Roger Garrett, George Rusch, and Ernest Falke) ✦ HCFC 141b; HFC 134a; Hydrogen cyanide; Hydrogen fluoride; Hydrogen sulfide; Otto Fuel II; Sulfur mustard (Agent HD); 1,1,1-Trichloroethane; and 1,2-Dichloroethene.
12:00	Lunch
1:00 PM	Review and Discussions of Proposed AEGLs from F R Notice (continued)
3:00	Break
4:00	Bromine (Zarena Post/Sylvia Talmage)
5:15	Adjourn for the day

Thursday, April 27, 2000

8:30 AM	Phosphine (Ernie Falke/Cheryl Bast)
10:30	Break
10:45	Review of 10-minute AEGLs ✦ Allylamine; Cyclohexamine; Chlorine trifluoride; Crotonaldehyde; Dimethyldichlorosilane; Epichlorohydrin; Ethylendiamine; Ethylenimine; Hydrogen chloride; Iron pentacarbonyl; Methyltrichlorosilane; Methyl isocynate; Nickel carbonyl; Peracetic acid; Phosphorus oxychloride; Phosphorus trichloride; Propylamine; and Toulene 2,4- & 2,6-diisocyanate.
12:00	Lunch
1:00 PM	Review of 10-minute AEGLs (continued)
2:30	Break
2:45	Review of 10-minute AEGLs (continued)
5:15	Administrative matters
5:30	Adjourn for the day

Friday, April 28, 2000

8:30 AM	Uranium hexafluoride (George Rusch/Cheryl Bast)
10:45	Break
11:00	Overview of Environmental and Occupational Health Sciences Institute (Bob Snyder)
12:00Noon	Adjourn meeting

NAC/AEGL-17
April 26-28, 2000
Rutgers University

Attachment 2

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FAX TRANSMITTAL # of pages ▶ 27

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NSN 7540-01-317-7368 5099-101 GENERAL SERVICES ADMINISTRATION

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Attachment 3

April 13, 2000

Environmental Protection Agency
Document Control Office (7407)
Office of Pollution Prevention and Toxics (OPPT)
Ariel Rios Bldg.
1200 Pennsylvania Ave., NW.
Washington, DC 20460

Re: Docket control number OPPTS-00289
AEGL for hydrogen cyanide

RECEIVED
2000 APR 18 AM 8:15
OPPT CBIC

Dear Sir or Madam:

The International Precious Metals Institute (IPMI) is an international association of producers, refiners and users of precious metals. We have long been active in domestic and international discussions regarding the regulation of precious metals and industries which use them, and we believe that we have been helpful to the Agency and the larger community, as well as to our members.

We support the Agency's efforts in creating Acute Exposure Guideline Levels to assist government agencies regarding short-term exposures to hazardous substances. We concur with the Agency that hydrogen cyanide is a hazardous substance, which must be understood by other agencies and communities, because it is potentially lethal at certain thresholds of exposure. We are concerned, however, that the Agency has stated that hydrogen cyanide is "used in electroplating and mining." (65 FR 14192) These industries use cyanide salts in solution to leach metals (in mining) or plate them (in electroplating). We are aware that these salts can be generated from hydrogen cyanide, but hydrogen cyanide is not the chemical used in the leaching or electroplating process. Our experience with the electroplating and mining industry is that it does not use, and is very careful to avoid the generation of hydrogen cyanide for not only a safety perspective, but to ensure against the loss of expensive salt reagents.

It is important in any response to a threat to public health that the nature of the threat be known and understood, and that responders and their communities not overreact to incorrect perceptions. There is a very significant difference to an emergency responder between the presence of hydrogen cyanide, a highly flammable, toxic and potentially lethal gas, and a cyanide electroplating solution, non-flammable, non-volatile, and unlikely to present a danger to a responder if not subjected to acid conditions, direct skin exposure or ingestion.

34751

American Petroleum Institute

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Lorraine E. Twerdok, Ph.D., DABT
Manager, Health Sciences

April 14, 2000

OPPTS Document Control Office
Environmental Protection Agency
East Tower Room G-099
Waterside Mall
401 M Street, SW
Washington, DC 20460

RE: Docket Control Number OPPTS-00289
Comments on Proposed AEGL Values for Hydrogen Fluoride and Hydrogen Sulfide

The American Petroleum Institute (API) is submitting these comments for consideration by the U.S. Environmental Protection Agency (EPA) and the National Advisory Committee (NAC), in response to the Federal Register Notice announcing the proposed Acute Exposure Guideline Levels (AEGLs). API is a national trade association representing over 400 member companies engaged in all aspects of the oil and gas industry, including exploration, production, transportation, refining, and marketing. API is interested in the important process of developing AEGLs and appreciates the opportunity to participate in this effort. To this end we have developed specific comments on the proposed AEGLs for hydrogen fluoride (HF) and hydrogen sulfide (H_2S).

API is concerned that the approach being taken in the development of the AEGLs is often overly conservative and thus results in establishing AEGLs far below their intended purpose. The AEGL values, by definition, should represent threshold levels of exposure to a chemical at (or above) which notable discomfort (AEGL-1), serious irreversible effects (AEGL-2), or lethality (AEGL-3) could occur. Our analysis of the proposed AEGLs for HF and H_2S found several instances where the choice of starting data, the uncertainty factors, and the scaling across time using a constant exponent results in proposed AEGL concentrations that are not useful for emergency planning purposes. The NAC must recognize that the AEGL values will have real impacts on local communities as they allocate emergency response resources. Planning for non-emergency situations takes away resources that could be used on real risks.

Contains No CBI

To illustrate our concern, in the AEGL for H_2S, the *n* exponent in the $C^n \times t = k$ equation in establishing the AEGL-1 and AEGL-2 values used the same *n*-value as established in the AEGL-3. In reality, different exponents should be used for each toxic end point. The use of a high exponent (in this case, 4.36) in the C term means that the time dimension becomes relatively unimportant. For lethal effects from H_2S (i.e., the AEGL-3 level), this makes sense because this is how the 4.36 factor was derived; however, at AEGL-1 or -2 levels, it becomes quite an overestimation of likely hazard, resulting in a substantial amount of conservatism being added into the longer timeframes. Even when deriving the AEGL-3 concentration the methodology (a 10x-uncertainty factor and the 4.36 exponent) results in unrealistic values. When the proposed 10-minute AEGL-3 of 76 PPM is juxtaposed to a 90-day subchronic study in rats at 80 PPM in which the only toxic effect was nasal irritation, it makes the likelihood of lethality in humans seem absurd. A recent study not reviewed by the NAC (Dorman *et al.*, 2000; included as an enclosure to this letter) exposed 4-day old baby rats and their nursing mothers to 80 PPM of H_2S for 6-hours a day for 17 consecutive days without measurable health consequences, certainly not lethality. We recognize that the rat is an obligate nose breather and that species to species adjustments must be made, but the 76 PPM proposal for a 10-minute AEGL-3 doesn't pass the bulletin board test.

Additionally, API has other specific concerns related to the AEGLs being proposed for HF (Attachment 1) and H_2S (Attachment 2 & 3), which are discussed in detail. API member companies may also be submitting additional comments on their own.

If you have any additional comment or questions regarding the above comments please contact me or Dr. George Woodall (202-682-8067; woodallg@api.org).

Sincerely,

Lorraine E. Twendok

Enclosures (3)

References

Emmen, H. H. and Hoogendijk, E. M. G. (1998) Report on ascending dose safety study comparing HFA-134a with CFC-12 and air, administered by whole-body exposure to healthy volunteers. TNO Report V98.754.

Hext, P. M. (1989) HFC 134a: Ninety day inhalation toxicity study in rats. Report No. CTL/P/2466. ICI Central Toxicology Laboratory.

Hext, P. M. and Parr-Dobrzanski, R. J. (1993) HFC 134a: Two year inhalation toxicity in the rat. Report No. CTL/P/3841. Zeneca Central Toxicology Laboratory.

Kennedy, G. L. (1979) Acute inhalation toxicity study of tetrafluoroethane (FC 134a). Report No. 422-79. DuPont Haskell Laboratory.

Attachment 1
API Letter to OPPT DCO (April 14, 2000)
Docket Control Number OPPTS-00289

Comments on the Proposed AEGLs for Hydrogen Fluoride (HF)

The American Petroleum Institute (API) is submitting these comments in reference to the proposed Adverse Effects Guideline Levels (AEGLs) for hydrogen fluoride (HF). As stated in the cover letter, the approach being taken in developing the AEGLs is generally too conservative. In the current set of comments on HF, API's focus of attention is on the proposed AEGL-2 values for 30 and 60 minutes (34 ppm and 24 ppm, respectively).

The basis for the 30-minute and 60-minute AEGL-2 values proposed by NAC is data from a study by Rosenholtz et al published in 1963. This study included an exposure of two dogs to 243 ppm HF for 60 minutes. Clinical signs of toxicity included, "blinking, periodic sneezing, coughing, and signs of general discomfort." The 60-minute value of 24 ppm that is being proposed by NAC was obtained by dividing the 1-hour 243 ppm value by a 10-fold uncertainty factor. The proposed 30-minute value of 34 ppm is obtained by starting with the results of the 60-minute exposure and scaling across time using $C^2 \times t = k$, and then applying an uncertainty factor of 10.

The basis for the AEGL-2 should be the studies by Dalbey *et al.* (1998 a,b) rather than Rosenholtz (1963).

API believes there are significant weaknesses with the Rosenholtz study, and that it should not be used as a basis for setting the 30-minute and 60-minute AEGL-2 values. Only very limited information on the study design and results were provided in this thirty-year old publication. In particular, the 60-minute exposure involved only two dogs and this small sample size precludes any statistical evaluation of the data. Moreover, only limited measures of effect were reported (ie, clinical signs and hematology). Given the age of this study, it is also likely that the analytical techniques used to verify the chamber concentrations significantly underestimated the HF concentrations actually present. More current techniques employ teflon-coated impingers which prevents the HF loss that occurs when the acid attacks the glass surfaces of older measuring devices.

As an alternative to the Rosenholtz study, API recommends that data from the recently published studies by Dalbey *et al.* (1998 a,b) be used to set the 30- and 60-minute values. In these studies, a series of acute inhalation exposures were conducted to establish the concentration response for nonlethal HF effects in rats. Most exposures were either 2 or 10 minutes long and concentrations ranged from 135 to 8621 ppm. A few additional exposures were performed for 60 minutes (20 to 48 ppm). A mouth breathing model with a tracheal cannula was used in most of the exposures to maximize delivery of HF to the lower respiratory tract and thus mimic human mouth breathing. Endpoints on the day after exposure included hematology, serum chemistry, bronchoalveolar lavage, pulmonary function, organ weights and

Attachment 1
API Letter to OPPT DCO (April 14, 2000)
Docket Control Number OPPTS-00289

histopathology. These data provide an integrated picture of the concentration-related effects of acute nonlethal exposures to HF.

API recommends that data from the Dalbey studies be used to establish the 30-minute and 60-minute AEGL-2 values, rather than the data reported by Rosenholtz. Following this approach, the NAC could use as a starting point the same 950 ppm NOAEL from the Dalbey study that was used to set the 10-minute AEGL-2 value. Thirty and sixty minute values of 55 ppm and 39 ppm, respectively, are then obtained by scaling across time (using $C^2 \times t = k$) and applying the same 10-fold uncertainty factor. However, because a NOAEL is not a threshold for effect, the NAC should also reexamine their basis for using the 950 ppm NOAEL as the starting point. As effects would be expected to occur at levels above the NOAEL, the NAC should consider using the1,454 ppm exposure level from the Dalbey study, the next-higher exposure level above the NOAEL. All of the animals in this treatment group survived and the effects observed are compatible with the AEGL-2 objective of representing threshold levels of exposure at which serious irreversible effects could occur. Using the 950 ppm NOAEL with a 10-fold uncertainty factor is an example of the compounded health conservative assumptions that result in AEGLs that are not in keeping with their intended purpose.

To summarize, API recommends that NAC revise their proposed AEGL-2 values for 30-minutes and 60- minutes using the data recently published by Dalbey *et al.* (1998 a,b). The basis for this recommendation is that the studies by Dalbey *et al.* are recent, high quality experiments specifically designed to evaluate AEGL-type effects.

References

Dalbey,W., Dunn,B. ,Bannister,R., Daughtrey,W., Kirwin,K., Reitman,F., Wells,M., and Bruce,J. (1998). Short-term exposures of rats to airborne hydrogen fluoride. Journal of Toxicology and Environmental Health, 55: 241-275.

Dalbey,W., Dunn,B., Bannister,R., Daughtrey,W., Kirwin,C., Reitman,F., Steiner,A., and Bruce,J. (1998). Acute effects of 10-minute exposure to hydrogen fluoride in rats and derivation of a short-term exposure limit for humans. Reg. Toxicol. Pharmacol. 27(3):207 - 216.

Rosenholtz, M., Carson, T., Weeks,M., Wilinski,F., Fords,D., and Oberst,V. (1963). A toxicopathological study in animals after brief single exposures to hydrogen fluoride. Am. Ind. Hyg. Assoc. J. 24: 253 - 261.

Attachment 2
API Letter to OPPT DCO (April 14, 2000)
Docket Control Number OPPTS-00289

Comments on the Proposed AEGLs for Hydrogen Sulfide (H_2S)

The American Petroleum Institute (API) is submitting these comments in reference to the proposed Adverse Effects Guideline Levels (AEGLs) for hydrogen sulfide (H_2S). As stated in the cover letter, the approach being taken in developing the AEGLs is generally too conservative. More specific comments related to the AEGLs developed for H_2S are provided below.

AEGL-1: Nondisabling

The National Advisory Committee (NAC) recommends an AEGL-1 for hydrogen sulfide of 0.03 ppm for 10 minutes, 30 minutes, one hour, four hours, and eight hours.

The basis for this AEGL-1 should be the study by Jappinen et al. (1990) rather than the report by TNRCC (1998).

The study by Jappinen *et al.* (1990) on 10 asthmatics exposed to 2 ppm hydrogen sulfide for 30 minutes provides a suitable scientific basis on which to estimate an AEGL-1 for hydrogen sulfide. This well controlled laboratory experiment was conducted on hypersensitive individuals (i. e., asthmatics); thus its findings represents a highly robust and conservative basis on which to set an AEGL-1. The medical consequences are consistent with the definition for an AEGL-1.

We note that, in 1998, the NAC proposed this study for the AEGL-1 for hydrogen sulfide, and estimated values of 2 ppm (30 minutes), 1.7 ppm (one hour), 1.2 ppm (four hours), and 1.1 ppm (eight hours) through the application of exponential scaling (equation of $C^{4.36} \times t = k$) used to derive the AEGL-3. Although this evaluation better represents adverse health effects associated with low dose exposures to hydrogen sulfide, it still includes an exponent factor that may not be relevant to the end point under consideration. The 4.36 exponent value used in AEGL-3 is relevant to the lethality end point but may not be appropriate for nonlethal effects being considered under AEGL-1 or AEGL-2. API encourages the NAC to consider an alternative scaling factor for calculating AEGL-1 and AEGL-2.

The basis recommended in the NAC's current proposal lies in sharp contrast to the data in the Jappinen *et al.* (1990) study. In its present proposal, USEPA relied on information described in a memorandum for the Texas Natural Resources Conservation Commission (TNRCC, 1998) pertaining to offsite air sampling conducted downwind of an oil refinery for approximately five hours. According to the NAC, this unpublished memorandum reported: "persistent odors, eye and throat irritation, headache, and nausea" for six workers over the test period at an average hydrogen sulfide concentration of 0.09 ppm. From this information, the NAC applied an uncertainty factor of three to account for intraspecies variability to derive a value of 0.03 ppm

for each duration based on a "flat-line" assumption.

However, in accepting the TNRCC memorandum as the basis of the AEGL-1, the NAC has ignored several important considerations regarding analytical sampling conducted in the field; the very least of which is the diverse nature of emissions which may have confounded the analysis referred to in TNRCC's memo. In fact, the NAC has acknowledged as much by noting that "sulfur dioxide, benzene, methyl t-butyl ether, and toluene were also detected." Therefore, the effects reported could not be attributable solely to hydrogen sulfide, as USEPA suggests. Although the NAC posits that the "concentrations of these chemicals would not be expected to cause health effects," clearly the mild irritant effects reported by TNRCC could be attributable to any number of airborne contaminants, including but certainly not limited to sulfur dioxide, benzene, methyl-t-butyl ether, toluene, and hydrogen sulfide.

Furthermore, the well known and extensive variability and unreliability of field monitoring instrumentation, in particular mobile equipment, raises serious doubts about the validity of the reported and as yet unsubstantiated concentrations.

Finally, the TNRCC data are anecdotal and have yet to be replicated. As such, the TNRCC report provides only marginal support for any AEGL-1 values.

Consequently, USEPA should rely on the findings of the Jappinen *et al.* study over the unsubstantiated report of TNRCC as the main basis on which to estimate an appropriate AEGL-1 value for exposures to hydrogen sulfide.

> **The flat-line approach for the AEGL-1 is not justified, and the NAC's traditional equation to adjust for duration of exposure should be employed for AEGL-1 as for the AEGL-2 and AEGL3.**

In its proposal, USEPA considered the "flat-line" approach to be relevant inasmuch as: "mild irritant effects generally do not vary greatly over time." The flat line approach has yet to be validated for hydrogen sulfide, and the majority of the toxicity data indicate that response is dependent not only on atmospheric concentration but also on duration of exposure. The application of the NAC's scaling equation (sometimes referred to as "Haber's Law") should be applied to the AEGL-1 as it is for the AEGL-2 and the AEGL-3.

The application of an uncertainty factor of three for intraspecies variability for the range of exposure durations is considered appropriate for the derivation of an AEGL-1 value since the variability in susceptibility is known to be relatively narrow and the effects do not appear to be cumulative over the time covered by the AEGL.

Consequently, USEPA should rely on the findings of the Jappinen *et al.* study to estimate an

Attachment 2
API Letter to OPPT DCO (April 14, 2000)
Docket Control Number OPPTS-00289

appropriate AEGL-1 value for exposures to hydrogen sulfide and apply the appropriate scaling, as articulated above and in the NAC's proposed 1998 AEGL-1 for hydrogen sulfide. In so doing, the resultant AEGL-1 values of 2 ppm (30 minutes), 1.7 ppm (one hour), 1.2 ppm (four hours), and 1.1 ppm (eight hours) would better represent adverse health effects associated with low dose exposures to hydrogen sulfide.

AEGL-2: Disabling

The NAC recommends AEGL-2 for hydrogen sulfide of 42 ppm (10 minutes), 32 ppm (30 minutes), 28 ppm (one hour), 20 ppm (four hours), and 17 ppm (eight hours).

> **The findings of the most appropriate studies were selected as the basis for the AELG-2; however, the air concentration level of 300 ppm, and not 200 ppm, conforms to the selection criteria for the AEGL-2.**

To derive the AEGL-2, USEPA relied on two studies (Green et *al.*, 199 1; Khan *et al.*, 1991), which reported:

> "No adverse clinical signs or gross lung pathology were observed in animals exposed to 200 ppm; however, there was a significant ($p<0.001$) increase in protein and lactate dehydrogenase. . . . Rats exposed to 300 ppm hydrogen sulfide were visibly stressed during the exposure period and lungs showed focal areas of red atelectasis and patchy alveolar edema with perivascular and peribronchial interstitial edema."

Likewise, Green *et al.* (1991) researchers reported the following at 300 ppm hydrogen sulfide:

> "... focal areas of red atelectasis and patchy alveolar edema with perivascular and peribronchial interstitial edema."

These data suggest that "*serious, long-lasting effects*" were evidenced at 300 ppm and not the 200 ppm cited by the NAC. In addition, when one examines the Khan *et al.* (1990) study, further corroboration of this conclusion is derived.

In the Khan *et al.* (1990) study, Fischer 344 rats were exposed to 0, 10, 50, 200, 400, and 500-700 ppm of hydrogen sulfide. While this study reported decreases in cytochrome *c* oxidase and other enzymatic activity in lung mitochondria, the researchers also reported oxidase activity returning to normal post-exposure. These data suggest a reversibility at lower exposure doses, including 200 ppm.

The conclusion that 200 ppm is an inappropriate basis for the AEGL-2 selection is further

supported by another Khan *et al.* study (1991) on Fischer 344 rats at similar exposure concentrations (0, 50, 200, and 400 ppm). In this study, the researchers reported significantly decreased cellular activity at 400 ppm. Based on these data, as well as the Green *et al.* (1991) and Khan *et al.* (1990) study, it is evident that the selection of 200 ppm for AEGL-2 derivation is inappropriate based on the weight-of-evidence presented in these studies.

In the preface of the proposed AEGL for hydrogen sulfide, the NAC specified the following definition of an AEGL-2:

> "AEGL-2 is the airborne concentration (expressed as ppm or mg/m3) of a substance at or above which it is predicted that the general population, including susceptible but excluding hyper-susceptible individuals, could experience *irreversible or other serious, long-lasting effects* or impaired ability to escape. Airborne concentrations below AEGL-2 but at or above AEGL-1 represent exposure levels which may cause notable discomfort." (emphasis added)

Clearly, the 300 ppm level, and not the 200 ppm level, meet the NAC's definition for the AEGL-2, and should be selected as the dose from which to estimate the AEGL-2 for each relevant duration of exposure.

> **With the 300 ppm atmospheric level of hydrogen sulfide selected as the pivotal exposure concentration, the AEGL-2 for 4 hours should be 30 ppm and not 20 ppm.**

The NAC originally applied an uncertainty factor of three to extrapolate from animals to humans and an additional uncertainty factor of three to account for sensitive individuals (total UF =10) to derive a 4-hour AEGL. This 10-fold uncertainty factor is appropriate to apply to the concentration level of 300 ppm, in which case the four-hour AEGL-2 is estimated to be 30 ppm. This four-hour value is then exponentially scaled, using USEPA's methodology (equation of $C^{4.36} \times t = k$), to the remaining exposure durations, resulting in AEGLs of 62 ppm (10 minutes), 48 ppm (30 minutes), 41 ppm (one hour), and 25 ppm (eight hours).

As noted on the comments on AEGL-1, the 4.36 exponent used in the scaling factor may not be appropriate for nonlethal effects. Use of a more appropriate scaling factor would also result in a modification to the AEGL-2 values.

AEGL-3: Lethal

The NAC recommends AEGL-3 for hydrogen sulfide of 76 ppm (10 minutes), 60 ppm (30 minutes), 50 ppm (one hour), 37 ppm (four hours), and 31 ppm (eight hours). To derive this

value, the USEPA has relied on a study by MacEwen and Vernot (1972) which reported: "A 1-hour no-effect-level for death in rats (504 ppm)."

> **NAC should adopt the 100 ppm Emergency Response Planning Guideline (ERPG-3) value developed by the American Industrial Hygiene Association (AIHA) in 1991 as the one-hour AEGL-3 value and use the scaling equation to derive the other time points.**

The development of the ERPG-3 and its subsequent use by the industry and governmental agencies (including EPA) for the past decade is based on protecting "...all individuals ... for up to 1 hour without experiencing or developing life-threatening health effects." The ERPG-3 value was established following an extensive and comprehensive peer-review process. In light of the ERPG-3 value of 100 ppm for a 1-hour exposure, it does not make sense that a 76 ppm exposure for 10 minutes is approaching a lethal concentration. If the ERPG-3 value of 100 ppm were to be adopted as the 1-hour AEGL-3 for H_2S, there would be no need to apply any uncertainty factors due to their incorporation in the ERPG-3.

Following the recommendation above as the starting point for the time scaling factor ($C^{4.36} \times t = k$), the calculated AEGL-3 values for H_2S would be: 151 ppm for 10 minute exposures; 117 ppm for 30 minute exposures; 100 ppm for 1-hour exposures; 73 ppm for-4-hour exposures; and 62 ppm for 8-hour exposures.

Another approach to establishing a more realistic AEGL-3 is to reevaluate the uncertainty factor used in the current proposal. The MacEwan and Vernot (1972) study appears to be appropriate to develop a scaling factor for time for the AEGL-3. However, the use of an uncertainty factor of 10 with the MacEwan and Vernot data seems overly conservative. Once the "scrubbing capacity" of the rat nose has been overwhelmed, it would be expected that all the H_2S would go to the lung. Humans and rats will likely have comparable effects at high atmospheric concentrations and the steep H_2S dose-response for lethality in the rat would be expected in humans as well. Therefore, the use of a 3x uncertainty factor is justified but not the 10x factor.

Additional Data Recommended for Inclusion in the AEGL Documentation

The NAC has provided a reasonably complete compendium of the relevant literature on the acute inhalation toxicity of hydrogen sulfide. The study of Dorman *et al.* (2000), not described in the proposed AEGL documentation, is recommended for inclusion in the supporting documentation. The findings of this study are summarized as follows:

> Dorman *et al.* (2000) examined perinatal exposure via inhalation to hydrogen sulfide in Sprague-Dawley rats. The study explored the potential for hydrogen sulfide to induce adverse impacts on pregnancy outcomes, developmental aberrations, and offspring behavior. Male and female

> Sprague-Dawley rats were exposed to 0, 10, 30, or 80 ppm of hydrogen sulfide six hr/day, seven days/wk for two weeks prior to breeding. Results included a statistically significant decrease in feed consumption, but no statistically-significant decrease in reproductive performance (i.e., number of females with live pups, litter size, average length of gestation, number of implants per female). Hydrogen sulfide did not affect pup growth, development, or performance in behavioral tests. The authors concluded that hydrogen sulfide is "neither a reproductive toxicant nor a developmental neurotoxicant in the rat at occupationally relevant concentrations (≤10 ppm)."

Data from this study help to clarify the uncertainty associated by the findings of Xu *et al.* (1998). Xu *et al.* (1998) conducted a retrospective epidemiological study of female workers in a Chinese petrochemical facility, and reported an increased odds ratio for spontaneous abortion. However, the attribution of the effects to hydrogen sulfide was inappropriate since the investigators failed to control for a number of potential confounders, particularly significant exposures to other chemicals in the work place. The Dorman *et al.* study, therefore, is particularly relevant in demonstrating the lack of reproductive or developmental toxicity associated with hydrogen sulfide in a carefully controlled investigation.

Furthermore, the Dorman *et al.* study either clarifies or confirms other reproductive or developmental toxicity studies presented in the proposed AEGL document, including that of Saillenfait *et al.* (1989), Hayden *et al.* (1990a and b), and Hannah and Roth (1991) which found no treatment-related adverse reproductive or developmental outcomes associated with exposures to hydrogen sulfide.

Attachment 2
API Letter to OPPT DCO (April 14, 2000)
Docket Control Number OPPTS-00289

References

AIHA (American Industrial Hygiene Association). 1991. Emergency Response Planning Guidelines for Hydrogen sulfide. AIHA, Akron, OH.

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Khan, A.A., S.Yong, M.G. Prior, *et al.* 1991. Cytotoxic effects of hydrogen sulfide on pulmonary alveolar macrophages in rats. J. Toxicol. Env. Health. 33: 54-64 *(as cited in the USEPA, 2000).*

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Attachment 2
API Letter to OPPT DCO (April 14, 2000)
Docket Control Number OPPTS-00289

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USEPA. 2000. National Advisory Committee-for Acute Exposure Guideline Levels (AEGLs) for Hazardous Substances; Proposed AEGL Values - Hydrogen Sulfide. Fed. Reg., Vol. 65, No. 51: 14186-14197. 15 March.

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rph@thesapphiregroup.com on 04/14/2000 04:22:24 PM

To: NCIC OPPT/DC/USEPA/US@EPA
cc:

Subject: Comments on Proposed AEGLs for Hydrogen Sulfide

OPPT Document Control Office
East Tower Rm. G-099
Waterside Mall
401 M Street, SW
Washington, D.C.

To Whom It May Concern:

On behalf of IBP, Inc., attached please find our report entitled Comments on USEPA s Proposed Acute Exposure Guideline Levels (AEGLs) for Hydrogen Sulfide. This report provides a critique of USEPA s report entitled Proposed Acute Exposure Guideline Levels (AEGLs) pertaining specifically to Hydrogen Sulfide, CAS Reg. No. 7783-06-4. For your convenience, we have attached this report in both ASCII and WordPerfect 6 formats.

If you have any questions about this information, I would be pleased to assist you. Please call me at your earliest convenience.

Sincerely,

Richard P. Hubner, M.P.H.
The Sapphire Group, Inc.

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Comments on
USEPA's Proposed Acute Exposure
Guideline Levels (AEGLs) for Hydrogen Sulfide

to enlighten the Agency's final selection of AEGL values for hydrogen sulfide that meet the prescribed definitions of each type of AEGL with the soundest scientific basis.

We agree with the Agency's conclusion that sufficient evidence exists to establish AEGL-1, AEGL-2, and AEGL-3 values. However, we specifically disagree with some of the Agency's interpretations of toxicological data supporting the derivation of AGEL-1 and AEGL-2 for hydrogen sulfide. Our comments, presented below, are confined to AGEL-1 and AEGL-2 values.

AEGL-1: Nondisabling

The Agency recommends an AEGL-1 for hydrogen sulfide of 0.03 ppm for 10 minutes, 30 minutes, one hour, four hours, and eight hours.

Based on the scientific strength of evidence, the basis for this AEGL-1 should be the study by Jappinen et al. (1990) rather than the report by TNRCC (1998).

The study by Jappinen et al. (1990) on 10 asthmatics exposed to 2 ppm hydrogen sulfide for 30 minutes provides a suitable scientific basis on which to estimate an AEGL-1 for hydrogen sulfide. This well controlled laboratory experiment was conducted on hypersensitive individuals (i.e., asthmatics); thus its findings represents a highly robust and conservative basis on which to set an AEGL-1. The medical consequences are consistent with the definition for an AEGL-1.

We note that, in 1998, the Agency proposed this study for the AEGL-1 for hydrogen sulfide, and estimated values of 2 ppm (30 minutes), 1.7 ppm (one hour), 1.2 ppm (four hours), and 1.1 ppm (eight hours) through the application of exponential scaling (equation of $c^{4.36} \times t = k$) used to derive the AEGL-2 and AEGL-3. This evaluation better represents adverse health effects associated with low dose exposures to hydrogen sulfide.

The basis recommended in the Agency's current proposal lies in sharp contrast to the data in the Jappinen et al. (1990) study. That contrast is heightened when one observes that the resulting value proposed in its present proposal represents a 98.5% reduction from the value proposed in 1998. Such a reduction must be supported by sound scientific analysis, not anecdotal data at best.

In its present proposal, USEPA relied on information described in a memorandum for the Texas Natural Resources Conservation Commission (TNRCC, 1998) pertaining to offsite air sampling conducted downwind of an oil refinery for approximately five hours. According to the Agency, this unpublished memorandum reported: "persistent odors, eye and throat irritation, headache, and nausea" for six workers over the test period at an average hydrogen sulfide concentration of 0.09 ppm. From this information, the Agency applied an uncertainty factor of three to account for intraspecies variability to derive a value of 0.03 ppm for each duration, based on a "flat-line" assumption.

However, in accepting the TNRCC memorandum as the basis of the AEGL-1, the Agency has ignored several important considerations regarding analytical sampling conducted in the field; the very least of which is the diverse nature of emissions which may have confounded the analysis referred to in TNRCC's memo. In fact, the Agency has acknowledged as much by noting that "sulfur dioxide, benzene, methyl t-butyl ether, and toluene were also detected." Therefore, the effects reported could not be attributable solely to hydrogen sulfide, as USEPA suggests. Although the Agency posits that the "concentrations of these chemicals would not be expected to cause health effects," clearly the mild irritant effects reported by TNRCC could be attributable to any number of airborne contaminants, including but certainly not limited to sulfur dioxide, benzene, methyl-t-butyl ether, toluene, and hydrogen sulfide.

Furthermore, the well known and extensive variability and unreliability of field monitoring instrumentation, in particular mobile equipment, raises serious doubts about the validity of the reported and as yet unsubstantiated concentrations.

Finally, the TNRCC data are anecdotal and have yet to be replicated. As such, the TNRCC report provides only marginal support for any AEGL-1 values.

Consequently, USEPA should rely on the findings of the Jappinen et al. study over the unsubstantiated report of TNRCC as the main basis on which to estimate an appropriate AEGL-1 value for exposures to hydrogen sulfide.

The flat-line approach for the AEGL-1 is not justified, and the Agency's traditional equation to adjust for duration of exposure should be employed for AEGL-1 as for the AEGL-2 and AEGL-3.

In its proposal, USEPA considered the "flat-line" approach to be relevant inasmuch as: "mild irritant effects generally do not vary greatly over time." The flat line approach has yet to be validated for hydrogen sulfide, and the majority of the toxicity data indicate that response is dependent not only on atmospheric concentration but also on duration of exposure. The application of the Agency's scaling equation (sometimes referred to as "Haber's Law") should be applied to the AEGL-1 as it is for the AEGL-2 and the AEGL-3.

The application of an uncertainty factor of three for intraspecies variability for the range of exposure durations is considered appropriate for the derivation of an AEGL-1 value since the variability in susceptibility is known to be relatively narrow and the effects do not appear to be cumulative over the time covered by the AEGL.

Consequently, USEPA should rely on the findings of the Jappinen et al. study to estimate an appropriate AEGL-1 value for exposures to hydrogen sulfide and apply the appropriate scaling, as articulated above and in the Agency's proposed 1998 AEGL-1 for hydrogen sulfide. In so doing, the resultant AEGL-1 values of 2 ppm (30 minutes), 1.7 ppm (one hour), 1.2 ppm (four hours), and 1.1 ppm (eight hours) would better represent adverse health effects associated with low dose exposures to hydrogen sulfide.

AEGL-2: Disabling

The Agency recommends AEGL-2 for hydrogen sulfide of 42 ppm (10 minutes), 32 ppm (30 minutes), 28 ppm (one hour), 20 ppm (four hours), and 17 ppm (eight hours).

The findings of the most appropriate studies were selected as the basis for the AELG-2; however, the air concentration level of 300 ppm, and not 200 ppm, conforms to the selection criteria for the AEGL-2.

To derive the AEGL-2, USEPA relied on two studies (Green et al., 1991; Khan et al., 1991), which reported:

"No adverse clinical signs or gross lung pathology was noted effects was observed in animals exposed to 200 ppm; however, there was a significant ($p<0.001$) increase in protein and lactate dehydrogenase. ... Rats exposed to 300 ppm hydrogen sulfide were visibly stressed during the exposure period and lungs showed focal areas of red atelectasis and patchy alveolar edema with perivascular and peribronchial interstitial edema."

Likewise, Green et al. (1991) researchers reported the following at 300 ppm hydrogen sulfide:

"...focal areas of red atelectasis and patchy alveolar edema with perivascular and peribronchial interstitial edema."

These data suggest that "serious, long-lasting effects" were evidenced at 300 ppm and not the 200 ppm cited by the Agency. In addition, when one examines the Khan et al. (1990) study, further corroboration of this conclusion is derived.

In the Khan et al. (1990) study, Fischer 344 rats were exposed to 0, 10, 50, 200, 400, and 500-700 ppm of hydrogen sulfide. While this study reported decreases in cytochrome c oxidase and other enzymatic activity in lung mitochondria, the researchers also reported oxidase activity returning to normal post-exposure. These data suggest a reversibility at lower exposure doses, including 200 ppm.

The conclusion that 200 ppm is an inappropriate basis for the AEGL-2 selection is further supported by another Khan et al. study (1991) on Fischer 344 rats at similar exposure concentrations (0, 50, 200, and 400 ppm). In this study, the researchers reported significantly decreased cellular activity at 400 ppm. Based on these data, as well as the Green et al. (1991) and Khan et al. (1990) study, it is evident that the selection of 200 ppm for AEGL-2 derivation is inappropriate based on the weight-of-evidence presented in these studies.

In the preface of the proposed AEGL for hydrogen sulfide, the Agency specified the following definition of an AEGL-2:

"AEGL-2 is the airborne concentration (expressed as ppm or mg/m3) of a substance at or above which it is predicted that the general population, including susceptible but excluding hyper-susceptible individuals, could experience irreversible or other serious, long-lasting effects or impaired ability to escape. Airborne concentrations below AEGL-2 but at or above AEGL-1 represent exposure levels which may cause notable discomfort." (emphasis added)

Clearly, the 300 ppm level, and not the 200 ppm level, meet the Agency's definition for the AEGL-2, and should be selected as the dose from which to estimate the AEGL-2 for each relevant duration of exposure.

With the 300 ppm atmospheric level of hydrogen sulfide selected as the pivotal exposure concentration, the AEGL-2 for 4 hours should be 30 ppm and not 20 ppm.

The Agency originally applied an uncertainty factor of three to extrapolate from animals to humans and an additional uncertainty factor of three to account for sensitive individuals (total UF = 10) to derive a 4-hour AEGL. This 10-fold uncertainty factor is appropriate to apply to the concentration level of 300 ppm, in which case the four-hour AEGL-2 is estimated to be 30 ppm. This four-hour value is then exponentially scaled, using USEPA's methodology (equation of $c4.36 \times t = k$), to the remaining exposure durations, resulting in AEGLs of 62 ppm (10 minutes), 48 ppm (30 minutes), 41 ppm (one hour), and 25 ppm (eight hours).

Conclusions

Given that 90% of all atmospheric hydrogen sulfide is derived from natural sources (ATSDR, 1997), the establishment of appropriate and defensible Acute Exposure Guideline Levels (AEGL) for hydrogen sulfide not only serves an important role in health protection but also provides unique challenges.

AEGL-1 values are not correct by failing to accommodate duration of exposure and are not supported by the strongest scientific evidence; they should be revised accordingly. Likewise, the AEGL-2 values are unjustifiably low, and should be increased in accordance with the supporting data. In each case, the data are sufficient to derive reasonably confident AEGL values; however, the databases for each are admittedly limited and should prompt some consideration by the Agency for additional research.

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Jappinen, P., V. Vilkka, O. Marttila et al. 1990. Exposure to hydrogen sulfide and respiratory function. Br. J. Ind. Med. 47: 824-828.

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USEPA. 2000. National Advisory Committee for Acute Exposure Guideline Levels (AEGLs) for Hazardous Substances; Proposed AEGL Values - Hydrogen Sulfide. Fed. Reg., Vol. 65, No. 51: 14186-14197. 15 March.

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American Flint Glass Workers Union
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Coalition of Black Trade Unionists
William Lucy President

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V. Daniel Radford Board Chairman

April 13, 2000

Document Control Office (7407)
Office of Pollution Prevention and Toxics (OPPT)
EPA
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Washington, D.C. 20406

Docket Control Number: OPPTS-00289

Dear AEGL Committee:

I would like to raise a concern regarding one of the values recommended by the AEGL Committee for Otto Fuel (propylene glycol dinitrate). I believe that the committee's extrapolation of the existing data to arrive at an AEGL 2 of 6 ppm level for 10 minutes is inappropriate and dangerous.

I am unconvinced that this level will not result in a significant proportion of the general population experiencing the disabling headaches found in the Stewart study. These headaches forced the termination of the 1.5 ppm exposure after 3.2 hours (the highest exposure for any human study). The extrapolation to shorter time periods should only be done where there exists better data that demonstrates the safety of such an extrapolation.

I recommend that the flat lining of the AEGL 1 value between 30 minutes to 10 minutes should be done for the AEGL 2 value also.

Sincerely,

John S. Morawetz

c: Frank D. Martino
Secretary Treasurer's Office
Eric Bray
Michael Sprinker
Bill Kojola, AFL-CIO

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April 13, 2000

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Docket Control Number: OPPTS-00289

Dear AEGL Committee:

I would like to raise concerns regarding the values recommended by the AEGL Committee for 1,1,1 trichloroethane. I believe that the AEGL 3 endpoint, in particular the value of 4,800 ppm for both 10 and 30 minutes, is excessive given the available human data.

The draft AEGL document states that for human data "concentration-duration exposure relationships were not reliably reported". The Jones (1983) article does give exposure duration data to give the committee cause for concern. If the Committee believes that simulation exercises "are not reliable" and do not provide any useful data, this study can be ignored. However these published studies do contribute information which should be used to limit exposure to populations potentially exposed during chemical spills.

In one of two fatalities reported by Jones, the work tasks were repeated with the same amount of material (100 to 200 ml of solvent) and time weighted averages measured. The measured exposure was 36 ppm for 27 minutes. When deliberately using "excessive amounts of solvent" they measured 440 ppm for 6 min. The authors report that three times that amount were found 15 cm above the floor (108 to 1,320 ppm). They then spilled 100 ml of the solvent on a cloth which was placed on the floor. A 9 minute sample resulted in 6,410 while the level was 515 ppm for 15 minutes measured 15 cm above the floor. The level of 6,410 ppm only 2.5 cm above the floor is an area level not one that the deceased breathed.

Although not a definitive level that occurred at the time of death these results give significant cause for concern. Even if the highest measured value found 15 cm above the floor is used to calculate a 10 minute value (1,320 ppm), a safety factor needs to be introduced. The current recommendations raise serious concerns that a general population exposed to 4,800 ppm for 30 minutes would experience some fatalities.

I therefore urge the committee to reconsider all AEGL 3 levels.

Sincerely,

John S. Morawetz

c: Frank D. Martino
Secretary Treasurer's Office
Eric Bray
Michael Sprinker
Bill Kojola, AFL-CIO

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April 13, 2000

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1200 Pennsylvania Ave. NW
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Docket Control Number: OPPTS-00289

Dear AEGL Committee:

I would like to raise concerns regarding the values recommended by the AEGL Committee for HFC-134a (1,1,1,2 tetrafluoroethane). I believe that the committee's use of no uncertainty factor from a study of 8 healthy young people exposed to 8,000 ppm for 1 hour is inappropriate. The committee should use human exposure studies in arriving at recommended levels but they need to have a safety factor for a number of reasons.

The subjects were all young healthy adults. An uncertainty factor should be used to account for sub populations.

With only 8 subjects, a 10% effect could not be detected. An uncertainty factor should be used due to the limited number of subjects and human variability.

With a lack of significant findings for this outcome we should either not set an AEGL 1 value or use an uncertainty factor for the use of one study with small numbers of young, healthy subjects to extrapolate to the general population. I urge the committee to reconsider the AEGL 1 levels for all time periods.

Sincerely,

John S. Morawetz

c: Frank D. Martino
Secretary Treasurer's Office
Eric Bray
Michael Sprinker
Bill Kojola, AFL-CIO

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Coalition of Black Trade Unionists
William Lucy President

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Greater Cincinnati Occupational Health Center
V. Daniel Radford Board Chairman

April 13, 2000

Document Control Office (7407)
Office of Pollution Prevention and Toxics (OPPT)
EPA
Ariel Rios Building
1200 Pennsylvania Ave. NW
Washington, D.C. 20406

Docket Control Number: OPPTS-00289

Dear AEGL Committee:

I would like to raise concerns regarding the values recommended by the AEGL Committee for HFC-141b (1,1-Dichloro-1-fluoroethane). I believe that the committee's use of no uncertainty factor from a study of 8 healthy young people to 1,000 ppm for 4 hour (and only 2 subjects for an additional 2 hours) is inappropriate. The committee should use human exposure studies in arriving at recommended levels but they need to have a safety factor for a number of reasons.

The subjects were all young healthy adults. An uncertainty factor should be used to account for sub populations.

With only 8 subjects, a 10% effect could not be detected. An uncertainty factor should be used due to the limited number of subjects and human variability.

There is a lack of significant findings for this outcome therefore we should either not set an AEGL 1 value or use an uncertainty factor for the use of one study with small numbers of young, healthy, subjects to extrapolate to the general population. I urge the committee to reconsider the AEGL 1 levels for all time periods.

Sincerely,

John S. Morawetz

c: Frank D. Martino
Secretary Treasurer's Office
Eric Bray
Michael Sprinker
Bill Kojola, AFL-CIO

34749

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April 13, 2000

By Hand

OPPT Document Control Office (DCO)
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Waterside Mall
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Washington, DC

Docket Control Number: 00289

Proposed Acute Exposure Guideline Levels for HFC 134a (CAS: 811-97-2)

Dear Sir:

I am pleased to take this opportunity to comment on the approach employed in setting the proposed values for the acute exposure guideline levels (AEGLs) for HFC 134a and the bases for their derivation published in the Federal Register of March 15, 2000.

Context for Concern

It is recognized that, in selecting AEGL values, it can be difficult to balance the need to "err on the safe side" and to avoid incorporating an unnecessarily large safety factor. In some cases where the confidence in the AEGL value is low, the safety margin must be wider to accommodate uncertainty. This is not the case for HFC 134a where the results of recent, high quality, relevant studies are available. The following analysis shows that the proposed AEGL values are based upon unnecessarily large safety factors.

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Contains No CBI

The concern regarding lower than necessary AEGL values arises because, apart from the special case of ammonia, HFC 134a alone among refrigerants has been subject to the AEGL setting process. The proposed AEGLs for HFC 134a are lower than values resulting from similar exposure limit development exercises such as the American Society of Heating and Air-conditioning Engineers' (ASHRAE) Acute Toxicity Exposure Limit (ATEL) and its international equivalent, the ISO Safety Classification of Refrigerants. Problems arise because no other refrigerants have AEGLs for comparison with that of HFC 134a and thus false conclusions regarding the safety of HFC 134a relative to that of other refrigerants may be drawn by comparison of an overly conservative HFC 134a AEGL with ATELS for other refrigerants. It should be noted that the ATEL and ISO procedures have been rigorously standardized and are tailored to the properties and uses of refrigerants. One potential remedy would be for the AEGL process to include a wide range of refrigerants: fluorochemical, hydrocarbon and carbon dioxide.

Since the ATEL is an exposure level for 30 minutes calculated to not impede a vulnerable member of the general population from escaping from a refrigerant filled building, it is most similar to ATEL-2, 30 minutes exposure. The ATEL for HFC 134a is 50,000 ppm and, in contrast, AEGL-2 is 13,000 ppm.

Time-dependence of AEGLs

The decision to "flat-line" each of the three AEGL types for HFC 134a across time is appropriate, being founded in the nature of the toxicological endpoints being considered (i.e. responses concentration dependent) and information on the uptake and distribution in animals and man showing rapid establishment of equilibrium.

Interpretation of Cardiac Sensitization Data

The treatment of cardiac sensitization data dominates, as it should, the setting of AEGLs for HFC 134a. As acknowledged in the Federal Register notice, the design of the cardiac sensitization test in dogs makes it "supersensitive". Not only does this mean that no interspecies adjustment in dose is required but an adjustment for the "sensitive individual" is also unnecessary. For example, it is improbable that a human with a cardiac condition would be any more sensitive than dogs primed with high doses of

epinephrine. The removal of any intra-species uncertainty factor makes a significant difference to the AEGL values and brings AEGL-2 into line with ATEL and ISO limits.

Note that a NOEL for cardiac sensitization of 50,000 ppm has been established (reference to be supplied) and this should be used in deriving AEGLs rather than the 40,000 ppm in the proposal. This same study showed the onset of effects at 75,000 ppm and this should be used in place of the 80,000 ppm currently being employed.

AEGL-1

The human volunteer study of Emmen and Hoogendijk (1998) is valuable in that it shows, unequivocally, that humans experience no adverse effect of any kind inhaling a level of 8,000 ppm of HFC 134a for I hour. However, there is no direct evidence to show how far above 8,000 ppm the absence of effects extends – the true no effect level may be considerably higher. It is necessary to turn to the results of animal studies to resolve this question.

As explained above, the NOEL for HFC 134a in the cardiac sensitization test is 50,000 ppm and this does not require adjustment for inter-species conversion or inter-individual variability. In acute toxicity tests in the rat, the LC_{50} is >360,000 ppm, initial signs of anesthesia have not been observed in any study at dose levels of 80,000 ppm and below and no signs of (non-neoplastic) toxicity have been seen at the top dose level of 50,000 ppm in rat 90-day, 1 year or even 2-year studies (Kennedy, 1979; Hext, 1989; Hext and Parr-Dobrzanski, 1993).

The evidence clearly indicates that the true NOEL for humans lies well above the proposed 8,000 ppm for AEGL-1. Cardiac sensitization provides the most appropriate basis for developing AEGLs for HFC 134a. Although, the results of the cardiac sensitization studies support a conclusion that 50,000 ppm may reasonably be considered a NOEL for this end-point in man, a true safety factor of 2 could be considered for AEGL-1 to yield a value of 25,000 ppm.

AEGL-2

As discussed above, it is clear that no "escape impairing" or "disabling" effects would be expected to result from human exposures to HFC 134a at

50,000 ppm and below, and this would apply even for the sensitive individual. The appropriate AEGL-2 value is 50,000 ppm which matches the ATEL value derived by ASHRAE methodology.

AEGL-3

The lowest level at which significant cardiac sensitization effects have been observed in dogs is 75,000 ppm; these were not life threatening. Repeating the argument that the cardiac sensitization test is sufficiently stringent that no uncertainty factors need to be applied for inter-species conversion or inter-individual variability, a value between the NOEL (50,000 ppm) and the lowest dose shown to induce effects (75,000 ppm) meets the definition of AEGL-3. A level of 60,000 ppm is thus recommended for AEGL-3.

Conclusions

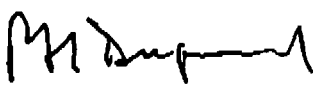
The proposed AEGLs for HFC 134a are overly conservative when judged against the nature of the toxicological evidence, the results obtained by other limit setting groups using rigorous procedures, and the AEGL values for other more toxic materials. It is recommended that the "flat-line" of individual AEGLs across exposure times be retained but that the AEGL values be adjusted to the following inhalation levels:

AEGL-1:- 25,000 ppm

AEGL-2:- 50,000 ppm

AEGL-3:- 60,000 ppm

Respectfully submitted.



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April 11, 2000

Proposed Acute Exposure Guideline
Levels for Hydrogen Fluoride
Docket Control No. OPPTS-00289

00MR 148

MR 3486

Environmental Protection Agency
Office of Pollution Prevention and Toxics (OPPT)
Document Control Office (7407), Room G-099
401 M Street, SW
Washington, DC

This letter is submitted on behalf of ExxonMobil in response to the proposed Acute Exposure Guideline Levels (AEGLs) for hydrogen fluoride (HF). ExxonMobil supports the National Advisory Committee (NAC) in their efforts to develop AEGLs. We commend the NAC on their efforts to develop AEGLs for HF. We specifically note the following.

- The draft technical support document is very comprehensive and well written.
- In response to industry suggestions on the need to evaluate shorter-term events, the NAC included recommendations for 10-minute AEGLs.
- To determine the overall uncertainty factor used to set the AEGL 2 values and to protect public health, the NAC carefully considered the direct-acting nature of the HF-induced toxicity and the high quality nature of the Petroleum Environmental Research Forum (PERF) study, which used a sensitive mouth-breathing model and many sensitive measures of effect.
- The NAC used the best available data to set the AEGL-1 values, the AEGL-3 values, and the 10-minute, 4-hour, and 8-hour AEGL 2 values.
- The Committee deliberations have been conducted in an open forum, allowing for consideration of new health effects data, for example, the PERF acute toxicity study.

Our concerns on the proposed AEGLs centers on the 30-and 60-minute AEGL 2 values. The NAC has proposed to use results from a study by Rosenholtz *et al.* (1963) to set these values. The 60-minute value is obtained by dividing the 1-hour 240 ppm exposure level by 10. The proposed 30-minute value of 34 ppm is obtained by extrapolating the results of the 60-minute exposures in the Rosenholtz *et al.* study to 30 minutes using concentration squared times time

equal to a constant ($C^2 \times t = k$) and applying an uncertainty factor of 10.

We recommend using the acute HF toxicity study conducted by PERF to set the 30-and 60-minute AEGL 2 values. The recommended 30-and 60 minute AEGL-2 values of 55 ppm and 39 ppm, respectively, are obtained by extrapolating the results of the10-minute exposures to 30 and 60 minutes using $C^2 \times t = k$ and applying the 10-fold uncertainty factor. Our rationale for preferring the PERF study and an exponent of 2 is discussed in more detail in the attachment.

The difference between a 30 minute AEGL 2 value of 55 ppm versus 34 ppm and a 60 minute value of 39 ppm versus 24 ppm may not appear to be very significant from a health viewpoint. However, this is a very critical issue for practical application of the values. In addition, the use of two different data sets to establish the 10-minute versus the 30- and 60-minute AEGL 2 values results in a discontinuous progression in the exposure duration range most critical to HF accidental release scenarios. As described in Ken Steinberg's presentation to the AEGL Committee on June 8, 1998, a discontinuous progression of AEGL values significantly confounds the interpretation of results from consequence dispersion modeling. As noted in the presentation, this discontinuous progression for HF is not found in the AEGL values for chlorine. The need for continuity in AEGLs to facilitate the analysis of results from dispersion modeling is a general concern that applies to all hazardous chemical AEGLs.

We appreciate the opportunity to provide these comments. Please contact me at 908 730-1025 if you have questions.

Sincerely,

Richard Phillips, Ph.D.
Director, Toxicology Division
Exxon Biomedical Sciences, Inc.

Linda Hoffmann
Manager
Environmental, Safety, Civil and Marine Division
ExxonMobil Research and Engineering Company

RDP:jmk

Attachment

Comments on the Proposed AEGLs for Hydrogen Fluoride (HF)

General Comments

The technical support document (TSD) includes all of the best available toxicology data and is clearly written. The National Advisory Committee (NAC) has included recommendations for 10- minute AEGLs essential for evaluating short-term simulated accidental releases. The NAC based the 10-minute "level 3" and "2" values on the high quality acute toxicity study conducted by PERF. Similarly, the Committee has used the best available data to set all of the AEGL 1 and 3 values and the 4 and 8-hour AEGL 2 values.

To determine the overall uncertainty factor (UF) needed to set the AEGL 2 values protective of human health, the NAC carefully considered the lower degree of variability observed in how individuals respond to pulmonary irritants such as HF. This contrasts with the higher degree of complexity and variability, which may be observed in how individuals respond to chemicals that produce certain systemic toxic effects, for example methemoglobinemia. Also, in their deliberations on the UF, the NAC considered the sensitive nature of the cannulated rat model and the sensitive toxicological effects assessed in the PERF study. In our view, the chemical-specific, data-derived approach used by the NAC to determine the UF for AEGL 2 is consistent with the *Guidelines for Developing Emergency Exposure Level Guidelines* published by the National Research Council.

Toxicology Concerns on the Proposed 30-and 60-Minute AEGL 2 Value

We have several concerns with the approach used by the NAC to derive the 30-and 60-minute AEGL 2 values. The basis was the study by Rosenholtz *et al.*, which involved a 60-minute exposure in only two dogs. This small number of animals precludes statistical treatment of the data. In addition, this study has several other weaknesses. Very limited measures of effect, essentially only clinical signs of toxicity and hematology, were assessed. Clinical signs of toxicity can be a relatively subjective and insensitive measure of response. The hematology, which was conducted many days after the HF exposures, is of limited use for evaluating HF vapor toxicity, which centers on effects in the pulmonary system. Only very limited information on the study design and results were provided in the publication.

Moreover, it is very likely that the measurement techniques used to verify the HF exposure levels in the Rosenholtz *et al.* study underestimated the HF levels actually present in the chambers. First, Rosenholtz *et al.* used an all-glass sampling system to measure HF chamber concentrations. Recent techniques employ Teflon-coated impingers which prevent HF loss that occurs when the acid attacks the glass surfaces. In a recent study by Dupont (1990), concentrations reported with all glass impingers were 18-28% lower than when Teflon-coated impingers were employed. Also, Rosenholtz *et al.* used a less than optimal air sampling flow rate, 0.4-liters/minute. Current methods recommend 1.4-1.6 liters/minute (Dupont, 1990). The lower sampling rates are known to collect less HF, again lowering the reported HF chamber concentrations.

In contrast, the acute toxicity study in rats conducted by the Petroleum Environmental Research Forum (PERF) is a high-quality study designed specifically to evaluate AEGL 2 effects (see Table). In this study, 20 animals/group were used, ten/group for bronchoalveloar lavage

(BAL), serum chemistry and ten/group for pulmonary function tests, histopathology, and organ weights. Statistical treatment of the data was performed. As described above, multiple and sensitive measures of effect were used. The three volume 300+ page report provides complete information on the study design, results, and conclusions. The most up-to-date measurement techniques were used to verify HF exposure concentrations. Finally, a sensitive, cannulated rat model was used to mimic human mouth breathing. In order to link to the existing HF database, exposures in nose-breathing animals were also conducted, and the results of the two models were compared.

In establishing the proposed 30-and 60-minute AEGL 2 values, the NAC did not quantitatively account for the less serious effects observed in dogs versus the effects described in the definition for AEGL 2. In dogs exposed to 243 ppm HF for 1 hour, the clinical signs of toxicity reported were "blinking, periodic sneezing, coughing, and signs of general discomfort." These effects are much less serious than those described in the definition for AEGL 2, which are irreversible or other serious long-lasting effects or impaired ability to escape. Rather, the effects in dogs are similar to those described in the definition for AEGL 1, namely notable discomfort, mild odor or taste, or other sensory irritation.

To establish the 30- and 60-minute AEGL values, we recommend using the data reported by PERF rather than the data reported by Rosenholtz *et al.*, 1963 for the reasons cited above. Both approaches involve extrapolation. However, our view is that the PERF study is stronger scientifically. In this study, a sensitive cannulated rat model was used and the study design included a thorough evaluation of toxic effects relevant to AEGL 2. The exposure concentrations were verified using up-to-date techniques that limit the loss of HF and underreporting of chamber concentrations. Using the same 950 ppm No-Observed-Adverse-Effect Level as the NAC used to derive the 10-minute AEGL, extrapolating to 30- and 60 minutes using $C^2 \times t = k$ as per the NAC, and applying the same 10-fold uncertainty factor, the resulting 30-and 60-minute AEGL-2 values are 55 and 39 ppm, respectively.

Use of the $C^2 \times t = k$ relationship to extrapolate to different timeframes is supported by various studies. For example, to estimate a time adjustment factor for HF for estimating the ratio of concentrations producing equivalent responses for different exposure durations, Alexeeff *et al.* (1993) applied a least-squares linear curve fit of the graph of log time vs. log LC_{50}. The result was the equation $y = 7.69 - 1.89 x$ with an R^2 of 0.995 and a slope of 1.89, which the authors rounded to 2. This value compares well with the value of 2 derived by ten Berge et al. (1986) using probit analysis. Use of the $C^2 \times t = k$ relationship to derive both AEGL-3 and AEGL-2 is a reasonable approach to establishing AEGLs for multiple timeframes. HF is a direct acting pulmonary irritant. Both the life-threatening and serious effects produced by HF are related to the chemical's irritant potential.

The difference between a 30-minute AEGL 2 value of 55 versus 34 ppm and a 60 minute AEGL 2 value of 39 versus 24 ppm may not appear to be very different from a health perspective. However, in addition to the issue of accuracy, as described in the presentation by Ken Steinberg on June 8, use of different data sets to establish the 10-minute versus the 30-and 60- minute values causes a discontinuity in the consequence analysis results using dispersion modeling. This discontinuity confounds the interpretation of ambient impact prediction for a given hypothetical accidental release. However, as noted in this presentation, this discontinuous

progression occurred with HF but was not found with the AEGLs for chlorine. The need for continuity in the analysis of results from dispersion modeling is a general concern that applies to all hazardous chemical AEGLs.

Table

Comparison of the Rosenholtz and PERF HF Acute Toxicity Studies

Quality Criteria	Rosenholtz *et al.*	PERF
Number of animals/group	2	20
Statistics performed	No	Yes
Toxic effects evaluated	Clinical signs, hematology	Clinical signs, pulmonary function, histopathology, bronchoalveolar lavage
Completeness of the report (study, results, conclusions)	Very limited, incomplete information provided	Extensive and complete information provided
Accuracy of HF air sampling technique	All glass; likely under estimated exposures	Teflon coated; accurately measured exposure
Sensitivity of the animal model	Moderately sensitive dog whole body exposure	More sensitive cannulated rat used, simulating human mouth breathing; results compared to rat whole body exposures

References

Alexeeff, G., et al. (1993) Estimation of Potential Health Effects from Acute Exposure to Hydrogen Fluoride Using a Benchmark Dose Approach. Risk Analysis 13, No.1, 63-69.

Ten Berge, W.F. et al. (1986). Concentrations-Time Mortality Response Relationship of Irritant and Systemically Acting Vapors and Gases. J. Haz. Mat. 13, 301-309.

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EPA (199?). Guideline On Air Quality Models (Revised). EPA-450/2-78-027R United States Environmental Protection Agency Office of Air Quality Planning and Standards, Research Triangle, Park, NC.

PERF (1996). Evaluation of the Toxicity of Hydrogen Fluoride at Short-Term Exposure Times. PERF Project No. 92-09. Petroleum Environmental Research Forum. Performed at Stonybrook Laboratories, Inc., P.O. Box 1029. Princeton, NJ 08543.

Rosenholtz, M. *et al.* (1963). A Toxicopathologic Study in Animals After Brief Single Exposure to Hydrogen Fluoride. *AIHAJ*, May-June, 253-261.

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Steinberg, K. (1998). Influence of Toxicity Averaging Time on Cloud Penetration for Accidental Releases. Presented to the AEGL National Advisory Committee, June 8.

LAG:jmk
April 3, 2000

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MR 34633

April 10, 2000

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RE: Docket Control Number OPPTS-00289

BP Amoco is submitting the following comments to the National Advisory Committee for Acute Exposure Guideline Levels (NAC/AEGL Committee) for their consideration. These comments are in response to the Federal Register Notice, dated March 15, 2000, announcing the proposed AEGL values for hydrogen fluoride (HF). BP Amoco is a major international petrochemical company with significant operations throughout the United States. We use HF in both our refining and chemical operations. We have, therefore, a vested interest in the proposed AEGL values for HF.

In general, BP Amoco is concerned with the overly conservative nature of the proposed AEGL values for HF. We believe that many of the proposed values are too low and, thus, do not meet the intended definition of AEGL values. The AEGL values, by definition, should represent threshold levels of exposure to HF at (or above) which notable discomfort (AEGL-1), serious irreversible effects (AEGL-2), or lethality (AEGL-3) could occur. We do not take exception to the proposed AEGL-1 values of 2 ppm and 1 ppm as thresholds for notable discomfort. However, based on the available acute toxicity data for HF, we do take exception to the proposed AEGL-2 and AEGL-3 values as thresholds for serious irreversible effects and lethality, respectively. Our specific comments focus on the proposed AEGL-2 and -3 values.

The NAC Committee has selected the Dalby *et al.* study as a basis for the 10-minute AEGL-2 value. We agree with this selection. The Dalby study was well designed and conducted, and yielded relevant, high-quality data. The committee has selected the 950 ppm exposure level as the starting point for deriving the 10-minute AEGL-2 value. We disagree with this selection. The 950 ppm exposure level in the Dalby study established a clear no-observed-adverse-effect level (NOAEL), as acknowledged by the NAC

Committee in the Federal Register Notice. A NOAEL is not a threshold for effect and, thus, should not be used as a basis for the AEGL-2 value. As effects would be expected to occur at levels above the NOAEL, we propose that a more appropriate basis for the 10-minute AEGL-2 value is the 1,454 ppm exposure level from the Dalby study, the next-higher exposure level above the NOAEL. All of the animals in this treatment group not only survived, but were functioning normally after the recovery period. We recommend that the NAC Committee revise the proposed AEGL-2 values by starting with the 1,454 ppm exposure level from the Dalby study. An intraspecies safety factor should be applied to this value to account for sensitive human individuals; an intraspecies safety factor of 5 is recommended. An additional interspecies safety factor is not warranted because of the acute, irritant nature of HF's effects, as the Committee has justified in several other instances in the Federal Register Notice. Based on the above approach, we recommend a 10-minute AEGL-2 value of 290 ppm.

We disagree with the NAC Committee's selection of the Rosenholtz study as a basis for the 30-minute and 1-, 4-, and 8-hour AEGL-2 values. The Rosenholtz study is of inferior quality compared to the Dalby study. We recommend that the NAC Committee use the above-recommended 290 ppm 10-minute AEGL-2 value as a basis for deriving the other AEGL-2 values, and then apply the $c^2 \times t = k$ relationship.

The NAC Committee has selected the 1,764 ppm exposure level from the Dalby *et al.* study as a basis for the proposed 10-minute AEGL-3 value. While we agree with the selection of this exposure level as a threshold for lethality, we disagree with the committee's justification for using an uncertainty factor of 10. The mouse may be a more sensitive species than the rat, but the Darmer *et al.*[1] study reveals a lethality threshold for HF in non-human primates of 1,035 ppm for a 60-minute exposure. The results of the Darmer study indicate that non-human primates are less sensitive than the mouse. It is not clear, however, why the committee has chosen the mouse data over the primate data. The Darmer *et al.* data indicate that the application of an uncertainty factor of 10 to the rat data is excessive. Using the Darmer data as support, we recommend that the committee consider applying an intraspecies safety factor of 5 to the rat data, to protect sensitive human individuals. This approach would result in a 10-minute AEGL-3 of 350 ppm. The relationship $c^2 \times t = k$ could then be used to derive the 30-minute and 1-, 4-, and 8-hour AEGL-3 values. Alternatively, the lethality threshold of 1,035 ppm in non-human primates from the Darmer *et al.* study could be used as a basis for the 1-hour

AEGL-3 value. By applying a safety factor of 5 to protect sensitive human individuals, and by using the $c^2 \times t = k$ relationship, the other AEGL-3 value could be derived.

In conclusion, BP Amoco believes that the NAC Committee has derived AEGL-2 and AEGL-3 values for HF that are too low and, thus, not consistent with the definition of these criteria. We recommend that the NAC Committee revise the proposed AEGL-2 and -3 values upward to represent more accurately the acute toxicity data on HF.

Sincerely,

James D. Jernigan, Ph.D.
Director, Product Stewardship & Toxicology

[1] Darmer *et al.*, Am. Ind. Hyg. Assn. J., 33, 661, 1972.

Serving The Industry Since 1906.

Sherry L. Edwards
Director
Legislative & Regulatory Affairs

MR 34861

April 14, 2000

U.S. Environmental Protection Agency
Office of Pollution Prevention and Toxics
Document control Office (7407)
Ariel Rios Building
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Washington, DC 20460

RE: Proposed Acute Exposure Guideline Levels (AEGLs) Docket No. OPPTS-00289

Dear Sir or Madam:

The American Meat Institute (AMI) appreciates the opportunity to comment on the Environmental Protection Agency's (EPA or the agency) proposed Acute Exposure Guideline Levels (AEGLs). 65 *Fed. Reg.* 14186, March 15, 2000. AMI is the national organization representing the interests of meat and poultry slaughterers and processors and their suppliers throughout North America. AMI's members produce the majority of meat and poultry products manufactured in the United States.

AMI is particularly concerned with the levels proposed for hydrogen sulfide. The agency has failed to demonstrate a sufficient scientific basis for the proposed AEGL value. Therefore, AMI urges the agency to withdraw the proposed values until the agency conducts or presents additional scientific studies or data to support the values and makes this information available for public comment.

AMI appreciates EPA's considerations of our concerns. Please call me at (703) 841-2400 or email me at sedwards@meatami.org if you have any questions or comments regarding this issue.

Sincerely,

Sherry L. Edwards

sedwards@meatami.org on 04/14/2000 04:23:25 PM

To: NCIC OPPT/DC/USEPA/US@EPA
cc:

Subject: AMI Comments on AEGLs Proposal

The attached document are the American Meat Institute's comments on EPA's proposed Acute Exposure Guideline Levels Docket No. OPPTS-00289. Please let me know if you have trouble opening the document.

<<AMI AEGL comments.doc>>

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 - AMI AEGL comments.doc

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April 14, 2000

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SUBJECT: OPTS-00289

The following comments are being offered pursuant to the Federal Register Notice issued March 15, 2000, regarding Proposed Acute Exposure Guidance Levels (AEGL).

1. Comments on the derivation of AEGLs for cis- and trans-1,2-dichloroethylene

The AEGL documentation was quite thorough in explaining how the AEGL values were derived for cis- and trans-1,2-dichlororthylene (DCE). However, the following comments might be considered before the AEGL's are finalized.

The two-fold difference in toxicity between the trans-DCE and cis-DCE isomers was used throughout this document to derive the cis-DCE AEGL values from trans-DCE data. However, it would seem that in some cases, the cis-DCE AEGL could have been derived directly from the cis-DCE toxicity data without modifying the trans-DCE based AEGL. For example, the 4 and 8 hour AEGL-3 for cis-DCE was based on the rat 4-hour trans-DCE lethal concentration 50 (LC50) from Kelly, 1999. The study by Kelly also reports a 4-hour LC50 for the cis-DCE, which could have been used to determine the cis-DCE AEGL-3 directly. It is more appropriate to use chemical specific data for the chemical in question when possible, rather than applying some modifying factor to data from another chemical.

There might also be a brief discussion of why another agency's minimum risk levels (MRLs) are equivalent rather than having a two-fold difference between the two MRL's. For instance, the Agency for Toxic Substance & Disease Registry (ATSDR) has equivalent acute MRLs for both cis- and trans-DCE. Is the lack of a difference in the cis-DCE and trans-DCE MRL a result of the other agency not believing there is a difference in toxicity between the cis-DCE and trans-DCE?

2. Comments on the derivation of AEGLs for hydrogen fluoride (HF)

The derivations for the AEGL-1 appear to be well documented and accurately derived.

The AEGL-2 10-minute value uses an interspecies uncertainty factor of 3 citing three separate reasons. Two of the reasons, i.e. that HF is a primary irritant and that the irritation endpoint seen in the key study is appropriate for human risk assessment, are valid. However, the argument regarding LC50 differences between the mouse and rat does not seem appropriate, based on other descriptions in the text. The text on page 28 of the technical support document notes that humans may be more sensitive than animals. There are no adequate exposure concentrations associated with lethality in humans for comparison with the rodent values. Therefore, the use of an interspecies factor that simply compares two rodent species' acute lethality values may not incorporate the full range of interspecies uncertainty. The use of the full 10-fold uncertainty factor would seem warranted, given the above considerations. The same rationale may be used to indicate the lack of support for a reduced interspecies uncertainty factor in the AEGL-3 30-minute, 1-hour, 4-hour and 8-hour values. These derivations used an interspecies uncertainty factor of 1 stating that the mouse was the most sensitive species. The reduction of the interspecies uncertainty factor to a value of 3 is particularly troubling in the instance of the AEGL-3 10-minute value, since the key study used an exposure level that was fatal to 1/20 rats

examined.

An intraspecies uncertainty factor of 3 was used in derivations of all AEGL-2 values. The text states that "HF reacts chemically with tissues of the respiratory tract and effects are unlikely to differ between individuals." However, Table 2 describes exposure concentrations associated with mild irritant effects in humans ranging from 0.2 to 7.8 parts per million (ppm) from the same author. This represents an almost 40x difference. A reduced intraspecies uncertainty factor is not supported if the studies by Lund are valid. In addition, the Agency for Toxic Substances and Disease Registry reports that people who are elderly, have magnesium deficiency, or with cardiovascular or kidney problems may be predisposed to the toxic effects of excess hydrogen fluoride (ATSDR, 1991, DRAFT, "Toxicological Profile for Fluorides, Hydrogen Fluoride and Fluorine"). This citation does not indicate whether this is true at acute exposures. If it is true in those cases, it indicates there may be significant numbers of individuals in the general population who are sensitive. The same rationale can be used to indicate lack of support for a reduced intraspecies uncertainty factor in the AEGL-3 derivations.

3. Comments on the derivation of AEGLs for hydrogen cyanide

The technical support document notes (page 20) that the AEGL-2 30-minute value is the same as the present U.S. Occupational Safety and Health Administration (OSHA) permissible exposure limit (PEL) and the 1-, 4- and 8-hour values are below the present OSHA PEL. This statement is presumably made in support of the AEGL-2 values providing appropriate protection. However, this author notes that the AEGL-2 values for 10-minute, 30-minute and 1 hour all exceed the National Institute for Occupational Safety and Health (NIOSH) short-term exposure limit (STEL) (and the previous OSHA PEL) of 4.7 ppm. The STEL is defined as the value that should not be exceeded at any time during a workday. Although the STEL is designed to provide protection against the disabling effects allowed by the AEGL-2 values, the STEL is created for the population of "healthy" adult workers. The AEGL values are designed for the general population, including sensitive individuals. The database of information on human exposures to hydrogen cyanide is not large. The fact that the AEGL-2 values exceed the STEL does not provide supportive evidence that they are appropriate for a population including sensitive individuals. This is particularly true if the data from Blanc, et al., (J. Am. Med. Assoc., 1985, v. 253, p. 367-371) are valid. They reported workers having symptoms including dizziness and paresthesia at 15 ppm. This value indicates that "healthy workers" experienced disabling symptoms below the AEGL-2 10 minute value.

4. Comments on the derivation of AEGLs for hydrogen sulfide

Of the three proposed AEGL values being established for hydrogen sulfide, AEGL-2 and AEGL-3 values appear to be justifiable based on their respective studies. However, the AEGL-1 value (0.03 ppm) causes concern due to the key study on which it is based. The key study for this value was a Texas Natural Resources Conservation Commission (TNRCC) memo from one staff member to another describing a mobile laboratory sampling trip to an oil refinery. The six staff members who were downwind of this site experienced eye, nose, and throat irritation allegedly due to hydrogen sulfide concentrations during a five-hour sampling episode. While

chemical exposure from oil refinery emissions could be measured, there was no forethought of scientific controls. Despite the eye, nose, and throat irritation, a number of confounding factors could have influenced these health effects. Some of these factors are: personal sensitivities, exposure to chemicals not measured, synergistic effects of the chemicals measured, and length of exposure. It is mentioned in the guidance document that a flat-lining approach was considered appropriate since mild irritant effects generally do not vary greatly over time. However, hydrogen sulfide deadens the sense of smell. This effect does vary over time. It is questionable whether duplication of this event would provide similar findings. The memo should be made available for review to determine if confounding factors were addressed. Overall, it would seem more plausible to base the AEGL-1 value on the state of California's "odor annoyance" threshold as stated in the guidance document. This method seems to have been conducted using scientific principles in an experimental setting. Maybe the California study should be used as the key reference and the TNRCC memo as supporting anecdotal documentation.

5. Comments on the derivation of AEGLs for 1,1,1,2-tetrafluoroethane

The technical support document was reviewed and appears well done.

Comments on the derivation of AEGLs for 1,1,1-trichloroethane

The technical support document was reviewed and appears well done.

Sincerely

Mary Lee Hultin
Toxics and Compliance Support Section
Air Quality Division
517-373-9845

MLH:SLB
cc: Cathy Simon, MDEQ
Gary Butterfield, MDEQ
Marco Bianchi, MDEQ

AF&PA

34750

AMERICAN FOREST & PAPER ASSOCIATION
Regulatory Affairs

BY HAND

April 14, 2000

OPPT Document Control Office
East Tower Room G-099
Waterside Mall
401 M St., S.W.
Washington, D.C.

Re: OPPTS – 00289
AEGLs – Hydrogen Sulfide

Ladies and Gentlemen:

The American Forest & Paper Association (AF&PA) is responding to the March 15, 2000 notice in the *Federal Register* (65 *Fed. Reg.* 14186) requesting comments on the proposed Acute Exposure Guideline Levels (AEGLs) for certain chemicals, including hydrogen sulfide. We appreciate the opportunity to comment.

AF&PA is commenting specifically on the proposed AEGL-1, the "non-disabling" level for hydrogen sulfide, of 0.03 ppm for all time periods. The proposal indicates that the basis for this value is found in a memorandum from the staff of a mobile laboratory operated by the Texas Natural Resources Conservation Commission (TNRCC). We have reviewed that internal memorandum and the "public draft" of the supporting documentation dated January 2000. AF&PA also reviewed an earlier draft of the AEGL documentation, and the contrast gives us cause for concern because the revised AEGL is not based on sound, peer-reviewed and published data.

Earlier Draft Based on Published, Controlled Study Selected from Literature Review

The earlier draft of the documentation for the AEGLs (marked NAC/Pro Draft 2: 7/98) prepared by Oak Ridge National Laboratory for discussion at the September 1998 public meeting proposed an AEGL-1 of 2.0 ppm (30 minute); 1.7 ppm (one hour); 1.2 ppm (four hours); and 1.1 ppm (eight hours). (hereinafter referred to as the 2 ppm proposal).

- That draft described extensive scientific literature on the acute effects of hydrogen sulfide, including numerous case reports and epidemiologic studies, as well as experimental studies. (1998 draft pp. 4-12.)

- The draft recounted the results of a number of controlled studies indicating that "no adverse effects were observed in male or female volunteers exposed to 5 or 10 ppm hydrogen sulfide while exercising to exhaustion." (1998 draft at 13, citing Bambhani and Singh 1991, Bambhani et al. 1996a, 1996b, Bambhani et al. 1994.)

- After review of the numerous published, peer-reviewed studies from literature, that draft proposed to rely upon an experimental study of asthmatics for the AEGL-1 (Jappinen et al. 1990). However, in our review of that study, we note that the authors conclude "when asthmatic subjects were exposed in controlled conditions to 2 ppm of hydrogen sulphide for 30 minutes, no significant changes in respiratory function occurred." Moreover, the authors state that this exposure did not produce any clinical symptoms among the 10 asthmatic subjects studied.

The 1998 draft identified the reviewers for hydrogen sulfide by name, phone number and e-mail, although not by affiliation. Based on the e-mail addresses, the three reviewers included a representative of TNRCC, a representative with what appears to be a California government address, and another state representative.

Revised Proposal Relying on Unpublished Data

The proposal in the March 15, 2000 *Federal Register* dramatically changes course. The 2 ppm proposal has disappeared, and in its place is a proposed AEGL-1 of 0.03 ppm.

Rejecting the numerous published case reports, epidemiologic studies and experimental studies without a stated basis for rejection, the proposal instead relies on an unpublished memorandum by a staff member of the TNRCC. With all due respect to the TNRCC, reliance on such data is inconsistent with the mission of the AEGL Advisory Committee and seemingly contrary to sound science.

- The TNRCC memorandum is unpublished and has not been subjected to peer review of any kind as far as we know. The memorandum is not even an official document of the TNRCC, but rather a trip report written by a single staff person. The AEGL Advisory Committee has no basis to rely on such data when extensive published, peer-reviewed data are available.

- The memorandum reports on field sampling downwind of a refinery and multiple other industrial facilities. The memorandum notes that one to four members of the sampling team experienced symptoms such as headaches and eye or throat irritation during various sampling events. It is not clear from the report how many staff members were present or whether the affected workers were the same in each instance. The draft AEGL documentation (p. 18) refers to six staff workers each experiencing all of the reported symptoms, which appears inconsistent with the memorandum. In any event, the reported symptoms represent unvalidated case reports of subjective symptoms, which have not been published in a scientific or medical journal. The persons reporting the symptoms may have experienced some reporting or recall bias, as they were the individuals conducting the air monitoring. They may also have been subjected to other influencing factors.

- The sampling encompassed not only hydrogen sulfide, but also benzene, MTBE, toluene, butadiene, cumene and sulfur dioxide. Any irritation experienced by the staff persons cannot be definitively attributed to a single chemical. MTBE and sulfur dioxide, for example, are irritants, and toluene can cause headaches. Further, it is not at all clear that the staff person reporting on the sampling is qualified to make such an assessment, or that if qualified, had adequate information to make an accurate diagnosis or attribution of causation.

- The California document cited in support of the AEGL-1 proposal (Amoore, "Perception of Hydrogen Sulfide Odor in Relation to Setting an Ambient Standard, April 10, 1985, ARB Contract A4-046-33) notes (at pages 34-35) that:

> Despite the relative convenience, precision and objectivity of ambient hydrogen sulfide measurements, it becomes apparent that they can be reliable as a basis for odor pollution control only in certain narrowly-defined situations, such as:
>
> 1. Where hydrogen sulfide is the sole, or at least the predominant and lowest-threshold, odorous species in the effluent.
> 2. Where the chemical mixture in the effluent is constant, and the hydrogen sulfide concentration has been previously demonstrated to be a consistent indicator of the overall odor threshold of the mixture. (Emphasis in original.)

These conditions are not satisfied in the TNRCC sampling.

- The air monitoring was conducted in a mobile van. It is not clear whether the symptoms occurred based on indoor or outdoor exposure. See, e.g., page 18 (symptoms occurred in workers exposed "in a monitoring van downwind from an oil refinery.") The presence of exhaust or generator fumes, build-up of gases used by sampling equipment, increasing carbon dioxide levels, exposure to solvents or reagents, or other factors could have affected the staff members.

In short, this anecdotal memorandum, while no doubt useful for purposes of TNRCC targeting its enforcement efforts, cannot be equated with the body of published literature on hydrogen sulfide, nor can its findings be reconciled with the peer-reviewed literature (including controlled studies) cited in the draft documentation.

The proposed documentation (at p. 18) cites a 1985 California document for information indicating that when an odor reaches approximately five times its odor threshold, "odor annoyance" occurs. The documentation asserts that the odor threshold for hydrogen sulfide – 0.008 ppm – times five is 0.04 ppm, a level of calculated "annoyance" comparable to the 0.03 ppm proposed AEGL-1. However, the reliability of this calculation is suspect.

- First, the AEGL documentation itself on page 1 puts the odor threshold for hydrogen sulfide at 0.02 to 0.13 ppm.

- Second, the 0.008 ppm odor threshold level used in the California document is the geometric mean of 26 separate reports of widely varying quality. (California document Table I, p. 12.) As the California document notes:

> "An immediately disturbing feature of this compilation is [the] wide range of values reported. Valentin's (1848) threshold is 20,000 times higher than Henning's (1924). Since then, the experimental techniques have evidently improved somewhat, and the range of values reported in the other 24 papers does not exceed a *500-fold variation.*" (Id. at 14, emphasis added.)

- Third, the multiplier of five applied to odor detection to identify the level of odor annoyance is based on a study of other chemicals. There is no evidence it is applicable to hydrogen sulfide. Respondents were asked to quantify emotional and social reactions as well as sensory and physiological responses. As the California document (p. 33) notes: "the California ambient standard [of 0.03 ppm] is basically intended to minimize odor annoyance and psychosomatic symptoms, such as those described by Winneke and Kastka (1977)." The AEGLs, on the other hand, are not intended to address psychosomatic symptoms.

Thus, the unpublished California review is not sufficient to support the unpublished Texas memorandum.

The March 2000 public draft continues to present the published case reports, epidemiologic and experimental data, in language identical to the earlier Oak Ridge 1998 draft. The proposal offers no basis for not relying on published, peer-reviewed literature in favor of the unpublished TNRCC report. We do not believe that the anecdotal and unscientific reports from the monitoring van episode should form the basis for setting the AEGL.

We urge the Committee to rethink this approach, and to use the best available published, peer-reviewed scientific evidence in establishing the AEGLs for hydrogen sulfide. This is particularly important if the values are to be used as "Interim" AEGL values prior to review by the National Research Council/National Academy of Sciences.[1]

We hope these comments will assist the Committee to establish AEGLs based on the best available science.

Respectfully submitted,

John L. Festa, Ph.D.
Senior Scientist

Susan S. Crowley
Director, Environmental Affairs

cc: Susan Wayland, OPPTS
William Sanders, OPPT
Joe Carra, OPPT

[1] 65 *Fed. Reg.* at 14187. We do not understand precisely what legal status EPA intends to accord such interim values.

AF&PA®

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AMERICAN FOREST & PAPER ASSOCIATION
Regulatory Affairs

BY HAND

April 14, 2000

OPPT Document Control Office
East Tower Room G-099
Waterside Mall
401 M St., S.W.
Washington, D.C.

Re: OPPTS – 00289
AEGLs – Hydrogen Sulfide

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AF&PA is commenting specifically on the proposed AEGL-1, the "non-disabling" level for hydrogen sulfide, of 0.03 ppm for all time periods. The proposal indicates that the basis for this value is found in a memorandum from the staff of a mobile laboratory operated by the Texas Natural Resources Conservation Commission (TNRCC). We have reviewed that internal memorandum and the "public draft" of the supporting documentation dated January 2000. AF&PA also reviewed an earlier draft of the AEGL documentation, and the contrast gives us cause for concern because the revised AEGL is not based on sound, peer-reviewed and published data.

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We urge the Committee to rethink this approach, and to use the best available published, peer-reviewed scientific evidence in establishing the AEGLs for hydrogen sulfide. This is particularly important if the values are to be used as "Interim" AEGL values prior to review by the National Research Council/National Academy of Sciences.[1]

We hope these comments will assist the Committee to establish AEGLs based on the best available science.

Respectfully submitted,

John L. Festa

John L. Festa, Ph.D.
Senior Scientist

Susan S. Crowley

Susan S. Crowley
Director, Environmental Affairs

cc: Susan Wayland, OPPTS
William Sanders, OPPT
Joe Carra, OPPT

[1] 65 *Fed. Reg.* at 14187. We do not understand precisely what legal status EPA intends to accord such interim values.

34900

CHEMICAL MANUFACTURERS ASSOCIATION

COURTNEY M. PRICE
VICE PRESIDENT
CHEMSTAR

April 14, 2000

U.S. Environmental Protection Agency
Office of Pollution Prevention and Toxics
Document Control Office (7407)
Ariel Rios Building
1200 Pennsylvania Avenue, N.W.
Washington, D.C. 20460

Re: Proposed Acute Exposure Guideline Levels (AEGLs),
Docket # OPPTS-002890

Dear Sir or Madam:

The Hydrogen Sulfide Panel of the Chemical Manufacturers Association (CMA) is pleased to submit these comments on EPA's proposed Acute Exposure Guideline Levels (AEGLs) for hydrogen sulfide. 65 Fed. Reg. 14186 (Mar. 15, 2000). The Panel includes individual companies and trade groups.

For the reasons stated in the appended comments, the Panel urges EPA to withdraw the proposed AEGLs for hydrogen sulfide and replace them with the Emergency Response Planning Guideline (ERPG) levels for hydrogen sulfide established in 1991 by the American Industrial Hygiene Association (AIHA) Emergency Response Guideline Committee. The Panel additionally urges EPA to revise the supporting documentation as recommended in the appended comments.

BEFORE THE
UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

COMMENTS OF THE CHEMICAL MANUFACTURERS ASSOCIATION HYDROGEN SULFIDE PANEL IN RESPONSE TO EPA'S PROPOSED AEGLs FOR HYDROGEN SULFIDE

National Advisory Committee for Acute Exposure Guideline Levels (AEGLs) for Hazardous Substances, Proposed AEGL Values Notice, 65 Fed. Reg. 14186 (Mar. 15, 2000)	)	OPPTS - 00289 FRL-6492-4

Courtney M. Price
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April 14, 2000

CHEMICAL MANUFACTURERS ASSOCIATION
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EXECUTIVE SUMMARY

The Hydrogen Sulfide Panel of the Chemical Manufacturers Association (CMA) submits these comments on EPA's proposed Acute Exposure Guideline Levels (AEGLs) for hydrogen sulfide. 65 Fed. Reg. 14186 (Mar. 15, 2000). The Panel includes domestic companies and trade groups.

These comments address only issues specific to hydrogen sulfide. The Panel additionally supports and incorporates by reference the comments separately submitted by the American Forest & Paper Association on the proposed values for hydrogen sulfide.

EPA should withdraw the proposed AEGLs for hydrogen sulfide and replace them with the American Industrial Hygiene Association's Emergency Response Planning Guideline levels for hydrogen sulfide. EPA at the least should withdraw the AEGL-1 values because they are scientifically indefensible. In addition, EPA should correct various errors and misstatements in the "Public Draft" Background Document.

TABLE OF CONTENTS

INTRODUCTION

The Hydrogen Sulfide Panel of the Chemical Manufacturers Association (CMA) submits these comments on EPA's proposed Acute Exposure Guideline Levels (AEGLs) for hydrogen sulfide. 65 Fed. Reg. 14186 (Mar. 15, 2000). The Panel includes domestic companies and trade groups.[1/]

These comments address only issues specific to hydrogen sulfide. The Panel additionally supports and incorporates by reference the comments separately submitted by the American Forest & Paper Association on the proposed values for hydrogen sulfide.

EPA proposes AEGL values for hydrogen sulfide (ppm(mg/m^3)) as follows:

Classification	10-min.	30-min.	1-hour	4-hour	8-hour
AEGL-1 (Nondisabling)	0.03 (0.04)	0.03 (0.04)	0.03 (0.04)	0.03 (0.04)	0.03 (0.04)
AEGL-2 (Disabling)	42 (59)	32 (45)	28 (39)	20 (28)	17 (24)
AEGL-3 (Lethality)	76 (106)	60 (85)	50 (71)	37 (52)	31 (44)

I. EPA SHOULD WITHDRAW THE PROPOSED AEGLS FOR HYDROGEN SULFIDE AND REPLACE THEM WITH AIHA'S ERPG LEVELS FOR HYDROGEN SULFIDE

The American Industrial Hygiene Association (AIHA) established in 1991 the

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1/ Panel members are: American Forest & Paper Association, American Petroleum Institute, Carbon Disulfide Panel of the Chemical Manufacturers Association, Metam-Sodium Task Force, and Montana Sulfur & Chemical Company.

Emergency Response Planning Guideline (ERPG) levels for hydrogen sulfide.[2/] ERPG levels consist of a three-tiered standard with one common denominator, a one-hour contact duration. ERPG-1 is 0.1 ppm; ERPG-2 is 30 ppm; and ERPG-3 is 100 ppm.[3/] The AIHA Emergency Response Committee, which established the ERPG for hydrogen sulfide, is composed of qualified representatives drawn from academia, government, and industry with backgrounds in industrial hygiene, medicine, and toxicology. The ERPG levels for hydrogen sulfide were established after an extensive and comprehensive peer review process.

EPA relied upon ERPG-2 levels as the basis for toxic endpoints specified for use in off-site consequence analyses for EPA's Risk Management Plan (RMP) regulations codified at 40 C.F.R. Part 68. As ERPG levels for hydrogen sulfide have been in use for almost a decade and are widely recognized by industry and others, it is unclear why the National Advisory Committee (NAC)/AEGL Committee is proposing different values.

2/ EPA, "Computer-Aided Management of Emergency Options (CAMEO®), Public Exposure Guidelines," <http://www.epa.gov/swercepp/cameo/expguide.htm>.

3/ ERPG levels are defined as follows:

> ERPG-3 is the maximum airborne concentration below which it is believed that nearly all individuals could be exposed for up to 1 hour without experiencing or developing life-threatening health effects.
>
> ERPG-2 is the maximum airborne concentration below which it is believed that nearly all individuals could be exposed for up to 1 hour without experiencing or developing irreversible or other serious health effects or symptoms which could impair an individual's ability to take protective action.
>
> ERPG-1 is the maximum airborne concentration below which it is believed that nearly all individuals could be exposed for up to 1 hour without experiencing other than mild transient adverse health effects or perceiving a clearly defined, objectionable odor.

Id.

This is particularly true given the dramatic departure of the values published in the *Federal Register* from the 1998 draft documentation for the AEGLs.[4/] The 1998 draft documentation proposed the following AEGL-1 values: 2.0 ppm (30 minutes); 1.7 ppm (one hour); 1.2 ppm (four hours); and 1.1 ppm (eight hours). These values were based on an extensive review of studies and the literature. EPA has offered no valid basis for its departure from them.

The Hydrogen Sulfide Panel thus urges EPA to withdraw the AEGL values and replace them with the AIHA ERPG levels, or explain why the ERPG levels are not scientifically defensible for these purposes.

II. EPA AT THE LEAST SHOULD WITHDRAW THE AEGL-1 VALUES BECAUSE THEY ARE SCIENTIFICALLY INDEFENSIBLE

EPA derived the AEGL-1 values on limited "human data" reportedly found in a Texas Natural Resources Conservation Commission (TNRCC) memorandum.[5/] According to the "Public Draft" Background Document for hydrogen sulfide, the AEGL-1 values were derived as follows:

> Since human data are available, they will be used to derive AEGL-1 values. Persistent odors, eye and throat irritation, headache, and

---

4/ Oak Ridge National Laboratory, NAC/Pro Draft 2: 7/98.

5/ 65 Fed. Reg. at 14194 (col 2). TNRCC (1998). Memorandum from Tim Doty to Joanne Wiersma. Corpus Christie Mobile Laboratory Trip, January 31-February 6, 1998; Real-Time Gas Chromatography and Composite Sampling, Sulfur Dioxide, Hydrogen Sulfide, and Impinger Sampling (Apr. 20, 1998).

> nausea were observed in six workers exposed to a mean concentration of 0.09 ppm [hydrogen sulfide] for approximately 5 hours in a monitoring van downwind from an oil refinery (TNRCC, 1998). An uncertainty factor of 3 was applied to account for intra species variability since minor irritation is not likely to vary greatly between individuals. The value was flat-lined across the 10-, and 30-minute, 1-, 4-, and 8-hour exposure time points. The flatlining approach was considered appropriate since mild irritant effects generally do not vary greatly over time. The AEGL-1 values for hydrogen sulfide are presented in Table 5, and the calculations for these AEGL-1 values are presented in Appendix A.[5/]

EPA cannot rely upon these data for several reasons. First, these data do not appear to be verified or scientifically valid. The TNRCC memorandum is unpublished and has not been subjected to any peer review. Indeed, it appears to be merely a trip report. EPA should not rely on such a document for standard setting, especially when, as here, extensive published peer review data are available.

Second, the six workers downwind of an oil refinery reportedly were exposed to concentrations of 0.09 ppm hydrogen sulfide, and other specified and unspecified contaminants, including sulfur dioxide. The effects noted, which include persistent odors, eye and throat irritation, headache, and nausea, could have been caused by any one or more of the constituents to which the six workers reportedly were exposed during the period in question. EPA wrongly

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5/ United States Environmental Protection Agency, Office of Polution Prevention and Toxics, "Hydrogen Sulfide, CAS Reg. No. 7783-06-4, Proposed Acute Exposure Guideline Levels (AEGLs), Public Draft" at 18 (Background Document).

assumes that each of these health effects was caused by exposure to hydrogen sulfide alone. There is nothing, however, in the record to support this conclusion.

Third, EPA offers no basis for using these limited, unverified data for any standard setting purpose.

EPA also believes that these AEGL-1 values are justified by "information stating that when an unpleasant odor reaches approximately 5-times its odor threshold, odor annoyance is attained."[2/] EPA relies upon a 1985 California Air Resources Board (CARB) memorandum that apparently applies this rule of thumb in certain, unstated circumstances in California. EPA should not rely upon this anecdotal rule of thumb, presumably used in California, as support for its derivation of an AEGL-1 value for hydrogen sulfide.

The Panel requested, but was unable to obtain, a copy of this guidance from CARB or EPA. The fact that the State of California uses this approach does not make it appropriate for purposes of deriving AEGL values. The fact that the guidance was not in the public docket limits the Panel's right under the Administrative Procedure Act to review and comment on information that EPA has relied upon in determining AEGL values. For this reason, EPA's reliance on the guidance is therefore inappropriate and unlawful.

Even if the document were available, there is no reason to believe that reliance on one State's "guidance" for establishing "odor annoyance" correlates in any meaningful way to the derivation of an AEGL-1 value for hydrogen sulfide. In the absence of any explanation for this reliance, the Agency has not provided an adequate basis for supporting the AEGL-1 value.

2/ *Id.* The value was derived as follows: the geometric mean of hydrogen sulfide's odor threshold was multiplied by five (0.008 ppm x 5 = 0.04 ppm).

For these reasons, AEGL-1 values for hydrogen sulfide for all durations should be withdrawn.

III. EPA SHOULD CORRECT VARIOUS ERRORS AND MISSTATEMENTS IN THE "PUBLIC DRAFT" BACKGROUND DOCUMENT

The Background Document contains numerous errors and misstatements. As an example, on page 1, the introduction states that hydrogen sulfide is "synthesized for use in rayon manufacturing, as an agricultural disinfectant, and as an additive in lubricants." This is incorrect. Hydrogen sulfide is not synthesized for use in rayon manufacture. It is, however, a byproduct of the viscose process which is used to manufacture a number of different cellulosic products, including rayon. Additionally, the Panel does not understand hydrogen sulfide to be used as an agricultural disinfectant. Rather, hydrogen sulfide is a byproduct emission of certain soil fumigants, including metam-sodium. Finally, hydrogen sulfide is not a lubricant additive, but can be generated as certain lubricant packages (ZDP-containing) "wear" and break down during normal use.

Finally, the Panel urges EPA to clarify its references to the Occupational Safety and Health Administration (OSHA) permissible exposure limit (PEL) for hydrogen sulfide. Pages 21 and 24 of the Background Document cite the PEL as "OSHA 1997." This may be erroneously interpreted to mean that OSHA established or revised the PEL in 1997. The Panel urges EPA to revise the cite to correct any such potential misimpression.[8/]

[8/] Additionally, the Panel notes that page 21 of the Background Document erroneously refers to the "Occupational Safety and Health Association." The Panel urges EPA to change the word "Association" to "Administration."

PPG Industries, Inc. One PPG Place Pittsburgh, Pennsylvania 15272

James A. Barter, Ph.D.
Director, Environmental Health Sciences
Environment, Health & Safety

Phone: 412-434-2801
Fax: 412-434-3193

April 14, 2000

Subject: Docket Control Number OPPTS-00289

To whom it may concern:

The attached comments are submitted in response to the March 15,2000 Federal Register Notice and request for comments on the National advisory Committee for Acute Exposure Guideline Levels (AEGLs)for Hazardous Substances; Proposed AEGL values.

Thank you for your consideration of these comments.

Sincerely yours,

James A. Barter, Ph.D. DABT

Comments on the Derivation of Acute Exposure Guideline Levels (AEGLs) for *trans*-1,2-Dichloroethylene and *cis*-1,2-Dichloroethylene

The following comments are directed to the Technical Support Document for the development of the AEGLs and the derivation of the AEGL values.

Description:

The document states " 1,2-Dichloroethylene is a flammable liquid existing in both *cis*- and *trans*-forms and as a mixture of these two isomers. It has been used as an intermediate in the production of chlorinated solvents and as a low-temperature extraction solvent for decaffeinated coffee, dyes, perfumes, lacquers, and thermoplastics." Although this statement correctly summarizes the historical information on 1,2-dichloroethylenes, it does not characterize the present information on uses of these materials in the United States. Today, dichloroethylenes are produced as one of a number of C2 chlorocarbons produced in the reaction mixture resulting from processes involved in the chlorination of ethylene to produce chlorinated monomers and solvents. The only commercial dichloroethylene product in the United States is *trans*-1,2-dichloroethylene, produced by PPG Industries, Inc. This material is isolated by distillation and sold as a highly purified product. The only market for this product is for use in precision cleaning of electronic equipment, where the material is used as a major ingredient in formulations that also contain fluorinated organic cleaning agents. These formulations are generally used in aerosol cans.

Genotoxicity:

The document states "No data concerning the genotoxicity of 1,2-dichloroethylene were identified in the available literature". There are several studies on genotoxicity available from the literature. The ATSDR Toxicological Profile for Dichloroethylenes lists several of these studies and PPG will provide a list of studies if requested. In general, *trans*-1,2-dichloroethylene has been negative in these assays, whereas the data on *cis*-1,2-dichloroethylene are equivocal in some of the assays.

Derivation of AEGL Values:

In deriving AEGL values for the dichloroethylenes, human data from a study by Lehman and Schmidt-Kehl (1936) were used extensively. Although human data are appropriately used in preference to animal data where robust human data exists, careful judgement must be exercised to evaluate the quality of the human data. With regard to this particular study, there are several issues which suggest that these data should not be given overarching credence to the exclusion of data from animal studies. The studies were conducted in 1936 using what was good technique at the time. However, there are valid questions concerning both the composition of the test material and the experimental methodology for the human exposures.

The test material in the Lehman and Schmidt-Kehl study was described as *trans*-1,2-dichloroethylene that had been purified by fractional distillation and was characterized by physical properties such as refractive index, boiling point, etc. In 1936, analytical capabilities were limited and all of the sophisticated instrumental methods for identification of impurities were yet to be developed. It is likely that the test material utilized in these experiments contained some unknown amount of *cis*-1,2-dichloroethylene. Data from the literature, as well as recently conducted studies submitted to the Agency as part of the ongoing AEGL process, have established that *cis*-1,2-dichlorethylene is more toxic than *trans*-1,2-dichloroethylene. Therefore, the results obtained in this study may not be characteristic of the responses that would be produced by exposure to pure *trans*-1,2-dichloroethylene.

The human responses reported in the Lehman and Schmidt-Kehl study are based on the self-recorded subjective observations of only two (2) subjects who self-administered the test material. The relative significance of these data compared to the robust data set from recent animal experiments conducted under

Good Laboratory Practices must be considered when choosing information from which to derive AEGL values.

Recommendations:

AEGL-1
This value should be based on ocular irritation in rats observed in Hurt et al., 1993.

AEGL-2
This value should be based on narcosis in rats observed in Hurt et al., 1993.

AEGL-3
This value should be based on No Effect Level for death in Rats observed in Kelly, 1998 and 1999.

References:

Hurt, M.E., Valentine, R., and Alvarez, L. 1993. Developmental toxicity of inhaled *trans*-1,2-dichloroethylene in the rat. Fund. Appl. Toxicol. 20: 225-230.

Kelly, D.P. 1998. *trans*-1,2-Dichloroethylene: 90-Day Inhalation toxicity study in the rat. E.I. du Pont de Nemours and Company, Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE. Laboratory Project No. HL-1998-00952.

Kelly, D.P. 1999. t*rans*-1,2-Dichloroethylene and *cis*-1,2-dichloroethylene: Inhalation median lethal concentration (LC50) study in rats. E.I. du Pont de Nemours and Company, Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE. Laboratory Project ID: DuPont-2806.

Comments on USEPA's Proposed Acute Exposure Guideline Levels (AEGLs) for Hydrogen Sulfide

Prepared for
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On Behalf of
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14 April 2000

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Comments on USEPA's Proposed Acute Exposure Guideline Levels (AEGLs) for Hydrogen Sulfide

On 15 March 2000, the US Environmental Protection Agency (USEPA) issued the recommendations of the National Advisory Committee for Acute Exposure for Hazardous Substances (NAC/AEGL Committee), under the authority of the Toxics Substances Control Act and its Amendments, for AEGL values of three types for 10 chemicals, including hydrogen sulfide (USEPA, 2000). In this notice, the USEPA has requested comments on the proposed values and their underlying scientific foundation as expressed not only the Executive Summaries but also to a greater degree in the Agency's Technical Support documents.

The comments contained herein address the proposed AEGLs solely for hydrogen sulfide, and are offered to enlighten the Agency's final selection of AEGL values for hydrogen sulfide that meet the prescribed definitions of each type of AEGL with the soundest scientific basis.

We agree with the Agency's conclusion that sufficient evidence exists to establish AEGL-1, AEGL-2, and AEGL-3 values. However, we specifically disagree with some of the Agency's interpretations of toxicological data supporting the derivation of AGEL-1 and AEGL-2 for hydrogen sulfide. Our comments, presented below, are confined to AGEL-1 and AEGL-2 values.

AEGL-1: Nondisabling

The Agency recommends an AEGL-1 for hydrogen sulfide of 0.03 ppm for 10 minutes, 30 minutes, one hour, four hours, and eight hours.

> **Based on the scientific strength of evidence, the basis for this AEGL-1 should be the study by Jappinen *et al.* (1990) rather than the report by TNRCC (1998).**

The study by Jappinen *et al.* (1990) on 10 asthmatics exposed to 2 ppm hydrogen sulfide for 30 minutes provides a suitable scientific basis on which to estimate an AEGL-1 for hydrogen sulfide. This well controlled laboratory experiment was conducted on hypersensitive individuals (*i.e.*, asthmatics); thus its findings represents a highly robust and conservative basis on which to set an AEGL-1. The medical consequences are consistent with the definition for an AEGL-1.

We note that, in 1998, the Agency proposed this study for the AEGL-1 for hydrogen sulfide, and estimated values of 2 ppm (30 minutes), 1.7 ppm (one hour), 1.2 ppm (four hours), and 1.1 ppm (eight hours) through the application of exponential scaling (equation of $c^{4.36} \times t = k$) used to derive the AEGL-2 and AEGL-3. This evaluation better represents adverse health effects associated with low dose exposures to hydrogen sulfide.

The basis recommended in the Agency's current proposal lies in sharp contrast to the data in the Jappinen *et al.* (1990) study. That contrast is heightened when one observes that the resulting value proposed in its present proposal represents a 98.5% reduction from the value proposed in 1998. Such a reduction must be supported by sound scientific analysis, not anecdotal data at best.

In its present proposal, USEPA relied on information described in a memorandum for the Texas Natural Resources Conservation Commission (TNRCC, 1998) pertaining to offsite air sampling conducted downwind of an oil refinery for approximately five hours. According to the Agency, this unpublished memorandum reported: "persistent odors, eye and throat irritation, headache, and nausea" for six workers over the test period at an average hydrogen sulfide concentration of 0.09 ppm. From this information, the Agency applied an uncertainty factor of three to account for intraspecies variability to derive a value of 0.03 ppm for each duration, based on a "flat-line" assumption.

However, in accepting the TNRCC memorandum as the basis of the AEGL-1, the Agency has ignored several important considerations regarding analytical sampling conducted in the field; the very least of which is the diverse nature of emissions which may have confounded the analysis referred to in TNRCC's memo. In fact, the Agency has acknowledged as much by noting that "sulfur dioxide, benzene, methyl t-butyl ether, and toluene were also detected." Therefore, the effects reported could not be attributable solely to hydrogen sulfide, as USEPA suggests. Although the Agency posits that the "concentrations of these chemicals would not be expected to cause health effects," clearly the mild irritant effects reported by TNRCC could be attributable to any number of airborne contaminants, including but certainly not limited to sulfur dioxide, benzene, methyl-*t*-butyl ether, toluene, and hydrogen sulfide.

Furthermore, the well known and extensive variability and unreliability of field monitoring instrumentation, in particular mobile equipment, raises serious doubts about the validity of the reported and as yet unsubstantiated concentrations.

Finally, the TNRCC data are anecdotal and have yet to be replicated. As such, the TNRCC report provides only marginal support for any AEGL-1 values.

Consequently, USEPA should rely on the findings of the Jappinen *et al.* study over the unsubstantiated report of TNRCC as the main basis on which to estimate an appropriate AEGL-1 value for exposures to hydrogen sulfide.

The flat-line approach for the AEGL-1 is not justified, and the Agency's traditional equation to adjust for duration of exposure should be employed for AEGL-1 as for the AEGL-2 and AEGL-3.

In its proposal, USEPA considered the "flat-line" approach to be relevant inasmuch as: "mild irritant effects generally do not vary greatly over time." The flat line approach has yet to be validated for hydrogen sulfide, and the majority of the toxicity data indicate that response is dependent not only on atmospheric concentration but also on duration of exposure. The application of the Agency's scaling equation (sometimes referred to as "Haber's Law") should be applied to the AEGL-1 as it is for the AEGL-2 and the AEGL-3.

The application of an uncertainty factor of three for intraspecies variability for the range of exposure durations is considered appropriate for the derivation of an AEGL-1 value since the variability in susceptibility is known to be relatively narrow and the effects do not appear to be cumulative over the time covered by the AEGL.

Consequently, USEPA should rely on the findings of the Jappinen *et al.* study to estimate an appropriate AEGL-1 value for exposures to hydrogen sulfide and apply the appropriate scaling, as articulated above and in the Agency's proposed 1998 AEGL-1 for hydrogen sulfide. In so doing, the resultant AEGL-1 values of 2 ppm (30 minutes), 1.7 ppm (one hour), 1.2 ppm (four hours), and 1.1 ppm (eight hours) would better represent adverse health effects associated with low dose exposures to hydrogen sulfide.

AEGL-2: Disabling

The Agency recommends AEGL-2 for hydrogen sulfide of 42 ppm (10 minutes), 32 ppm (30 minutes), 28 ppm (one hour), 20 ppm (four hours), and 17 ppm (eight hours).

The findings of the most appropriate studies were selected as the basis for the AELG-2; however, the air concentration level of 300 ppm, and not 200 ppm, conforms to the selection criteria for the AEGL-2.

To derive the AEGL-2, USEPA relied on two studies (Green *et al.*, 1991; Khan *et al.*, 1991), which reported:

> "No adverse clinical signs or gross lung pathology was noted effects was observed in animals exposed to 200 ppm; however, there was a significant ($p<0.001$) increase in protein and lactate dehydrogenase. ... Rats exposed to 300 ppm hydrogen sulfide were visibly stressed during the exposure period and lungs showed focal areas of red atelectasis and patchy alveolar edema with perivascular and peribronchial interstitial edema."

Likewise, Green *et al.* (1991) researchers reported the following at 300 ppm hydrogen sulfide:

> "...focal areas of red atelectasis and patchy alveolar edema with perivascular and peribronchial interstitial edema."

These data suggest that "*serious, long-lasting effects*" were evidenced at 300 ppm and not the 200 ppm cited by the Agency. In addition, when one examines the Khan *et al.* (1990) study, further corroboration of this conclusion is derived.

In the Khan *et al.* (1990) study, Fischer 344 rats were exposed to 0, 10, 50, 200, 400, and 500-700 ppm of hydrogen sulfide. While this study reported decreases in cytochrome *c* oxidase and other enzymatic activity in lung mitochondria, the researchers also reported oxidase activity returning to normal post-exposure. These data suggest a reversibility at lower exposure doses, including 200 ppm.

The conclusion that 200 ppm is an inappropriate basis for the AEGL-2 selection is further supported by another Khan *et al.* study (1991) on Fischer 344 rats at similar exposure concentrations (0, 50, 200, and 400 ppm). In this study, the researchers reported significantly decreased cellular activity at 400 ppm. Based on these data, as well as the Green *et al.* (1991) and Khan *et al.* (1990) study, it is evident that the selection of 200 ppm for AEGL-2 derivation is inappropriate based on the weight-of-evidence presented in these studies.

In the preface of the proposed AEGL for hydrogen sulfide, the Agency specified the following definition of an AEGL-2:

> "AEGL-2 is the airborne concentration (expressed as ppm or mg/m^3) of a substance at or above which it is predicted that the general population, including susceptible but excluding hyper-susceptible individuals, could experience *irreversible or other serious, long-lasting effects* or impaired ability to escape. Airborne concentrations below AEGL-2 but at or above

AEGL-1 represent exposure levels which may cause notable discomfort." (emphasis added)

Clearly, the 300 ppm level, and not the 200 ppm level, meet the Agency's definition for the AEGL-2, and should be selected as the dose from which to estimate the AEGL-2 for each relevant duration of exposure.

With the 300 ppm atmospheric level of hydrogen sulfide selected as the pivotal exposure concentration, the AEGL-2 for 4 hours should be 30 ppm and not 20 ppm.

The Agency originally applied an uncertainty factor of three to extrapolate from animals to humans and an additional uncertainty factor of three to account for sensitive individuals (total UF = 10) to derive a 4-hour AEGL. This 10-fold uncertainty factor is appropriate to apply to the concentration level of 300 ppm, in which case the four-hour AEGL-2 is estimated to be 30 ppm. This four-hour value is then exponentially scaled, using USEPA's methodology (equation of $c^{4.36} \times t = k$), to the remaining exposure durations, resulting in AEGLs of 62 ppm (10 minutes), 48 ppm (30 minutes), 41 ppm (one hour), and 25 ppm (eight hours).

Conclusions

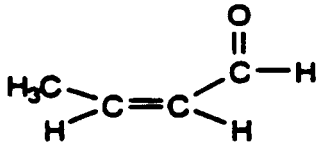
Given that 90% of all atmospheric hydrogen sulfide is derived from natural sources (ATSDR, 1997), the establishment of appropriate and defensible Acute Exposure Guideline Levels (AEGL) for hydrogen sulfide not only serves an important role in health protection but also provides unique challenges.

AEGL-1 values are not correct by failing to accommodate duration of exposure and are not supported by the strongest scientific evidence; they should be revised accordingly. Likewise, the AEGL-2 values are unjustifiably low, and should be increased in accordance with the supporting data. In each case, the data are sufficient to derive reasonably confident AEGL values; however, the databases for each are admittedly limited and should prompt some consideration by the Agency for additional research.

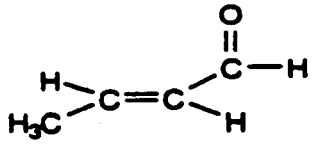
NAC/Draft 2: 4/2000

ACUTE EXPOSURE GUIDELINE LEVELS (AEGLs) FOR CROTONALDEHYDE

[CAS Reg. No. 4170-30-3 (mixture of cis and trans isomers) and 123-73-9 (trans isomer)]



Cis isomer



Trans isomer

ORNL Staff Scientist: Sylvia Milanez

Chemical Manager: Doan Hansen

Chemical Reviewers: George Alexeeff and Larry Gephart

April 27, 2000

NAC/AEGL Committee Members:

AEGL values for the 30-min, 1-, 4-, and 8-hour time points for crotonaldehyde were approved by the NAC/AEGL Committee in June, 1998. The crotonaldehyde document has been revised to include newly derived 10-minute AEGL values (i.e., 2nd draft). Only the 10-minute values are presently under consideration by NAC/AEGL Committee.

Sylvia Milanez,
ORNL

AEGL-1 VALUES FOR CROTONALDEHYDE – Apply to *trans*-crotonaldehyde (123-73-9) and commercial *cis/trans*-crotonaldehyde mixture (> 95% *trans* isomer; 4170-30-3)				
10 minutes	30 minutes	1 hour	4 hours	8 hours
0.19 ppm [0.53 mg/m^3]	0.19 ppm [0.53 mg/m^3]	0.19 ppm [0.53 mg/m^3]	0.19 ppm [0.53 mg/m^3]	0.19 ppm [0.53 mg/m^3]

Reference: Fannick, N. 1982. Sandoz Colors and Chemicals, East Hanover, New Jersey (Health Hazard Evaluation Report, No. HETA-81-102-1244), Cincinnati, OH, United States National Institute for Occupational Safety and Health, Hazard Evaluations and Technical Assistance Branch.

Test Species/Strain/Sex/Number: Humans; number not specified but likely <10

Exposure Route/Concentrations/Durations: Inhalation for < 8 hours to 0.56 ppm; highest measured air concentration was 1.1 ppm.

Effects: Slight eye irritation.

Endpoint/Concentration/Rationale: Workers exposed to 0.56 ppm for a portion of their 8-hour work shift occasionally had mild eye irritation.

Uncertainty Factors/Rationale:
Total uncertainty factor: 3
Interspecies: Not applicable
Intraspecies: 3: The critical effect (slight eye irritation) was mild; it is not expected that the degree of eye irritation would vary greatly among humans.

Modifying Factor: None

Animal to Human Dosimetric Adjustment: Not necessary.

Time Scaling: Not performed because another human study suggested it was not appropriate (the degree of irritation was much greater at shorter time periods than longer time periods for the same Ct); the same value is adopted for 10 minute to 8-hour exposures.

Data Quality and Support for AEGL-1 Values: Database was limited but included human data. The key study was conducted by NIOSH and crotonaldehyde concentrations were measured analytically. A possible confounding factor was the co-exposure of the workers to several other airborne chemicals, although crotonaldehyde was probably the most irritating and the degree of toxicity in the key study was mild.

AEGL-2 VALUES FOR CROTONALDEHYDE – Apply to *trans*-crotonaldehyde (123-73-9) and commercial *cis/trans*-crotonaldehyde mixture (> 95% *trans* isomer; 4170-30-3)				
10 minutes	30 minutes	1 hour	4 hours	8 hours
27 ppm [76 mg/m^3]	8.9 ppm [25 mg/m^3]	4.4 ppm [13 mg/m^3]	1.1 ppm [3.2 mg/m^3]	0.56 ppm [1.6 mg/m^3]

Reference: Rinehart, W. 1967. The effect on rats of single exposures to crotonaldehyde vapor. Amer. Ind. Hyg. Assoc. J. 28:561-566.

Test Species/Strain/Sex/Number: Male Sprague-Dawley rats; 12-16 per Ct (concentration x time) range

Exposure Route/Concentrations/Durations: Inhalation for 5 -240 minutes; individual concentrations and exposure times were not given but only the C x t values, which ranged from 100-32,000 ppm-minutes.

Effects: Decreased pulmonary function (manifest as a reduction in carbon monoxide and ether uptake rates compared to pre-exposure values) was seen at ≥2000 ppm-min, respiratory bronchiole proliferative lesions at ≥8000 ppm-min, and death at ≥16,000 ppm-min.

Endpoint/Concentration/Rationale: Pulmonary impairment in rats (20-40% decreased rate of carbon monoxide and ether uptake) and microscopic bronchiole proliferation at 8000 ppm-min. The endpoint is expected to also occur in humans.

Uncertainty Factors/Rationale: Total uncertainty factor: 30

Intraspecies: 3 - Crotonaldehyde acts primarily as a surface-contact irritant and the degree of irritation is not expected to vary greatly among humans.

Interspecies: 10 - Based on lack of actual concentration and time data and the stated variability in the animal responses, and the absence of supporting animal or human studies.

Modifying Factor: None

Animal to Human Dosimetric Adjustment: Not applied

Time Scaling: Concentration and time appeared to be roughly equally important for toxicity, i.e., $C^1 \times t = k$. Only Ct values were given in study, and not actual exposure concentrations and times. AEGL-2 values were calculated by dividing 8000 ppm-min by 10, 30, 60, 240, or 480 minutes.

Data Quality and Support for AEGL Values: The database of appropriate studies was small. The key study appeared to be well-conducted and crotonaldehyde air concentrations were measured, although the actual exposure concentrations and times were not given.

Pulmonary responses of rats exposed to 10-580 ppm crotonaldehyde for 5 minutes to 4 hours (data from Rinehart, 1967)				
Conc. x time range (ppm-min)	Geometric mean conc. x time	No. animals	CO uptake rate (% pre-exposure ± SD)	Ether uptake rate (% pre-exposure ± SD)
Controls	0	12	99.5 ± 12.5	103.1 ± 12.8
1000-2000	1330	12	92.9 ± 9.0	94.8 ± 9.4
2000-4000	2730	12	89.9 ± 5.6**	92.8 ± 5.7*
4000-8000	5390	12	86.7 ± 11.3**	91.0 ± 14.9*
8000-16,000	10,940	12	73.3 ± 12.8**	81.2 ± 9.6**
16,000-32,000	21,430	10	58.3 ± 10.8**	67.0 ± 9.2**
16,000-32,000 (animals died)	28,900	4	< 40	<40

Significantly different from controls: *$p \leq 0.10$ **$p < 0.05$

- Proliferative respiratory bronchiole lesions were found 3 days after exposure above 8000 ppm-min. Edema was seen only where death occurred within 24 hrs.

- Concentration and time were ~similarly important for toxicity.

NAC/Draft 2: 4/2000

ACUTE EXPOSURE GUIDELINE LEVELS (AEGLs)

FOR

ALLYLAMINE

(CAS Reg. No. 107-11-9)

$$H_2C{=}C{-}CH_2{-}NH_2$$

ORNL Staff Scientist: Sylvia Milanez

Chemical Manager: Loren Koller

Chemical Reviewers: Mark McClanahan, Robert Hazen

April 27, 2000

Allylamine 2nd Draft TSD major changes

The Technical Support Document (TSD) for cyclohexylamine was originally presented at the June 1997 NAC/AEGL meeting. The NAC approved AEGL-2 and AEGL-3 values and determined that there were inadequate data to develop AEGL-1 values. The cyclohexylamine TSD was presented to the COT/AEGL subcommittee in November 1999. It was recommended that AEGL-1 values be developed and that an n-value (in $C^n t = k$) be calculated from the cardiotoxicity data of Guzman et al. (1961) and used to time-scale AEGL-2 values. The following major changes are reflected in the 2nd draft TSD:

- An AEGL-1 value is proposed for 10 minutes to 1 hour based on a human 5-minute study
- Different values are proposed for the AEGL-2 based on the same key study (Guzman et al., 1961), but using a different exposure scenario and n-value (in $C^n t=k$) derived from the key study.
- The rationale for using the (same) uncertainty factors was altered slightly
- Tables 4, 5, and 6 were expanded and/or reorganized
- **10-minute values were developed for all three AEGL levels**

Metabolism and Mechanism of Toxicity

- No human or animal inhalation exposure metabolism studies were located.

- Allylamine causes severe myocardial damage followed by vascular smooth muscle injury (in aorta and medium-sized and small muscular arteries) in a variety of animal species.

- Orally administered allylamine was shown to be metabolized to acrolein and hydrogen peroxide. The mechanism of cellular damage is proposed to be lipid peroxidation by acrolein, and to involve the modulation of glutathione status and damage of the mitochondrial membranes by acrolein (or another unknown metabolite) and hydrogen peroxide.

- The metabolite acrolein has been detected in both rat and human aorta, myocardium, and liver homogenates incubated with allylamine.

- Rats gavaged with radiolabeled allylamine had radioactivity in many organs, the greatest amount in aorta and coronary arteries. A fraction (30-40%) of the animals, however, had counts in aorta 10 to 20-fold lower than others (intraspecies variability).

AEGL-1

Key study: Hine et al., 1960. Humans (35 volunteers) were exposed for 5 minutes to ≥2.5 ppm allylamine.

Toxicity endpoint: Sensory irritation (eye and nose irritation and pulmonary discomfort)
Scaling: None: 2.5 ppm = *k* (flat-lining across time was considered appropriate since mild irritant effects generally do not vary greatly over time)

Total uncertainty factor: 3
Interspecies - none
Intraspecies - 3: degree of sensory irritation is not expected to vary greatly among humans

AEGL-1 FOR ALLYLAMINE				
10 minute	**30 minute**	**1 hour**	**4 hours**	**8 hours**
0.83 ppm [1.9 mg/m^3]	0.83 ppm [1.9 mg/m^3]	0.83 ppm [1.9 mg/m^3]	NR [1]	NR [1]

[1]NR = Not Recommended because exposure could cause effects within scope of AEGL-2

- Supported by mouse RD_{50} = 9 ppm (study of Gagnaire et al., 1989; 1993): Alarie (1981) proposed that exposure to 0.1 x RD_{50} (i.e. 0.9 ppm) for hours-days is expected to produce some sensory irritation.

- Human odor threshold for allylamine is unknown but shown in key study to be < 2.5 ppm

AEGL-2

Key study: Guzman et al. (1961). Male Long-Evans rats (1-20/group) were exposed to 20-100 ppm allylamine for 4-48 hours and sacrificed for analysis after 8 hours-14 days. In key scenario, exposure for 14 hours to 60 ppm resulted in cardiovascular lesions (scattered myofibril fragments with loss of striation, perivascular edema, and cellular infiltration).

Toxicity endpoint: Cardiovascular lesions

Scaling: $C^n \times t = k$ where $n = 1.71$, based on regression analysis of data from key study

Uncertainty factors: Total uncertainty factor: 100

Interspecies- 10 to account for the lack of acute toxicity studies and toxicokinetic and metabolism data from other species

Intraspecies- 10 because significant intraspecies variation occurred in the rat cardiotoxic responses in the key study, and there was no data to determine the human variability of allylamine-induced cardiotoxicity

AEGL-2 FOR ALLYLAMINE				
10 minute	**30 minute**	**1 hour**	**4 hours**	**8 hours**
8.0 ppm [18 mg/m^3]	4.2 ppm [9.8 mg/m^3]	2.8 ppm [6.5 mg/m^3]	1.2 ppm [2.8 mg/m^3]	0.83 ppm [1.9 mg/m^3]

COMPARISON OF CURRENT 2ND DRAFT AND EARLIER PROPOSED AEGL-2 KEY SCENARIOS AND VALUES FOR ALLYLAMINE

CARDIOTOXIC EFFECTS IN RATS AFTER A SINGLE ALLYLAMINE INHALATION EXPOSURE (Data from Guzman et al., 1961)					
Exposure hours	**Conc. (ppm)**	**Total no. rats exposed**	**Number rats sacrificed @ given time[2]**	**Lesion**	**Histologic heart changes**
0	0	5	all @ 14 days	0	Occasional suggestive areas of round-cell infiltration
CURRENT -- 2nd DRAFT					
14	60	4	1 @ 18 hrs 1 @ 2 days 2 @ 8 days	+ + +	Scattered myofibril fragments with loss of striation Perivascular edema, cellular infiltration
EARLIER PROPOSED					
16	40	20	11 @ 8-17 hrs 4 @ 7 days 5 @ 14 days	0 0 0	Occasional suggestive areas of round cell infiltration, edema of some small vessel walls

[1]Calculated from the beginning of the exposure period. Animals died by sacrifice except as noted.

AEGL-2						
UFs	**10 minute**	**30 minute**	**1 hour**	**4 hours**	**8 hours**	**Endpoint (Reference)**
Intra=10 Inter=10 **n=1.71**	**8.0 ppm**	**4.2 ppm**	**2.8 ppm**	**1.2 ppm**	**0.83 ppm**	Round cell infiltration of heart, edema of small coronary vessel walls
Intra=10 Inter=10 n=0.8458	Not proposed	11 ppm	4.7 ppm	0.91 ppm	0.40 ppm	Round cell infiltration of the heart, edema of small coronary vessel walls

AEGL-3

Key study: Hine et al., 1960. Rat inhalation LC_{50} study.

Toxicity endpoint: Lethality thresholds, estimated from LC_{01} values obtained by probit analysis:
1- hour LC_{01} = 533 ppm
4- hour LC_{01} = 104 ppm
8- hour LC_{01} = 69.2 ppm

Scaling: $C^n \times t = k$ where n=0.8458, based on regression analysis of key study; used only for derivation of the **10 and** 30 minute values by scaling from 1-hr LC_{01}

Uncertainty factors: Total uncertainty factor: 30
Intraspecies - 3 because lethality, as an endpoint associated with severe pulmonary edema, is not likely to vary considerably among humans
Interspecies - 10 **to account for the lack of acute toxicity studies and toxicokinetic and metabolism data from other species**

AEGL-3 FOR ALLYLAMINE				
10 minute	**30 minute**	**1 hour**	**4 hours**	**8 hours**
145 ppm [338 mg/m^3]	40 ppm (94 mg/m^3)	18 ppm (42 mg/m^3)	3.5 ppm (8.1 mg/m^3)	2.3 ppm (5.4 mg/m^3)

- Key study was extensive and the data were internally consistent; similar AEGL-3 values were obtained in another rat acute exposure study.

SUMMARY OF AEGL VALUES FOR ALLYLAMINE – 2nd DRAFT					
Classification	10 minute	30 minute	1 hour	4 hours	8 hours
AEGL-1	0.83 ppm [1.9 mg/m^3]	0.83 ppm [1.9 mg/m^3]	0.83 ppm [1.9 mg/m^3]	NR[1]	NR[1]
AEGL-2	8.0 ppm [18 mg/m^3]	4.2 ppm [9.8 mg/m^3]	2.8 ppm [6.5 mg/m^3]	1.2 ppm [2.8 mg/m^3]	0.83 ppm [1.9 mg/m^3]
AEGL-3	145 ppm [338 mg/m^3]	40 ppm (94 mg/m^3)	18 ppm (42 mg/m^3)	3.5 ppm (8.1 mg/m^3)	2.3 ppm (5.4 mg/m^3)

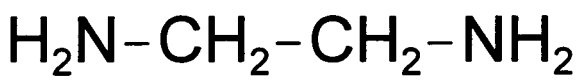
[1]NR = Not recommended because concentrations could cause effects within scope of AEGL-2

ACUTE EXPOSURE GUIDELINE LEVELS (AEGLs)

FOR

ETHYLENEDIAMINE

(CAS Reg. No. 107-15-3)



ORNL Staff Scientist: Sylvia Milanez

Chemical Manager: Mark McClanahan

Chemical Reviewers: Loren Koller, Richard Thomas

Ethylenediamine 2nd Draft TSD major changes

The Technical Support Document (TSD) for ethylenediamine (EDA) was originally presented at the March, 1999 NAC/AEGL meeting. The NAC approved AEGL-2 and AEGL-3 numbers based on a 30-exposure rat study, and AEGL-1 values were not proposed due to insufficient data. In November 1999, the EDA document was presented to the COT/AEGL subcommittee, which felt that using a 30-exposure study to derive AEGL values was not valid, and essentially asked that a different approach be taken. Values similar to those approved by the NAC were derived using single-exposure studies, and were supported by the 30-exposure study; AEGL-1 values were again not proposed.

The changes made in the 2nd draft TSD are:

- New AEGL-2 and AEGL-3 values, based on a different study, are presented. The total uncertainty factor was increased and the intraspecies and interspecies UF rationales were altered.
- Tables 2 and 3 were expanded and/or clarified
- 10-minute values were developed for the AEGL-2 and AEGL-3 values

Metabolism and Mechanism of Toxicity

- No human or animal inhalation exposure metabolism studies were located.
- EDA was extensively metabolized when given orally, but the role of metabolites in toxicity is unknown. Rats and mice given [^{14}C]EDA-2HCl orally excreted most of the radiolabel within 24 hours. Urine accounted for most of (39-70%) of radioactivity; feces for 4.5-31%; expired air for 5-22%.
- Mechanism of EDA toxicity or of its skin or respiratory sensitization properties is unknown. EDA is highly alkaline, water soluble and lipid-soluble, which causes it to be a potent skin and mucous membrane irritant. Effects reported in animal inhalation studies include liver, kidney, and lung lesions.
- Insufficient evidence exists to determine species variability: EDA toxicity in a species other than the rat was examined in only one inhalation study, but only one EDA concentration was tested and few experimental details were reported.
- EDA-sensitized workers report symptoms including chronic cough, phlegm, wheezing, and exertional breathlessness when exposed to EDA. They are considered "hypersusceptible" and may experience more severe effects at a given exposure time and/or concentration than predicted by the AEGL values.

AEGL-1

AEGL-1 values were <u>not</u> derived in either the **EARLIER PROPOSED** or in the **2nd DRAFT** EDA document because none of the available human or animal data were considered adequate.

TABLE 4. AEGL-1 Values for Ethylenediamine				
10 minutes	**30 minutes**	**1 hour**	**4 hours**	**8 hours**
Not determined due to insufficient data				

COMPARISON OF STUDIES USED TO DERIVE 2ND DRAFT AND EARLIER PROPOSED EDA AEGL-2 AND AEGL-3 VALUES

Species	Exposure time	Exposure conc. (ppm)	Endpoint and comments	Reference
Current (2nd Draft)				
Rat, Guinea pig	½, 1, 2, 4, or 8 hrs.	1000 (**AEGL-2**)	- 0/6 mortality; nominal conc., kidney cloudy swelling; lung edema	Carpenter et al., 1948
Rat	8 hours 8 hours	2000 (**AEGL-3**) 4000	- 0/6 mortality; nominal conc., no effects data - 6/6 mortality; nominal conc., no effects data	Smyth et al., 1951
SUPPORT for Current (2nd Draft)				
Rat	7 hrs/day for up to 30 days	59 132 (**AEGL-2**) 225 (**AEGL-3**) 484	- no effects noted - hair loss, 1/26 had "major" histo. lesions - 16/20 toxic deaths (mean 17.4 days); liver, kidney effects; alopecia - 0/27 toxic deaths (mean 11.4 days); liver, kidney, lung, adrenal effects; alopecia	Pozzani and Carpenter, 1954
Previously Proposed				
Rat	7 hrs/day for up to 30 days	59 (**AEGL-2**) 132 (**AEGL-3**) 225 484	- no effects noted - hair loss, 1/26 had "major" histo. lesions - 16/20 toxic deaths (mean 17.4 days); liver, kidney effects; alopecia - 0/27 toxic deaths (mean 11.4 days); liver, kidney, lung, adrenal effects; alopecia	Pozzani and Carpenter, 1954

AEGL-2

Key study: Carpenter et al., 1948. Rats and guinea pigs (6/group) exposed for 8 hours to ~484 ppm EDA (1000 ppm nominal) had bronchiolar edema of unspecified severity and "light cloudy kidney swelling" No other EDA concs. (other than control) were tested.

Toxicity endpoint: Bronchiolar edema and kidney swelling [**NOTE that** EDA-sensitized people ("hypersusceptible") may experience more severe effects]

Scaling: $C^n \times t = k$; ten Berge et al., 1986) using n=3 for time points < 8 hours to obtain conservative and protective AEGL values; no data were available to derive n.

Total uncertainty factor: 100

Intraspecies: 10: mechanism of toxicity and variability of the toxic response among humans is unknown

Interspecies: 10: key study tested only one EDA concentration and reported few experimental details, not providing a clear picture of species variability

AEGL-2 Values for Ethylenediamine				
10 minutes	**30 minutes**	**1 hour**	**4 hours**	**8 hours**
18 ppm [43 mg/m^3]	12 ppm [30 mg/m^3]	9.7 ppm [24 mg/m^3]	6.1 ppm [19 mg/m^3]	4.8 ppm [13 mg/m^3]

- Key study was supported by a rat study in which 30 exposures (7 hours/day) caused unspecified "major" lesions in 1/26 animals (Pozzani and Carpenter, 1954), and the AEGL-2 values for 10-60 minutes are similar to those derived from a challenged EDA-sensitized worker (15 min at 30 ppm).

AEGL-2 Values for EDA — 2nd DRAFT vs. based on 30-exposure study						
UFs	10 minute	30 minute	1 hour	4 hours	8 hours	Comment
Intra=10 Inter=10	**18 ppm**	**12 ppm**	**9.7 ppm**	**6.1 ppm**	**4.8 ppm**	**Single 8 hr exposure**
Intra=10 Inter=3	15 ppm	11 ppm	8.4 ppm	5.3 ppm	3.9 ppm	7 hrs/day for 30 days
Previously Proposed by NAC/AEGL						
Intra=3 Inter=3	N/P	14 ppm	11 ppm	7.1 ppm	5.2 ppm	7 hrs/day for 30 days

AEGL-3

Key study: Smyth et al. (1951). No rats (0/6) died after an 8-hour exposure to ~1000 ppm (2000 ppm nominal) but 6/6 died at ~2000 ppm (4000 ppm nominal). The estimated lethality threshold was ~1000 ppm. Toxic effects (other than death) were not described.

Toxicity endpoint: Estimated lethality threshold **[NOTE that** EDA-sensitized people ("hypersusceptible") may have severe effects at a lower concentration and/or duration]

Scaling: $C^n \times t = k$; ten Berge et al., 1986) using n=3 for time points < 8 hours to obtain conservative and protective AEGL values; no data were available to derive n.

Total uncertainty factor: 100

Intraspecies: 10: cause of death was not defined in key study and variability of the toxic response among humans cannot be predicted

Interspecies: 10: only one EDA concentration was tested, the cause of death was not defined in the key study, and there were no data from other species

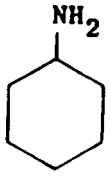
AEGL-3 Values for Ethylenediamine				
10 minutes	**30 minutes**	**1 hour**	**4 hours**	**8 hours**
36 ppm [89 mg/m^3]	25 ppm [62 mg/m^3]	20 ppm [49 mg/m^3]	13 ppm [31 mg/m^3]	10 ppm [26 mg/m^3]

- The proposed values are supported by a study in which rats (15/sex) exposed to 225 ppm 7 hours/day for 30 days had fractional mortality (Pozzani and Carpenter, 1954).

AEGL-3 Values for EDA — 2nd DRAFT vs. based on 30-exposure study						
UFs	10 minute	30 minute	1 hour	4 hours	8 hours	Comment
Intra=10 Inter=10	**36 ppm**	**25 ppm**	**20 ppm**	**13 ppm**	**10 ppm**	**Single 8 hr exposure**
Intra=10 Inter=3	26 ppm	18 ppm	14 ppm	9.0 ppm	6.6 ppm	7 hrs/day for 30 days
Previously Proposed by NAC/AEGL						
Intra=3 Inter=3	N/P	32 ppm	25 ppm	16 ppm	12 ppm	7 hrs/day for 30 days

SUMMARY OF AEGL VALUES FOR EDA — 2nd DRAFT						
Level	10 minute	30 minute	1 hour	4 hours	8 hours	Endpoint (Reference)
AEGL-1	Not recommended due to insufficient data					
AEGL-2	18 ppm	12 ppm	9.7 ppm	6.1 ppm	4.8 ppm	Bronchiolar edema, kidney swelling (Carpenter et al., 1948)
AEGL-3	36 ppm	25 ppm	20 ppm	13 ppm	10 ppm	Lethality threshold; no stated toxic effects (Smyth et al., 1951)

ACUTE EXPOSURE GUIDELINE LEVELS (AEGLs)
FOR
CYCLOHEXYLAMINE
(CAS Reg. No. 108-91-8)



ORNL Staff Scientist: Sylvia Milanez
Chemical Manager: Mark McClanahan
Chemical Reviewers: Nancy Kim and Richard Niemeier

Cyclohexylamine 2nd Draft TSD major changes

The Technical Support Document (TSD) for cyclohexylamine was originally presented at the December, 1998 NAC/AEGL meeting. The NAC approved AEGL-1 and AEGL-3 numbers based on a single-exposure rat (GLP) study, and AEGL-2 values based on a multiple-exposure, multi-species study. The cyclohexylamine TSD was presented to the COT/AEGL subcommittee in November 1999; it was recommended that a different study be used to derive AEGL-2 values. The following changes were made to the TSD:

- The Bio/dynamics, Inc (1990) GLP study is used instead of the Watrous and Schultz (1950) study to derive similar AEGL-2 values. The endpoint and UF rationales are slightly different and the modifying factor is omitted.

- The UF rationales for AEGL-1 and AEGL-3 were altered slightly but the AEGL-1 and AEGL-3 values are unchanged.

- Table 2 was expanded and clarified.

- 10-minute values were developed for all three AEGL levels.

AEGL-1, AEGL-2, and AEGL-3 KEY STUDY: Bio/dynamics, Inc., 1990

Conc. (ppm)	Mortality	Rats (5/sex) exposed for 4 hours had the following effects:
54.2	0/10	-Labored breathing, lacrimation, chromodacryorrhea, eyes partly closed, red nasal discharge
567	0/10	-Lacrimation, chromodacryorrhea red nasal discharge, tremors, labored breathing, gasping, rales, eyes closed, corneal opacity and ulceration, alopecia
542 ppm vapor + ~612 mg/m^3 aerosol	2/10	-As for 567 ppm; 1/5 male, 1/5 female died on day 2

AEGL-1

Key study: Bio/dynamics, Inc., 1990. Rats were exposed for 4 hours to 54.2 ppm, 567 ppm or a vapor/aerosol combination (542 ppm vapor and ~612 mg/m^3 aerosol).

Toxicity endpoint: NOAEL for respiratory and ocular irritation (causing mild or no irritation) was obtained by dividing 54.2 ppm by 3 (= 18.1 ppm)

Scaling: None; flat-lining across time was considered appropriate since mild irritant effects generally do not vary greatly over time

Total uncertainty factor: 10

Intraspecies: 3: mild sensory irritation from a surface-contact, very basic irritant gas is not likely to vary greatly among humans

Interspecies: 3: mild sensory irritation from a surface-contact, very basic irritant gas are not likely to vary greatly among species

AEGL-1 Values for Cyclohexylamine				
10 minutes	**30 minutes**	**1 hour**	**4 hours**	**8 hours**
1.8 ppm [7.3 mg/m^3]	1.8 ppm [7.3 mg/m^3]	1.8 ppm [7.3 mg/m^3]	1.8 ppm [7.3 mg/m^3]	1.8 ppm [7.3 mg/m^3]

AEGL-2

Key study: Bio/dynamics, Inc., 1990. Rats were exposed for 4 hours to 54.2 ppm, 567 ppm or a vapor/aerosol combination (542 ppm vapor and ~612 mg/m^3 aerosol).

Toxicity endpoint: Moderate respiratory effects and ocular irritation, NOAEL for irreversible ocular lesions at 54.2 ppm

Scaling: $C^n \times t = k$ (ten Berge et al., 1986); no data were available to derive n; used n=3 to extrapolate to < 4 hours and n=1 to extrapolate to > 4 hours to obtain conservative and protective AEGL values.

Uncertainty factors: 10

Intraspecies: 3: moderate respiratory and ocular irritation from a surface-contact, basic irritant gas is not likely to vary greatly among humans

Interspecies: 3: moderate respiratory and ocular irritation from a surface-contact, basic irritant gas is not likely to vary greatly among species

AEGL-2 Values for Cyclohexylamine				
10 minutes	**30 minutes**	**1 hour**	**4 hours**	**8 hours**
16 ppm [63 mg/m^3]	11 ppm [44 mg/m^3]	8.6 ppm [35 mg/m^3]	5.4 ppm [22 mg/m^3]	2.7 ppm [11 mg/m^3]

COMPARISON OF STUDIES USED TO DERIVE CURRENT 2ND DRAFT AND EARLIER PROPOSED CYCLOHEXYLAMINE AEGL-2 VALUES

Species	Exposure time	Conc. (ppm)	Time of death	Mortality	Effects, Comments (Reference)
CURRENT -- 2nd DRAFT (Bio/dynamics, Inc., 1990)					
Rat	4 hrs	54.2	(none)	0/10	-Labored breathing, lacrimation, eyes partly closed, red nasal discharge, chromodacryorrhea
	4 hrs	567	(none)	0/10	-As for 54.2 and tremors, gasping, rales, eyes closed, corneal opacity and ulceration, alopecia
	4 hrs	>>542*	Day 2	2/10	-As for 567 ppm; 2/10 died
PREVIOUSLY PROPOSED (Watrous and Schultz, 1950)					
Rat	7hr/d x 10 d.	150	≤ 10 day	1/5	-1 death; no other reported effects
		800	24 hrs	0-5/5‡	-Corneal opacity; death possibly (unclear)
		1200	7 hrs	4-5/5‡	-Extreme irritation, lung hemorrhage, opaque corneas, death
Guinea pig	7hr/d x 10 d.	150	≤ 10 day	0/2‡	-No reported effects
		800	14 hrs	2/?‡	-Corneal opacity; 2 deaths
		1200	7 hrs	All	-Extreme irritation, lung hemorrhage, opaque corneas, death
Rabbit	7hr/d x 10 d.	150	7 hrs	1/?‡	-1 death; no other reported effects
		800	14 hrs	1/?‡	-Corneal opacity ; 1 death
		1200	7 hrs	All	-Extreme irritation, lung hemorrhage, opaque corneas, death

? = Unknown; not reported

* = Highest conc. was 542 ppm vapor + ~612 mg/m^3 aerosol

‡ = Total number animals tested and/or responding over 10-day exposure period was not defined.

COMPARISON OF CURRENT 2ND DRAFT AND EARLIER PROPOSED AEGL-2 VALUES FOR CYCLOHEXYLAMINE

AEGL-2						
UFs	**10 minute**	**30 minute**	**1 hour**	**4 hours**	**8 hours**	**Endpoint (Reference)**
Intra=3 Inter=3	**16 ppm**	**11 ppm**	**8.6 ppm**	**5.4 ppm**	**2.7 ppm**	Moderate respiratory effects, ocular irritation; NOAEL for irreversible ocular lesions (Bio/dynamics, 1990).
Intra=3 Inter=3 MF=2	Not proposed	18 ppm	14 ppm	9.0 ppm	6.6 ppm	NOAEL for corneal opacity; may cause respiratory irritation (Watrous and Schultz, 1950).

AEGL-3

Key study: Bio/dynamics, Inc., 1990. Rats were exposed for 4 hours to 54.2 ppm, 567 ppm or a vapor/aerosol combination (542 ppm vapor and ~612 mg/m^3 aerosol).

Toxicity endpoint: Threshold for lethality, severe respiratory effects, irreversible ocular lesions

Scaling: $C^n \times t = k$ (ten Berge et al., 1986); no data were available to derive n. Used n=3 to extrapolate to < 4 hours and n=1 to extrapolate to > 4 hours to obtain conservative and protective values.

Uncertainty factors: 30

Intraspecies: 3: lethality response resulting from a basic irritant gas is not likely to vary greatly among humans

Interspecies: 10: significant variation was seen among species for the exposure causing lethality, and the data were insufficient to determine that rats were the most sensitive species

AEGL-3 Values for Cyclohexylamine				
10 minutes	**30 minutes**	**1 hour**	**4 hours**	**8 hours**
54 ppm [220 mg/m^3]	38 ppm [153 mg/m^3]	30 ppm [121 mg/m^3]	19 ppm [77 mg/m^3]	9.4 ppm [38 mg/m^3]

SUMMARY OF AEGL VALUES FOR CYCLOHEXYLAMINE – 2nd DRAFT						
Classifi-cation	**10 minute**	**30 minute**	**1 hour**	**4 hours**	**8 hours**	**Endpoint (Reference is Bio/dynamics, Inc., 1990)**
AEGL-1	**1.8 ppm**	1.8 ppm	1.8 ppm	1.8 ppm	1.8 ppm	NOAEL for respiratory and ocular irritation; may cause mild or no sensory irritation
AEGL-2	**16 ppm**	**11 ppm**	**8.6 ppm**	**5.4 ppm**	**2.7 ppm**	Moderate respiratory effects, ocular irritation; NOAEL for irreversible ocular lesions
AEGL-3	**54 ppm**	38 ppm	30 ppm	19 ppm	9.4 ppm	**Severe respiratory effects, irreversible ocular lesions, and** lethality threshold

8

Development of 10-Minute AEGL Values

Nickel Carbonyl
Iron Pentacarbonyl
Phosphorus Oxychloride
Phosphorus Trichloride

NAC/AEGL April 26-28, 2000

Attachment 8

AEGL VALUES FOR NICKEL CARBONYL						
Classification	**10-min**	**30-min**	**1-hour**	**4-hour**	**8-hour**	**Endpoint**
AEGL-1	**NR**	**NR**	**NR**	**NR**	**NR**	**not recommended**
AEGL-2	**0.096 ppm** --- *0.059 ppm*	**0.042 ppm** *0.042 ppm*	**0.021 ppm** *0.021 ppm*	**0.005 ppm** *0.011 ppm*	**NA**	**developmental toxicity in hamsters; gestational exposure (15 minutes, 8.4 ppm) (Sunderman et al., 1980)**
AEGL-3	**0.46 ppm** --- *0.32 ppm*	**0.32 ppm** *0.22ppm*	**0.16 ppm** *0.11 ppm*	**0.04 ppm**	**NA**	**estimated lethality threshold (30-min. LC_{01} of 3.17 ppm); mouse lethality data (Kincaid et al., 1953)**

Values in italics are current proposed AEGLs that were developed using a default n of 2.

- **10-minute exposure data not available**
- **No empirically derived *n* for $C^n \times t = k$; default assumption of $n = 1$ or 3**
- **UF for AEGL-2: 100 (10 each for intra- and interspecies variability)**
- **UF for AEGL-3: 10 (3 each for intra- and interspecies variability)**

AEGL VALUES FOR IRON PENTACARBONYL						
Classification	**10-min**	**30-min**	**1-hour**	**4-hour**	**8-hour**	**Endpoint (Reference)**
AEGL-1	**NR**	**NR**	**NR**	**NR**	**NR**	**Not recommended; insufficient data**
AEGL-2	**1.2 ppm** --- *1.2 ppm*	**0.4 ppm** *0.35 ppm*	**0.19 ppm** *0.17 ppm*	**0.05ppm** *0.044 ppm*	**NA**	**Based upon a three-fold reduction in the AEGL-3 values**
AEGL-3	**3.5 ppm** --- *3.5 ppm*	**1.2 ppm** *1.2 ppm*	**0.58 ppm** *0.58 ppm*	**0.15 ppm** *0.16 ppm*	**NA**	**Estimated lethality threshold in rats (6-hr exposure to 2.91 ppm) (BASF, 1995). $n = 1$; UF=30 (10 for interspecies variability, 3 for individual variability)**

Values in italics are currently proposed AEGLs developed using a default n of 2.

- **10-minute exposure data not available**
- **No empirically derived n for $C^n \times t = k$ but data suggest that n is close to unity**
- **UF for AEGL-2: 30 (as per AEGL-3 development)**
- **UF for AEGL-3: 30 (10 for interspecies variability; 3 for intraspecies variability)**

AEGL VALUES FOR PHOSPHORUS OXYCHLORIDE						
Classification	**10-min**	**30-min**	**1-hour**	**4-hour**	**8-hour**	**Endpoint (Reference)**
AEGL-1	**NR**	**NR**	**NR**	**NR**	**NR**	**Data unavailable for development**
AEGL-2	**NR**	**NR**	**NR**	**NR**	**NR**	**Data unavailable for development**
AEGL-3	**1.5 ppm** --- 	**1.1 ppm** *1.5 ppm*	**0.85 ppm** *1.1 ppm*	**0.54 ppm** *0.54 ppm*	**0.27 ppm** *0.38 ppm*	**Weeks et al., (1964). Estimate of lethality threshold in rats (16.1 ppm) based upon 3-fold reduction in 4-hr LC_{50} of 48.4 ppm.**

Values in italics are currently proposed AEGLs developed using a default n of 2.

- **10-minute exposure data not available**
- **No empirically derived n for $C^n \times t = k$; default assumption of $n = 1$ or 3**
- **UF for AEGL-3: 30 (10 for interspecies variability; 3 for intraspecies variability)**

AEGL VALUES FOR PHOSPHORUS TRICHLORIDE						
Classification	**10-min**	**30-min**	**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	**1.6 ppm** --- *1.6 ppm*	**1.1 ppm** *1.6 ppm*	**0.88 ppm** *1.1 ppm*	**0.56 ppm** *0.56 ppm*	**0.28 ppm** *0.39 ppm*	**Estimated lethality threshold based upon 3-fold reduction of guinea pig 4-hr LC_{50} (50.1 ppm/3 = 16.7 ppm) (Weeks et al., 1964)**

Values in italics are currently proposed AEGLs developed using a default n of 2.

- **10-minute exposure data not available**
- **No empirically derived n for $C^n \times t = k$; default assumption of $n = 1$ or 3**
- **UF for AEGL-30: 10 for interspecies variability; 3 for intraspecies variability**

Attachment 9

ACUTE EXPOSURE GUIDELINE LEVELS FOR HYDROGEN CHLORIDE

DEVELOPMENT OF 10-MIN. VALUES

NAC/AEGL-18
APRIL 26-28, 2000

CHEMICAL MANAGER: JOHN HINZ
ORNL STAFF SCIENTIST: CHERYL BAST

AEGL-1 VALUES				
10 minutes	30 minutes	1 hour	4 hours	8 hours
1.8 ppm	1.8 ppm	1.8 ppm	1.8 ppm	1.8 ppm

Reference: Stevens, B. et al. 1992. Respiratory effects from the inhalation if hydrogen chloride in young adult asthmatics. JOM. 34: 923-929.
Test Species/Strain/Number: Human/adult asthmatics/10
Exposure Route/Concentrations/Durations: inhalation at 0, 0.8, or 1.8 ppm for 45 minutes while exercising: (1.8 ppm was determinant for AEGL-1)
Effects: No treatment-related effects were observed in any of the individuals tested.
Endpoint/Concentration/Rationale: The highest concentration tested was a no-effect-level for irritation in a sensitive human population (10 asthmatic individuals tested) and was selected as the basis of AEGL-1. Effects assessed included sore throat, nasal discharge, cough, chest pain or burning, dyspnea, wheezing, fatigue, headache, unusual taste or smell, total respiratory resistance, thoracic gas volume at functional residual capacity, forced expiratory volume, and forced vital capacity. All subjects continued the requisite exercise routine for the duration of the test period.
Uncertainty Factors/Rationale: Interspecies: 1, test subjects were human Intraspecies: 1, test subjects were sensitive population (exercising asthmatics)
Modifying Factor: Not applicable
Animal to Human Dosimetric Adjustment: Insufficient data
Time Scaling: The AEGL-1 values for a sensory irritant were held constant across time because it is a threshold effect and prolonged exposure will not result in an enhanced effect. In fact one may become desensitized to the sensory irritation over time. Also, this approach was considered valid since the endpoint (no treatment-related effects at the highest concentration tested in exercising asthmatics) is inherently conservative.
Confidence and Support for AEGL values: The key study was well conducted in a sensitive human populationand is based on no treatment-related effects. Additionally,

AEGL-2 VALUES				
10 minutes	30 minutes	1 hour	4 hours	8 hours
130 ppm	43 ppm	22 ppm	5.4 ppm	2.7 ppm

Reference: Stavert et al. 1991. Relative acute toxicities of hydrogen chloride, hydrogen fluoride, and hydrogen bromide in nose- and pseudo-mouth-breathing rats. Fundam. Appl. Toxicol. 16: 636-655.

Test Species/Strain/Number: F344 rats/ 8 males/concentration

Exposure Route/Concentrations/Durations: Inhalation: 0, or 1300 ppm/30 minutes (1300 ppm was determinant for AEGL-2)

Effects:
- 0 ppm: no effects
- 1300 ppm: Nose breathers: severe necrotizing rhinitis, turbinate necrosis, thrombosis of nasalsubmucosa vessels
- 1300 ppm: Mouth breathers: severe ulcerative tracheitis accompanied by necrosis and luminal ulceration(determinant for AEGL-2)

Endpoint/Concentration/Rationale: 1300 ppm for 30 min; severe lung effects (ulcerative tracheitis accompanied by necrosis and luminal ulceration) or nasal effects (necrotizing rhinitis, turbinate necrosis, thrombosis of nasal submucosa vessels histopathology) in pseudo-mouth breathing male F344 rats.

Uncertainty Factors/Rationale:

Total uncertainty factor: 10

- Interspecies: 3- rodents (rats, mice, guinea pig) appear to be approximately 2-3 times more sensitive than primates to the irritative effects of HCl. Concentration-related decreases in respiratory frequency (RD_{50}), indicative of a protective mechanism, are observed in rodents, while primates exhibit increases in respiratory frequency, indicative of a compensatory response to hypoxia. For example, no AEGL-2 effects were observed in baboons exposed to 5,000 ppm hydrogen chloride, while rather severe respiratory necrosis and histopathology were observed in rats exposed to 1300 ppm hydrogen chloride.
- Intraspecies: 3- The mechanism of action, irritation, and the subsequent effect or response is not expected to differ greatly among individuals because HCl is a highly reactive and direct acting irritant.

Modifying Factor: 3- based on sparse database for AEGL-2 effects and the fact that the effects observed at the concentration used as the basis for AEGL-2 were somewhat severe

Animal to Human Dosimetric Adjustment: Insufficient data

Time Scaling: $C^n \times t = k$ where n = 1: based on regression analysis of combined rat and mouse LC_{50} data (1 min. to 100 min.) reported by ten Berge et al., 1986. Data point used to derive AEGL-2 was 30 minutes. AEGL-2 values for other specified exposure periods were based on extrapolation from the 30 minute value.

AEGL-3 VALUES				
10 minutes	30 minutes	1 hour	4 hours	8 hours
620 ppm	210 ppm	100 ppm	26 ppm	13 ppm

Reference: Vernot, E.H., MacEwen, J.D., Haun, C.C., Kinkead, E.R. 1977. Acute toxicity and skin corrosion data for some organic and inorganic compounds and aqueous solutions. Toxicol. Appl. Pharmacol. 42: 417-423.; Wohlslagel, J., DiPasquale, L..C., Vernot, E.H. 1976. Toxicity of solid rocket motor exhaust: effects of HCl, HF, and alumina on rodents. J. Combustion Toxicol. 3: 61-70.

Test Species/Strain/Sex/Number: Sprague-Dawley rats, 10 males perconcentration

Exposure Route/Concentrations/Durations: Inhalation at 0, 1813, 2585, 3274, 3941, or 4455 ppm for 1 hr

Effects:

Concentration	Mortality
0 ppm	0/10
1813 ppm	0/10
2585 ppm	2/10
3274 ppm	6/10
3941 ppm	8/10
4455 ppm	10/10

LC_{50}: reported as 3124 ppm (determinant for AEGL-3)

Endpoint/Concentration/Rationale: 1/3 of the 1-hr LC_{50} (3124 x 1/3 = 1041 ppm) to estimate a no-effect-level for death

Uncertainty Factors/Rationale:

Total uncertainty factor: 10

Interspecies: 3- rodents appear to be approximately 2-3 times more sensitive than primates to the irritative effects of HCl. Concentration-related decreases in respiratory frequency, indicative of a protective mechanism, are observed in rodents, while primates exhibit increases in respiratory frequency, indicative of a compensatory response to hypoxia. For example, no deaths were observed in baboons exposed to 11,400 ppm hydrogen chloride, while deaths were observed at 2585 ppm in rats.

Intraspecies: 3- The mechanism of action, irritation, and subsequent effect or response is not expected to differ greatly among individuals because HCl is a highly reactive and direct acting irritant.

Modifying Factor: Not applicable

Animal to Human Dosimetric Adjustment: Insufficient data

Time Scaling: $C^n \times t = k$ where n = 1, based on regression analysis of rat and mouse mortality data (1 min. to 100 min.) reported by ten Berge et al., 1986. Reported 1-hour data point was used to derive AEGL-3 values. AEGL-3 values for other specified exposure periods were based on extrapolation from the 1-hour value.

RELATIONAL COMPARISON OF AEGL VALUES FOR HYDROGEN CHLORIDE (ppm [mg/m^3])					
Classification	10-min	30-min	1-hour	4-hour	8-hour
AEGL-1 (Nondisabling)	1.8 [2.7]	1.8 [2.7]	1.8 [2.7]	1.8 [2.7]	1.8 [2.7]
AEGL-2 (Disabling)	130 [197]	43 [65]	22 [33]	5.4 [8.1]	2.7 [4.1]
AEGL-3 (Lethality)	620 [937]	210[313]	104 [155]	26 [39]	13 [19]

ERPG Values (AIHA, 1989):

ERPG-1: 3 ppm
ERPG-2: 20 ppm
ERPG-3: 100 ppm

NIOSH REL (CDC/NIOSH,1994): 5 ppm ceiling

OSHA PEL (CDC/NIOSH, 1994): 5 ppm ceiling

IDLH (CDC/NIOSH, 1994): 50 ppm

SPEGL (NRC, 1987): 1 ppm

EEGL (NRC, 1987): 20 ppm

Chronic RfC (U.S. EPA, 1995): 0.013 ppm

Attachment 10

ACUTE EXPOSURE GUIDELINE LEVELS FOR METHYLTRICHLOROSILANE

DEVELOPMENT OF 10-MIN. VALUES

NAC/AEGL-18
APRIL 26-28, 2000

CHEMICAL MANAGER: ERNEST FALKE
ORNL STAFF SCIENTIST: CHERYL BAST

AEGL-1 VALUES				
10 minutes	30 minutes	1 hour	4 hours	8 hours
0.6 ppm	0.6 ppm	0.6 ppm	0.6 ppm	0.6 ppm

Reference: U.S. EPA. 1997. Acute Exposure Guideline Levels for Hydrogen Chloride. Technical Support Document. (Stevens, B. et al. 1992. Respiratory effects from the inhalation if hydrogen chloride in young adult asthmatics. JOM. 34: 923-929.)

Test Species/Strain/Number: Human adult asthmatics/10

Exposure Route/Concentrations/Durations: inhalation at 0, 0.8, or 1.8 ppm hydrogen chloride for 45 minutes (exercising) (1.8 ppm was determinant for AEGL-1)

Effects: No treatment-related effects were observed in any of the individuals tested.

Endpoint/Concentration/Rationale: 1.8 ppm HCl for 45 minutes wås determined o be the no-effect-level for irritation in a sensitive human (asthmatic) population

Uncertainty Factors/Rationale:
Interspecies: 1, test subjects were human
Intraspecies: 1, test subjects were sensitive population(exercising asthmatics)

Modifying Factor: 3- a maximum of three moles of HCl may be produced by hydrolysis from one mole of methyltrichlorosilane

Animal to Human Dosimetric Adjustment: Insufficient data

Time Scaling: Values were held constant at the no-effect-level. This approach was considered valid since mild irritant effects are threshold effects and generally do not vary greatly over time and the selected endpoint concentration is inherently conservative (no-effect-level in exercising asthmatics).

Confidence and Support for AEGL values: AEGL-1 values for methyltrichlorosilane were determined using HCl, the known hydrolysis product, and likely source of respiratory irritation, as the basis. For each mole of methyltrichlorosilane, three moles of hydrogen chloride may be produced by hydrolysis. Thus, the hydrogen chloride AEGL-1 value was divided by a factor of 3 to approximate an AEGL-1 value for methyltrichlorosilane. Assuming complete hydrolysis, confidence in the AEGL-1 values is good.

AEGL-2 VALUES				
10 minutes	30 minutes	1 hour	4 hours	8 hours
37 ppm	12 ppm	6.2 ppm	1.6 ppm	0.78 ppm

Reference: Dow Corning. 1997. An acute whole body inhalation toxicity study with methyltrichlorosilane in Fischer 344 rats. Report No. 1997-I0000-43537. Study No. 8602. Dow Corning Corporation. Health & Environmental Sciences. Midland, MI.

Test Species/Strain/Number: F344 rats/ 5 males and 5 females/ concentration

Exposure Route/Concentrations/Durations: Inhalation at 622, 1047, 1439, or 3075 ppm for 1 hour (622 ppm was determinant for AEGL-2)

Effects: 622 ppm: ocular opacity, ocular irritation and alopecia, hunched posture.

1047, 1439, or 3075 ppm: death, ocular opacity, ocular alopecia, labored breathing, rales, gasping, hemorrhage of the thymus, ectasia of the lungs; submeningeal brain hemorrhage (3075 ppm only).

Endpoint/Concentration/Rationale: Rats/622 ppm for 1 hour/ ocular opacity and irritation, hunched posture. This level was considered to be the threshold for impairment of escape and the onset of serious irreversible health effects.

Uncertainty Factors/Rationale:
Total uncertainty factor: 30
Interspecies: 10-data from only one species available
Intraspecies: 3- effects appear to be due to irritation and are not expected to differ greatly among individuals

Modifying Factor: 3- sparse database for AEGL-2 effects (data in one species from one laboratory)

Animal to Human Dosimetric Adjustment: Insufficient data

Time scaling: $C^n \times t = k$ where $n = 1$, value reported for hydrogen chloride in reference by ten Berge et al., 1986: based on regression analysis of combined rat and mouse LC_{50} data (1 min. to 100 min.). The n value for hydrogen chloride was utilized for time scaling for methyltrichlorosilane since much of the acute toxicity appears to be due to hydrogen chloride, the methyltrichlorosilane hydrolysis product, and data were insufficient for deriving an n value for this chlorinated silane itself. The empirical data point used for AEGL-2 derivation was 1 hour. AEGL-2 values for other specified exposure periods were based on extrapolation from the reported 1 hour value.

Confidence and Support for AEGL values: Confidence is moderate due to the sparse data base.

AEGL-3 VALUES				
10 minutes	30 minutes	1 hour	4 hours	8 hours
170 ppm	56 ppm	28 ppm	7.0 ppm	3.5 ppm

Reference: Dow Corning. 1997. An acute whole body inhalation toxicity study of methyltrichlorosilane in Fischer 344 rats. Report No. 1997-I0000-43537. Study No. 8602. Dow Corning Corporation. Health & Environmental Sciences. Midland, MI.

Test Species/Strain/Sex/Number: F344 rats/ 5 males and 5 females/ concentration

Exposure Route/Concentrations/Durations: Inhalation at 622, 1047, 1439, or 3075 ppm for 1 hour (Calculated LC_{01} of 844 ppm was determinant for AEGL-3)

Effects:

Concentration	Mortality
622 ppm	0/10
1047 ppm	1/10
1439 ppm	6/10
3075 ppm	10/10

LC_{50}: 1365 ppm
LC_{01}: 844 ppm (determinant for AEGL-3 reported in study)

Endpoint/Concentration/Rationale: The calculated 1-hr LC_{01} (844 ppm) as a threshold for death in rats

Uncertainty Factors/Rationale:
Total uncertainty factor: 30
Interspecies: 10- data from only one species
Intraspecies: 3- effects resulting in death appear to be due to irritation and are not expected to differ greatly among individuals

Modifying Factor: none

Animal to Human Dosimetric Adjustment: Insufficient data

Time Scaling: $C^n \times t = k$ where n = 1, value reported for hydrogen chloride in reference by ten Berge et al., 1986: based on regression analysis of combined rat and mouse LC_{50} data (1 min. to 100 min.). The n value for hydrogen chloride was utilized for time scaling for methyltrichlorosilane since much of the acute toxicity appears to be due to hydrogen chloride, the methyltrichlorosilane hydrolysis product, and data were insufficient for deriving an n value for this chlorinated silane itself. Data point used for AEGL-3 derivation was 1 hour. AEGL-3 values for other specified exposure periods were based on extrapolation from the reported 1 hour value.

Confidence and Support for AEGL values: Confidence is moderate due to the sparse data base.

RELATIONAL COMPARISON OF AEGL VALUES FOR METHYLTRICHLOROSILANE (ppm [mg/m^3])					
Classification	10-min	30-min	1-hour	4-hour	8-hour
AEGL-1 (Nondisabling)	0.60 [3.7]	0.60 [3.7]	0.60 [3.7]	0.60 [3.7]	0.60 [3.7]
AEGL-2 (Disabling)	37 [226]	12 [73]	6.2 [38]	1.6 [9.8]	0.78 [4.8]
AEGL-3 (Lethality)	170 [1037]	56 [340]	28 [170]	7.0 [43]	3.5 [21]

1-hour ERPG values for methyltrichlorosilane (AIHA, 1996):

ERPG-1: 0.5 ppm
ERPG-2: 3 ppm
ERPG-3: 15 ppm

Attachment 11

ACUTE EXPOSURE GUIDELINE LEVELS FOR DIMETHYLDICHLOROSILANE

DEVELOPMENT OF 10-MIN. VALUES

NAC/AEGL-18
APRIL 26-28, 2000

CHEMICAL MANAGER: ERNEST FALKE
ORNL STAFF SCIENTIST: CHERYL BAST

AEGL-1 VALUES				
10 minutes	30 minutes	1 hour	4 hours	8 hours
0.9 ppm	0.9 ppm	0.9 ppm	0.9 ppm	0.9 ppm

Reference: U.S. EPA. 1997. Acute Exposure Guideline Levels for Hydrogen Chloride. Technical Support Document. (Stevens, B. et al. 1992. Respiratory effects from the inhalation if hydrogen chloride in young adult asthmatics. JOM. 34: 923-929.)

Test Species/Strain/Number: Human/adult asthmatics/10

Exposure Route/Concentrations/Durations: inhalation at 0, 0.8, or 1.8 ppm hydrogen chloride for 45 minutes (exercising) (1.8 ppm was determinant for AEGL-1)

Effects: No treatment-related effects were observed in any of the individuals tested.

Endpoint/Concentration/Rationale: No-effect-level for irritation in a sensitive human (asthmatic) population

Uncertainty Factors/Rationale:
Interspecies: 1, test subjects were human
Intraspecies: 1, test subjects were sensitive population(exercising asthmatics)

Modifying Factor: 2- a maximum of two moles of HCl may be produced by hydrolysis of one mole of dimethyldichlorosilane

Animal to Human Dosimetric Adjustment: Insufficient data

Time Scaling: Values were held constant at the no-effect-level. This approach was considered valid since mild irritant effects generally do not vary greatly over time and the endpoint is inherently conservative (no-effect-level in exercising asthmatics).

Confidence and Support for AEGL values: AEGL-1 values for dimethyldichlorosilane were determined by analogy to HCl. For each mole of dimethyldichlorosilane, two moles of hydrogen chloride may be produced by hydrolysis. Thus, the hydrogen

AEGL-2 VALUES				
10 minutes	30 minutes	1 hour	4 hours	8 hours
78 ppm	26 ppm	13 ppm	3.3 ppm	1.6 ppm

Reference: Dow Corning. 1997. An acute whole body inhalation toxicity study of dimethyldichlorosilane in Fischer 344 rats. Report No. 1997-I0000-43381. Study No. 8487. Dow Corning Corporation. Health & Environmental Sciences. Midland, MI.

Test Species/Strain/Number: F344 rats/ 5 males and 5 females/ concentration

Exposure Route/Concentrations/Durations: Rats/Inhalation at 1309, 2077, 2353, or 2726 ppm for 1 hour
(1309 ppm was determinant for AEGL-2)

Effects: 1309 ppm: corneal opacity, ocular alopecia, grey areas on lungs, dark red material in anterior chamber/inner cornea of the eye.
2077, 2353, or 2726 ppm: death, corneal opacity, ocular alopecia, swollen/necrotic paws, labored breathing, rales, hypoactivity, prostration, hemorrhage, congestion, and/or consolidation of the lungs, gaseous distension of the GI tract.

Endpoint/Concentration/Rationale: Rats/1309 ppm for 1 hour/ Corneal opacity, ocular alopecia, swollen/necrotic paws, grey areas on lungs, dark red material in anterior chamber/inner cornea of the eye.

Uncertainty Factors/Rationale:
Total uncertainty factor: 30
Interspecies: 10- data from only one species
Intraspecies: 3- effects appear to be due to irritation and are not expected to differ greatly among individuals

Modifying Factor: 3- sparse database for AEGL-2 effects (data in one species from one laboratory)

Animal to Human Dosimetric Adjustment: Insufficient data

Time Scaling: $C^n \times t = k$ where $n = 1$, value is for hydrogen chloride in reference by ten Berge et al., 1986: based on regression analysis of combined rat and mouse LC_{50} data (1 min. to 100 min.). The 'n' value for hydrogen chloride was utilized for time scaling for dimethyldichlorosilane since much of the acute toxicity appears to be due to hydrogen chloride and data were insufficient for deriving an n value for the silane itself. Data point used for AEGL-2 derivation was 1 hour. AEGL-2 values for other specified exposure periods were based on extrapolation from the 1 hour value.

Confidence and Support for AEGL values: Confidence is moderate due to the sparse data base.

AEGL-3 VALUES				
10 minutes	30 minutes	1 hour	4 hours	8 hours
320 ppm	106 ppm	53 ppm	13 ppm	6.6 ppm

Reference: Dow Corning. 1997. An acute whole body inhalation toxicity study of dimethyldichlorosilane in Fischer 344 rats. Report No. 1997-I0000-43381. Study No. 8487. Dow Corning Corporation. Health & Environmental Sciences. Midland, MI.

Test Species/Strain/Sex/Number: F344 rats/ 5 males and 5 females/ concentration

Exposure Route/Concentrations/Durations: Rats/Inhalation at 1309, 2077, 2353, or 2726 ppm for 1 hour (Calculated LC_{01} of 1589.5 ppm was determinant for AEGL-3)

Endpoint/Concentration/Rationale: The calculated 1-hr LC_{01} (1589.5 ppm) as a threshold for death in rats

Uncertainty Factors/Rationale:
Total uncertainty factor: 30
Interspecies: 10- data from only one species
Intraspecies: 3- effects appear to be due to irritation and are not expected to differ greatly among individuals

Modifying Factor: none

Animal to Human Dosimetric Adjustment: Insufficient data

Time Scaling: $C^n \times t = k$ where n = 1, value is for hydrogen chloride in reference by ten Berge et al., 1986: based on regression analysis of combined rat and mouse LC_{50} data (1 min. to 100 min.). The 'n' value for hydrogen chloride was utilized for time scaling for dimethyldichlorosilane since much of the acute toxicity appears to be due to hydrogen chloride and data were insufficient for deriving an n value for the silane itself. Data point used for AEGL-3 derivation was 1 hour. AEGL-3 values for other specified exposure periods were based on extrapolation from the 1 hour value.

Confidence and Support for AEGL values: Confidence is moderate due to the sparse data base.

RELATIONAL COMPARISON OF AEGL VALUES FOR DIMETHYLDICHLOROSILANE (ppm [mg/m^3])					
Classification	10-min	30-min	1-hour	4-hour	8-hour
AEGL-1 (Nondisabling)	0.90 [4.8]	0.90 [4.8]	0.90 [4.8]	0.90 [4.8]	0.90 [4.8]
AEGL-2 (Disabling)	78 [413]	26 [140]	13 [69]	3.3 [17]	1.6 [8.5]
AEGL-3 (Lethality)	320 [1696]	106 [560]	53 [280]	13 [69]	6.6 [35]

1-Hour ERPG Values for dimethyldichlorosilane (AIHA, 1996):

ERPG-1: 0.8 ppm
ERPG-2: 5 ppm
ERPG-3: 25 ppm

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21. Dezember 1999

Dr. Sylvia Talmage
Oak Ridge National Laboratory
1060 Commerce Park
Oak Ridge, TN 37830
U.S.A.

Re: AEGLs for Bromine and Chlorine

Dear Dr. Talmage,

thank you for your letter (undated) of November, 1999 with documents on bromine and chlorine effects at low concentrations in humans, and high concentrations in experimental animals. I apologize for being late in responding to your questions. However, to be substantial - after more than 35 years since the experiments described in our papers have been performed - I had to consult several papers quoted in your documents to allow comparison of experimental details, and argumentations brought forward by different authors. The collection of these papers took some time; although I am still missing some which may be important, I am going to submit my commentaries now in the hope that the key points may sufficiently be met by the presently available information.

The translation of the paper by Rupp and Henschler (1967), although abbreviated to some extent, is certainly correct. This refers particularly to the physiological/medical terms of symptoms and signs. Concern arises rather from the interpretation of these terms by different authors dealing with the same issue. I will explain this in more detail later on.

Since there is an internal coherence of the argumentations in context with our papers between your documents on chlorine and bromine, I will deal with the documents separately.

Chlorine. On Page 12, 1st para our paper (Rupp and Henschler 1967) is criticized for its lack of controls, for the possible presence of confounding chemicals, and differing results obtained by Anglen (1981) and Rotman et al.(1983).

- Lack of controls: Two different strategies are followed in quantitative toxicological experiments, (a) point assays, and (b) dose-response studies. For (a) you need controls, for (b) no control groups are used (e.g. in LD 50 or ED 50 determinations in which a suitable array of doses is used, one or more of which may be zero

response doses; these may be regarded as some sort of controls). Anglen and Rotman et al. did point assays (0.5; 1.0 and 2 ppm). Rupp and Henschler did a dose-response study, using 6 (Cl_2) or 7 (Br_2) dose-levels down to (almost) zero response levels. The aim of Rupp and Henschler was to establish thresholds of smell and irritations to sensitive mucous membranes of eyes and the respiratory tract, and not of changes in physiological functions; these were included in the Anglen and Rotman et al. studies. Therefore, the latter authors needed controls, which were inadequate in the dose response study of Rupp and Henschler. It should be kept in mind that Anglen and Rotman et al., as well as Joosting and Verberk (1974) did not determine thresholds; their lowest concentrations still induced considerable responses and changes at sensitive mucous membrane surfaces.- Based on these arguments, I see no reason to blame our study of not having used controls.

- Confounding chemicals: We saturated liquid paraffin (pharmaceutical quality, free from olefinic bonds) with chlorine to facilitate the precise dosing of a stream of low chlorine concentrations. This technique is used since long in preparative organic chemistry if small amounts of chlorine are needed. There is no evidence for the assumption that elemental chlorine will react with long chain saturated hydrocarbons under normal conditions. To be sure, I have again contacted an expert in chlorine organic chemistry who confirmed that the reaction of chlorine with paraffins needs high pressure and temperature conditions, and/or catalytical assistence. And even if some substitution reaction with impurities would occur: there is no indication of the formation of volatile derivates which could interfere with the exposure experiments. Thus, I think that - unless someone provides convincing evidence for the formation of confounders -the argument of confounding chemicals is flawed.

- Results of Anglen and Rotman et al. contradictory? As mentioned above, these authors - as well as Joosting and Verberk - started with 0.5 ppm as the lowest concentration. All three papers report on some subjective irritation at this lowest level (eye, nose and throat). Henschler and Rupp state that there were some subjective irritations below 0.5 ppm but only at or above this concentration the symptoms were rated as interfering with well feeling. I see no significant difference between the descriptions given in the four studies. Since the other authors (Anglen, Rotman et al., Joosting and Verberk) have not tested concentrations below 0.5 ppm, one can not extract from the published data that there is a discrepancy between the data provided by any of the four papers; of course this refers to subjective symptoms exclusively. Rather, I would rate the reported findings as comparable, and consistent.- One should keep in mind in this context that experiencing and reporting of subjective signs of irritation may grately be influenced - besides differences in experimental designs and materials used (such as construction of exposure cages, air flow rates, type and precision of analytical control of concentrations within the chambers which have not been fully described in some of the papers) - by *motivation*. Joosting and Verberk repoprt on an interesting experiment with ammonia in which the responses of committee members differ widely from those of students. Also, it seems important whether or not exposed volunteers are informed in advance of what they are exposed to (no information in the Rupp and Henschler study, information in the others), which may influence motivation considerably. - Nevertheless, despite the fact that a variety of factors may lead to varying results of subjective perceptions in different studies, the surprising

result is that all studies come to the same conclusion: the TLV for occupational exposures should be set at 0.5 ppm (8 hours average), which was put into operation in Germany in 1961, and in the US somewhen later (TLV - List). Also, there is consistency between the approaches exercised in Germany and the US to regulate peak exposures: 1 ppm/5 min 8times within a 8 hours shift (Germany, standard regulation for all local irritants), and - according to the proposal of Anglen - 2 ppm for any 15 min period in the US.- Taking all this information together, I would conclude: there seems to have been a misinterpretation of some results of the Rupp and Henschler study. In fact, they are comparable with data reported by other authors, particularly at the level of upcoming irritations, and have lead to identical conclusions with regard to the setting of occupational exposure standards for chlorine.

On Page 14, 1st para under 3.1 Acute Lethality it is stated that the finding of Schlagbauer and Henschler (1967) of a LC50 of 10 ppm for 3 hours exposure is contradicted by the non-lethal 6-hour exposure to 9.3 ppm (for 5 days) by Buckley et al. (1984). It is well-established knowledge that acute lethality studies in rodents may be considerably influenced by species and strain, age, gender, and a variety of conditions of handling of animals, as well as conditions of exposure. Visiting the paper of Buckley et al., I found out that they put groups of animals of 16 to 24 into a (rather small) glass aquarium of 102 liters in bulk. It is common experience that under exposure to strong irritants rodents put their noses under the fur of their neighbours, thus forming heaps, and making use of a protective filtering of the exposure atmosphere. In our experiments, we kept animals strictly separate by wire constructions, thus avoiding such protective behaviours of the animals. In other words: our mice will probably have been exposed to comparatively higher concentrations than those in the Buckley et al. experiments. This protective mechanism becomes the more effective, the longer the exposure time is. I suspect this explanation to be valid in view of the other toxicity figures: If one compares, as presented in your table 3 (page 15 of the document), the LC 50s for 30 min (Schlagbauer vs. Bitron and Zwart and Woutersen), 10 min (Alarie, Silver, Lipton), there are variations of 3- to 4-times at maximum. Such differences are not uncommon in acute toxicity testing results. I refer here for instance to the paper by Zbinden and Flury-Roversi, Arch.Toxicol. 47 (1981), 77-99 which lists the results of interlaboratory calibration tests with 65 participating laboratories from 8 countries, resulting in differences of LD50 determinations for 4 chemicals in rats ranging from 2.5- to 11.9-times, even when trying to standardise species, strain, age and environmental conditions of animal care. - In light of this, I think it inappropriate to characterize the results of Schlagbauer and Henschler as contradicted by others; rather, the results are in line with general experiences about variations of LD50 and LC50 determinations from different laboratories.

Bromine. Some inconsistencies of citing old literature may be mentioned:

- Lehmann and Hess (1887) is a misquotation. Lehmann published a paper on bromine (and some other irritants) in 1887 which is correctly listed in your file of references. Hess submitted a doctoral thesis at the university of Zurich in 1912. These two authors have never collaborated, nor written a paper together. Flury and Zernik (1931) made, in a chapter on bromine, reference to both authors in a floppy way (which was not uncommon those days) in the form of "Lehmann-Hess". The real background is as follows: L. Matt submitted a doctoral thesis in 1889 at the

University of Würzburg. It was sponsored by K.B. Lehmann. Matt investigated chlorine and bromine vapours in volunteers, and came to the conclusion that chlorine and bromine exert comparable irritant effects on mucous membranes: 0.001 - 0.002 ‰ "work possible without impairment"; 0.002 - 0.003 ‰ "work still possible but uncomfortable"; 0.004 ‰ "work impossible". Lehmann (1887) makes reference to these results; interestingly enough, the concentration of 0.004 ‰ has not been measured, due to mishandling of the analytical equipment, but just calculated from the amount of bromine evaporized. Hess, in his dissertation of 1912, cited these results; he himself has not contributed new data. Unfortunately, Flury and Zernik mistook the dimension of ‰ (vol/vol) as mg/m^3 (w/vol), so that they are quoted in the ensuing literature in two different versions (Withers and Lees 1986 describe this disscrepancy correctly). Nevertheless, many reviewers, eg. Patty, Henderson and Haggard, Fairhall, Elkins, and probably many others used the citation as published in Flury and Zernik as "Lehmann and Hess", as you did in your file. In fact, all of these citations are based on the work done by Matt. - If you wish to see the original booklet of Matt, please let me know, I will send you a copy.

- On page 7, first line it is stated that "the more recent studies of odor thresholds also call into question the results of the Rupp and Henschler study". It is my interpretation that this is based on the literature listed up in table 3 (pages 5 and 6) of your document. My literature search revealed that the following papers are just reviews of previous publications, without providing any new data on odor thresholds: Billings and Jonas (1981), Amoore and Hautala (1983), Ruth (1986), Alexandrow (1983), of course Lehmann and Hess (1887; see above), Elkins (1959), Henderson and Haggard (1943). An unprejudiced reader may get the impression that there is a variety of data available dealing with odor and irritation of bromine; some statement in your text refers to "more recent" publications. To my information, nobody except Matt and Rupp and Henschler have contributed original data. Therefore, may I recommend to shorten the table duely, or make clear that the bulk of citations just quotes the (only) old information.

- Page 3, last but one para, line 7/8: Rupp and Henschler did not state that bromine is a lacrimator below 1.0 ppm. The paper says that from 0.5 ppm onwards there is a stinging and burning sensation at the conjunctivae.

- Page 3. last but one para, last sentence (also in the middle of page 8): It is stated that chronic exposure to bromine resulting in excessive tissue levels of bromide ions (bromism) may lead to a variety of symptoms characteristic of bromism. To my information, this is quite unlikely to occur because the absolutely dominating symptom of bromine exposure is irritation of mucous membranes, the bromide levels from absorbed bromine are expected extremely low, and can by no means be compared with those resulting from bromide intake with centrally depressing drugs which are well documented in the relevant literature. I think this rather speculative conclusion should not be included in the document on bromine.

- Page 4, 3rd para, first sentence says "although it is a weaker oxidizing agent than fluorine or chlorine, Rupp and Henschler (1967) reported that bromine is more irritating than chlorine". The molecular mechanism of irritation by bromine or chlorine has not been evaluated. However, it is well established that the irritating capacities of different mucous membrane irritants are dependant on their water

solubility. This is - as described in the documents - much higher with bromine than with chlorine. Water solubility also determines the penetration of the gaseous compounds down the respiratory tract, which means that chlorine gets deeper than bromine. Thus, bromine is expected to react more intensely at the upper parts of the respiratory tract which are more sensitive to irritation in general than the lower parts. This difference in the deposition and pathological reaction between chlorine and bromine is substantiated by the histology of lesions as described in the paper of Schlagbauer and Henschler, as well as by other authors. Therefore, I see no reason to use the oxidizing capacity of the two gases as an argument for their potency of sensory irritation.

- Page 10/11, from last but one line on (also page 12, 2nd para, line 6/7): It is stated that the Schlagbauer and Henschler study did not use a control group, and that Withers and Lees (1986) also noted that the chlorine LC50 value of Schlagbauer and Henschler (1967) is lower than values of other researchers. - As pointed out above under chlorine, LC50 determinations do not need, and do not use control groups (see for instance the studies of Bitron and Aharonson 1978, Zwart and Woutersen 1988, and all the others which did not use control groups). With regard to the LC 50 values, the statement of Withers and Lees is correct, but does not indicate this to be an unusual finding, it is by no means contradictory to expectation (see above under chlorine), and does not justify to put into question the reliability of the study. In fact, Withers and Lees stated in their paper on bromine (1986) that the LC50 values of Bitron and Aharonson and of Schlagbauer and Henschler are - although obtained by different strategies - in accordance, as pointed out in fig 1 and table 3 of that paper, and Withers and Lees make use of the data of both experimental studies by averaging the results.

- Page 13, last para, line 3: The paper of Rupp and Henschler does not report that eye irritation occured at 0.006 ppm. As can be seen from the text and table 2, a concentration of 0.006 ppm has not been tested. The lowest concentration of bromine tested has been 0.01 ppm. Eye irritation was noted from 0.1 ppm on. I should be grateful for a correction of this misinterpretation of the data provided in the paper.

Finally, you ask for my comment on levels of bromine being uncomfortable, threshold of irreversible effects, and threshold of death. A threshold for uncomfortable (subjective) effects can be set, on the basis of our old findings, at 0.5 ppm ,which is in line with your AEGL-1. A threshold for irreversible effects, in the sense of irrepairable tissue damage, can not be derived from our studies and those of others; what can be said is that it should be expected to be higher than 2 ppm. A threshold for death can not be derived at present on a scientific basis, due to incomplete data from humans and experimental animals. I prefer to follow here the approach of Withers and Lees who start from (the much better) data on chlorine, using a conversion factor from animal toxicity data of both chlorine and bromine. The approach applied for the derivation of a AEGL-3 makes use of two uncertainty factors, the magnitude of which is set arbitrarily, and thus they constitute trans-scientific elements. To my mind, AEGL-1 and AEGL-2 are well based by scientific information. The only reservation is that we are lacking sound data to deal adequately with the "hypersusceptible" part of a population but I see no alternative to the way out of the dilemma than you took.

I hope my comments may be of some use for your efforts. If any uncertainties remain, please feel free to contact me again.

Sincerely yours,

D. Henschler

Attachment 13

ACUTE EXPOSURE GUIDELINE LEVELS FOR PHOSPHINE

Response to COT Suggestions and development of 10-min. values

NAC/AEGL-18
April 26-28, 2000

CHEMICAL MANAGER: ERNEST FALKE
ORNL STAFF SCIENTIST: CHERYL BAST

INTRODUCTION- PHOSPHINE

- **Colorless gas used as a fumigant against insects and rodents in stored grain and as a doping agent in the semiconductor industry**

- **Produced by hydrolysis of aluminum phosphide or the electrolysis of phosphorus in the presence of hydrogen**

- **Pure phosphine is odorless at concentrations up to 200 ppm. Garlic-like odor noted at 1.5 to 3 ppm is likely due to impurities in technical grade phosphine.**

DATA SUMMARY- PHOSPHINE

- **Human Data**

  - **There are numerous case reports concerning human phosphine exposure; however, reliable exposure duration and concentration terms were not available.**

  - **Common clinical signs include headache, nausea, vomiting, coughing, shortness of breath, paresthesia, weakness, tremors, and jaundice.**

  - **Post-mortem examination may reveal pulmonary congestion, pleural effusion, and congestive heart failure.**

  - **Children may be more sensitive than adults when exposed to presumably similar phosphine concentrations.**

    - **Two female children (ages 2 and 4.5 years) and 31 adult crew members were exposed to phosphine aboard a grain freighter. All adults and the 4 year-old child survived. The two-year old died as a result of the exposure. (Wilson et al., 1980).**

    - **Four males (ages 12, 35, 39, and 52 years) were discovered in a box car containing loose bulk lima beans that had been fumigated with aluminum phosphide. When discovered, the 12-year old was dead, while the three adults survived the exposure. (MMWR, 1994)**

DATA SUMMARY- PHOSPHINE

- **Animal Data**

  - **4-Hr. LC_{50} in male Charles River rats: 11 ppm (Waritz and Brown, 1975)**

  - **6-Hr. LC_{50} in male and female Sprague-Dawley rats: 28 ppm NOEL for death: 18 ppm (Newton, 1991)**

  - **Lethality data also available for mice, guinea pigs, cats, and rabbits. However, experimental details were not reported and exposure concentrations cannot be verified.**

  - **Non-lethal endpoints from acute exposure included decreased body weight, tremors, hunched appearance, decreased activity, and red mucoid discharge.**

  - **Non-lethal endpoints from repeated exposures included decreased lung weight, increased heart weight, kidney and liver histopathology, anemia, decreased white blood cell counts, and increased serum liver enzymes.**

ACUTE EXPOSURE GUIDELINES FOR PHOSPHINE (CAS NO. 7803-51-2)

AEGL-1 VALUES			
30 minutes	1 hour	4 hours	8 hours
Not appropriate	Not appropriate	Not appropriate	Not appropriate

Reference: Data unavailable

Test Species/Strain/Number: Not applicable

Exposure Route/Concentrations/Durations: Not applicable

Effects: Not applicable

Endpoint/Concentration/Rationale: Not applicable

Uncertainty Factors/Rationale: Not applicable

Modifying Factor: Not applicable

Animal to Human Dosimetric Adjustment: Not applicable

Time Scaling: Not applicable

Confidence: Appropriate data were not available for derivation of AEGL-1 values.

ACUTE EXPOSURE GUIDELINES FOR PHOSPHINE (CAS NO. 7803-51-2)

AEGL-2 VALUES			
30 minutes	1 hour	4 hours	8 hours
0.36 ppm	0.25 ppm	0.13 ppm	0.089 ppm

Reference: Newton et al. 1993. Inhalation toxicity of phosphine in the rat: acute, subchronic, and developmental. Inhalation Toxicol. 5: 223-239.

Test Species/Strain/Number: F344 rats/ 30/sex/concentration

Exposure Route/Concentrations/Durations: Inhalation: 0, 0.37, 1.0, 3.1, or 10 ppm, 6 hr/day, 5 days/week for 13 weeks

Effects:

0.37 ppm	no effects
1.0 ppm	decreased body weights and food consumption in males & females
3.1 ppm	decreased body weights and food consumption in males & females (determinant for AEGL-2)
10 ppm	lung congestion and kidney histopathology in both sexes, more severe in males than in females

Endpoint/Concentration/Rationale: 3.1 ppm,Exposure was for 6 hours a day, 5 days a week for 13 weeks.; no-effect-level for kidney pathology

Uncertainty Factors/Rationale:
Total uncertainty factor: 30
Interspecies: 3; Toxicity data exist for an AEGL-2 level effect in rats, but not mice, therefore the rat was used. Since data are from a multiple-exposure 13 week study in which no rats died, an uncertainty factor of 3 is used for the acute levels.
Intraspecies: 10 - Children appear to be more sensitive than adults to the effects of phosphine. There were two case reports where exposed children died but adults exposed under similar conditions survived.

Modifying Factor: NA

Animal to Human Dosimetric Adjustment: None; insufficient data

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

Confidence: AEGL-2 values are at least protective since they are based on a no-effect-level for serious effects in a repeated-exposure study.

ACUTE EXPOSURE GUIDELINES FOR PHOSPHINE (CAS NO. 7803-51-2)

AEGL-3 VALUES

30 minutes	1 hour	4 hours	8 hours
2.1 ppm	1.5 ppm	0.74 ppm	0.52 ppm

Reference: Newton, P.E. 1991. Acute inhalation exposures of rats to phosphine. Bio/Dynamics, Inc. East Millstone, NJ. Project No. 90-8271.

Test Species/Strain/Sex/Number: Sprague-Dawley rats, 5/sex/concentration or 10 males/concentration

Exposure Route/Concentrations/Durations: Inhalation: 0, 1.3, 6.0, or 28 ppm for 6 hr (5/sex/group); 0, 3.1, 10, or 18 ppm for 6 hr (10 males/group)

Effects: Exposure was for 6 hours.

Concentration	Mortality
0 ppm	0/10
1.3 ppm	0/10
3.1 ppm	0/10
6.0 ppm	0/10
10 ppm	0/10
18 ppm	0/10 (determinant for AEGL-3)
28 ppm	5/10

LC_{50}: 28 ppm

Endpoint/Concentration/Rationale: No-effect-level for death; 18 ppm, 6 hr.

Uncertainty Factors/Rationale:

Total uncertainty factor: 30

Interspecies: 3; This study was chosen because the use of other studies would have resulted in AEGL-3 levels which overlapped the AEGL-2 levels. However the AEGL-2 levels were set based upon data from a subchronic study. The OSHA PEL of 0.28 ppm was reported to have been exceeded in 5 separate human-exposure cases. Since adult humans can apparently tolerate this level without death a less conservative uncertainty factor of 3 is justified.

Intraspecies: 10 - Children appear to be more sensitive than adults to the effects of phosphine. There were two case reports where exposed children died but adults exposed under similar conditions survived.

Modifying Factor: Not applicable

Animal to Human Dosimetric Adjustment: Insufficient data

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

Confidence: Study is considered appropriate for AEGL-3 derivation since exposures are over a wide range of phosphine concentrations and utilize a sufficient number of animals.

ISSUES- PHOSPHINE

•Data indicate that the value of the exponent 'n' is approximately 1. The default value of n=2 is not correct.

•Better justification of the interspecies UF of 3.

•Derivation of AEGL-2 from a repeated-dose study is viewed as overly conservative.

-The experimental exposure was 6 hr/day, 5 days/week for 13 weeks.

-AEGL-2 values were calculated assuming a single 6 hour exposure.

•Suggest derivation of AEGL-1 values.

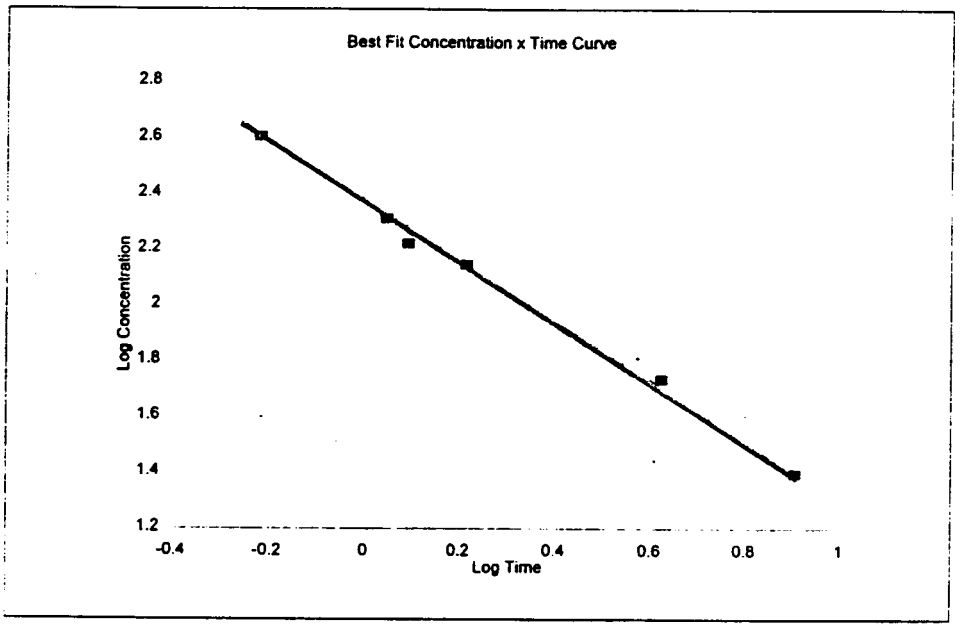
Time	Conc.	Log Time	Log Conc.
8	25	0.9031	1.3979
4.17	54	0.6201	1.7324
1.62	140	0.2095	2.1461
1.22	167	0.0864	2.2227
1.1	205	0.0414	2.3118
0.6	403	-0.2218	2.6053

Regression Output:	
Intercept	2.3553
Slope	-1.0468
R Squared	0.9968
Correlation	-0.9984
Degrees of Freedom	4
Observations	6

n = 0.96
k = 177.84

Minutes	Conc.
30	6.44
60	3.12
240	0.73
480	0.35

Hours	Conc.
0.5	468.12
1.0	226.60
4.0	53.09
8.0	25.70



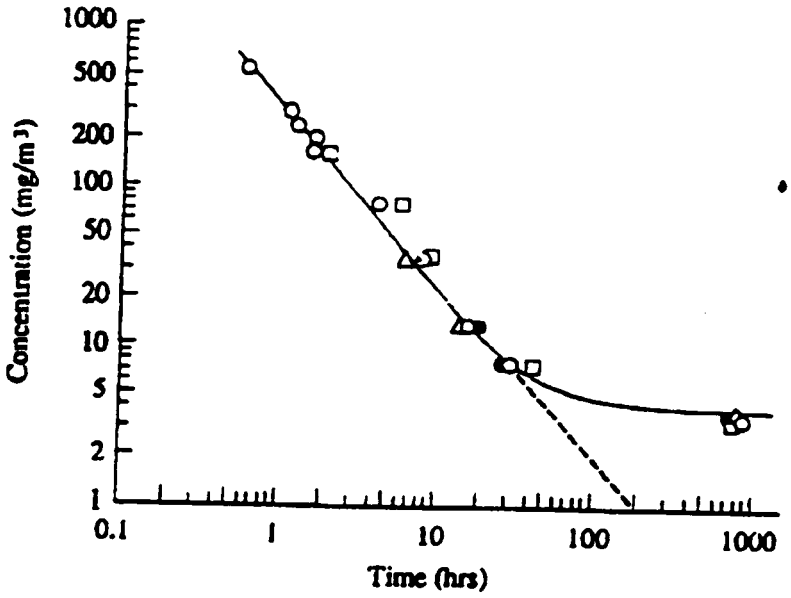


FIGURE 1. Phosphine concentration vs. Average time to death of rats (○), rabbits (△), guinea pigs (●), and cats (□).
(Gehring, 1991 from analysis of the data of Klimmer, 1969)

AEGL-1 FOR PHOSPHINE (ppm)				
AEGL Level	*30-min*	*1-hr*	*4-hr*	*8-hr*
AEGL-1	*2.4*	*1.2*	*0.30*	*0.15*

Species: *Rat*
Concentration: *6 ppm*
Time: *6 hr.*
Endpoint: *NOEL*
Reference: *Newton, 1991*

n = 1

Uncertainty Factor: 3 x 10 =30

Interspecies = 3 (Rat, rabbit, guinea pig, and cat lethality data suggest little species variability)

Intraspecies = 10 (Human data suggest that children are more sensitive than adults)

OR

0.3 ppm causes only headache in humans (secondary source cannot be verified)

AEGL-2 FOR PHOSPHINE (ppm [mg/m^3])					
AEGL Level	10-min	30-min	1-hr	4-hr	8-hr
AEGL-2	4.0 [5.6]	4.0 [5.6]	2.0 [2.8]	0.50 [0.71]	0.25 [0.35]

Species: Rat
Concentration: 10 ppm
Time: 6 hr.
Endpoint: Red nasal mucoid discharge
References: Newton et al., 1993

n = 1

Uncertainty Factor: 3 x 10 =30

Interspecies = 3 (Rat, rabbit, guinea pig, and cat lethality data suggest little species variability)

Intraspecies = 10 (Human data suggest that children are more sensitive than adults)

AEGL-3 FOR PHOSPHINE (ppm [mg/m^3])					
AEGL Level	10-min	30-min	1-hr	4-hr	8-hr
AEGL-3	7.2 [10]	7.2 [10]	3.6 [5.1]	0.90 [1.3]	0.45 [0.63]

Species: Rat
Concentration: 18 ppm
Time: 6 hr.
Endpoint: NOEL for death
References: Newton, 1991

n = 1

Uncertainty Factor: 3 x 10 =30

Interspecies = 3 (Rat, rabbit, guinea pig, and cat lethality data suggest little species variability)

Intraspecies = 10 (Human data suggest that children are more sensitive than adults)

RELATIONAL COMPARISON OF AEGL VALUES FOR PHOSPHINE (ppm [mg/m^3])					
Classification	**10-min**	**30-min**	**1-hour**	**4-hour**	**8-hour**
AEGL-1 (Nondisabling)	-	–	–	–	–
AEGL-2 (Disabling)	**4.0 [5.6]**	**4.0 [5.6]**	**2.0 [2.8]**	**0.50 [0.71]**	**0.25 [0.35]**
AEGL-3 (Lethality)	**7.2 [10]**	**7.2 [10]**	**3.6 [5.1]**	**0.90 [1.3]**	**0.45 [0.63]**

TWA PEL (OSHA): 0.28 ppm
TLV TWA (ACGIH, 1991): 0.3 ppm
TLV STEL (ACGIH, 1991): 1.0 ppm

ERPG-1 (AIHA, 1999): Not Appropriate
ERPG-2 (AIHA, 1999): 0.5 ppm (1 hour)
ERPG-3 (AIHA, 1999): 5 ppm (1 hour)

Appendix A

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

INTRODUCTION

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

GENERAL INTEREST ITEMS

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

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

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

C). AEGL values are not intended to apply to infrequent exposures. A request was made for NAS/AEGL members to submit thoughts/comments to Ernie Falke and John Morawetz for possible inclusion in the SOP document.

AEGL PRIORITY CHEMICALS

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

SUMMARY OF PROPOSED AEGL VALUES FOR SULFUR MUSTARD (AGENT HD)						
Classification	**10-min**	**30-min**	**1-hour**	**4-hour**	**8-hour**	**Endpoint (Reference)**
AEGL-1	0.060 ppm 0.40 mg/m^3	0.020 ppm 0.13 mg/m^3	0.010 ppm 0.067 mg/m^3	0.0026 ppm 0.017 mg/m^3	0.0012 ppm 0.008 mg/m^3	Conjunctival injection and minor discomfort with no functional decrement in human volunteers (Anderson, 1942)
AEGL-2	0.090 ppm 0.60 mg/m^3	0.030 ppm 0.20 mg/m^3	0.015 ppm 0.10 mg/m^3	0.0038 ppm 0.025 mg/m^3	0.0020 ppm 0.013 mg/m^3	Well marked, generalized conjunctivitis, edema, photophobia, and eye irritation in human volunteers (Anderson, 1942)
AEGL-3	0.91 ppm 6.1 mg/m^3	0.63 ppm 4.2 mg/m^3	0.32 ppm 2.1 mg/m^3	0.080 ppm 0.53 mg/m^3	0.041 ppm 0.27 mg/m^3	Lethality estimate in mice (Kumar and Vijayaraghavan, 1998)

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Thus, proposed values are as follows:

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

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

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

ADMINISTRATIVE ISSUES

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

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

Future NAS/COT meetings were also announced and included

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

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

LIST OF ATTACHMENTS

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

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

LIST OF APPENDICES

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

Appendix B

INTERIM VOTE (to accept PROPOSED)

NAC/AEGL Meeting 17: 4/26-28/2000 **Chemical:** HFC 134a #811-97-2

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

NAC Member	AEGL 1	AEGL 2	AEGL 3
Loren Koller	Y	Y	Y
Glenn Leach	A	A	A
Mark A. McClanahan	Y	Y	Y
John S. Morawetz	N	Y	Y
Richard W. Niemeier	N	Y	Y
Zarena Post	Y	Y	Y
George Rodgers	A	A	A
George Rusch, Chair	Y	Y	Y
Michelle Schaper	A	A	A
Bob Snyder	Y	Y	Y
Thomas Sobotka	A	A	A
Kenneth Still	Y	Y	Y
Judy Strickland (Membership pending)	(N)	(Y)	(Y)
Richard Thomas	A	A	A
Thomas Tuccin/ Doan ardi Hansen	A	A	A
TALLY	16/19	19/19	19/19

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

AEGL 1 **Motion:** L. Koller **Second:** J. Hinz

AEGL 2 **Motion:** J Morawetz **Second:** Mark McClanahan

AEGL 3 **Motion:** J Morawetz **Second:** Mark McClanahan

Approved by Chair: [signature] **DFO:** Paul S. Tobin **Date:** 4/26/00

Appendix C

INTERIM VOTE (to accept PROPOSED)

NAC/AEGL Meeting 17: 4/26-28/2000 **Chemical:** 1,1,1-TRICHLOROETHANE #71-55-06

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

NAC Member	AEGL 1	AEGL 2	AEGL 3
Loren Koller	Y	Y	Y
Glenn Leach	A	A	A
Mark A. McClanahan	Y	Y	Y
John S. Morawetz	N	N	N
Richard W. Niemeier	Y	Y	Y
Zarena Post	N	N	N
George Rodgers	A	A	A
George Rusch, Chair	Y	Y	Y
Michelle Schaper	A	A	A
Bob Snyder	Y	Y	Y
Thomas Sobotka	A	A	A
Kenneth Still	Y	Y	Y
Judy Strickland Membership pending	P	P	P
Richard Thomas	A	A	A
Thomas Tuccin/ Doan ardi Hansen	A	A	A
TALLY	13/19		

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

AEGL 1 **Motion:** Snyder **Second:** Barbee

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

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

Approved by Chair: _____ **DFO:** _____ **Date:** 4/26/00

Appendix D Ballot to move from Proposed → Interim

NAC/AEGL Meeting 17: 4/26-28/2000 **Chemical:** Sulfur Mustard

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

NAC Member	AEGL 1	AEGL 2	AEGL 3
Loren Koller			
Glenn Leach	A	A	A
Mark A. McClanahan			
John S. Morawetz			
Richard W. Niemeier			
Zarena Post			
George Rodgers	A	A	A
George Rusch, Chair			
Michelle Schaper	A	A	A
Bob Snyder			
Thomas Sobotka	A	A	A
Kenneth Still			
Judy Strickland Membership pending			
Richard Thomas	A	A	A
Thomas Tuccin/ Doan ardi Hansen	A	A	A
TALLY	UNANIMOUS		Y

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

AEGL 1 **Motion:** Mark McClanahan **Second:** Richard Niemeier

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

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

Approved by Chair: _____ **DFO:** _____ **Date:** 4/26/00

Appendix E

Ballot to move proposed AEGL → # INTERIM

NAC/AEGL Meeting 17: 4/26-28/2000 **Chemical:** 1,2-DICHLOROETHYLENE #540-59-0

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

NAC Member	AEGL 1	AEGL 2	AEGL 3
Loren Koller	Y	Y	Y
Glenn Leach	A	A	A
Mark A. McClanahan	Y	Y	Y
John S. Morawetz	Y	Y	Y
Richard W. Niemeier	Y	Y	Y
Zarena Post	A	A	A
George Rodgers	A	A	A
George Rusch, Chair	Y	Y	Y
Michelle Schaper	A	A	A
Bob Snyder	Y	Y	Y
Thomas Sobotka	A	A	A
Kenneth Still	Y	Y	Y
Judy Strickland Membership pending	Y	Y	Y
Richard Thomas	A	A	A
Thomas Tuccin/ Doan ardi Hansen	A	A	A
TALLY	19/19	19/19	19/19

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

AEGL 1 **Motion:** Mark McClanahan **Second:** Dave Belluck

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

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

Approved by Chair: [signature] **DFO:** [signature] **Date:** 4/26/00

Appendix F

NAC/AEGL Meeting 17: 4/26-28/2000 **Chemical:** INTERIM AEGLS * OTTO FUEL # 106602-80-6

NAC Member	AEGL 1	AEGL 2	AEGL 3 *	NAC Member	AEGL 1	AEGL 2	AEGL 3
George Alexeeff	Y	Y	Y A	Loren Koller	Y	Y	Y Y
Steven Barbee	Y	Y	Y Y	Glenn Leach	A	A	A A
Lynn Beasley	Y	Y	Y Y	Mark A. McClanahan	Y	Y	Y Y
David Belluck	Y	Y	Y A	John S. Morawetz	Y	Y	Y Y
Robert Benson	Y	Y	Y Y	Richard W. Niemeier	Y	Y	Y Y
Jonathan Borak	Y	Y	Y 14	Zarena Post	Y	Y	Y Y
William Bress	A	A	A A	George Rodgers	A	A	A Y
George Cushmac	Y	Y	Y Y	George Rusch, Chair	Y	Y	Y Y
Ernest Falke	Y	Y	Y Y	Michelle Schaper	A	A	A A
Larry Gephart	Y	Y	Y Y	Bob Snyder	Y	Y	Y Y
John Hinz	Y	Y	Y Y	Thomas Sobotka	A	A	A 14
Jim Holler	Y	Y	Y Y	Kenneth Still	Y	Y	Y Y
Thomas C. Hornshaw	A	A	A Y	Judy Strickland MEMBERSHIP PENDING	Y	Y	Y Y
Nancy Kim	A	A	A Y	Richard Thomas	A	A	A
M. Payton	A	A	A A	Thomas Tuccin/ Doan ardi Hansen	A	A	A
				TALLY	19/19	19/19	19/19 14

* Maintain all AEGL values as proposed, except Change AEGL-2 10 MIN 6PPM → 2PPM

PPM, (mg/m³) 10 MIN	30 Min	60 Min	4 Hr	8Hr
AEGL 1	,( )	,( )	,( )	,( )
AEGL 2 2PPM	,( )	,( )	,( )	,( )
AEGL 3 16PPM	,( )	,( )	,( )	,( )

+ AEGL 2 10 M TO 16PPM

AEGL 1 **Motion:** Benson **Second:** Niemeier

AEGL 2 **Motion:** Benson **Second:** Niemeier

AEGL 3 **Motion:** Falke **Second:** Hinz

Approved by Chair: [signature] **DFO:** Paul S. Tobin **Date:** 4/26/00

Appendix G Accept Proposed → Interim AEGLs

NAC/AEGL Meeting 17: 4/26-28/2000 **Chemical:** HCFC - 141b # 1717-00-6

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

NAC Member	AEGL 1	AEGL 2	AEGL 3
Loren Koller	Y	Y	Y
Glenn Leach	A	A	A
Mark A. McClanahan	Y	Y	Y
John S. Morawetz	N	Y	Y
Richard W. Niemeier	Y	Y	Y
Zarena Post	Y	Y	Y
George Rodgers	A	A	A
George Rusch, Chair	Y	Y	Y
Michelle Schaper	A	A	A
Bob Snyder	Y	Y	Y
Thomas Sobotka	A	A	A
Kenneth Still	Y	Y	Y
Judy Strickland MEMBERSHIP PENDING	N	Y	Y
Richard Thomas	A	A	A
Thomas Tuccin/ Doan ardi Hansen	A	A	A
TALLY	17/19	17/19	19/19

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

AEGL 1 **Motion:** McClanahan **Second:** Benson

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

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

Approved by Chair: _____ **DFO:** Paul S. Tobin **Date:** 4/26/00

Appendix H

Proposed AEGL → Interim AEGL

NAC/AEGL Meeting 17: 4/26-28/2000 **Chemical:** HYDROGEN SULFIDE # 7783-06-4

NAC Member	AEGL 1	*AEGL 2	*AEGL 3	NAC Member	AEGL 1	AEGL 2	AEGL 3
George Alexeeff	Y	Y	Y	Loren Koller	Y	Y	Y
Steven Barbee	Y	Y	Y	Glenn Leach	A	A	A
Lynn Beasley	Y	Y	Y	Mark A. McClanahan	A	Y	Y
David Belluck	Y	Y	Y	John S. Morawetz	Y	Y	Y
Robert Benson	Y	Y	Y	Richard W. Niemeier	Y	Y	Y
Jonathan Borak	Y	P A	P A	Zarena Post	Y	Y	Y
William Bress	A	A	A	George Rodgers	A	A	A
George Cushmac	Y	Y	Y	George Rusch, Chair	Y	Y	Y
Ernest Falke	Y	Y	Y	Michelle Schaper	A	A	A
Larry Gephart	Y	Y	N	Bob Snyder	Y	Y	Y
John Hinz	Y	P A	A P	Thomas Sobotka	A	A	A
Jim Holler	Y	Y	Y	Kenneth Still	Y	Y	Y
Thomas C. Hornshaw	Y	A	P	Judy Strickland (Membership pending)	N	(A)	(Y)
Nancy Kim	A	A	A	Richard Thomas	A	A	A
M. Payton	A	A	A	Thomas Tuccin/ Doan ardi Hansen	A	A	A
				TALLY	19/19	17/17	16/17

* ACCEPT AEGL-2 & 3 PROPOSED LEVELS AS INTERIM

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

AEGL 1 **Motion:** I. Belluck **Second:** E. Falke

AEGL 2 **Motion:** R Benson **Second:** E Falke

AEGL 3 **Motion:** ↓ **Second:** ↓

Approved by Chair: [signature] **DFO:** Paul S. Tobin **Date:** 4/26/00

Appendix I PROPOSED AEGL → INTERIM (2,3 only)

NAC/AEGL Meeting 17: 4/26-28/2000 **Chemical:** HYDROGEN CYANIDE # 74-90-8

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

NAC Member	AEGL 1	AEGL 2	AEGL 3
Loren Koller		Y	Y
Glenn Leach	A	A	A
Mark A. McClanahan		Y	Y
John S. Morawetz		Y	Y
Richard W. Niemeier		Y	Y
Zarena Post		Y	Y
George Rodgers		Y	Y
George Rusch, Chair		Y	Y
Michelle Schaper	A	A	A
Bob Snyder		Y	Y
Thomas Sobotka	A	A	A
Kenneth Still		Y	Y
Judy Strickland MEMBERSHIP PENDING	( )	(Y)	(Y)
Richard Thomas	A	A	A
Thomas Tuccin/ Doan ardi Hansen	A	A	A
TALLY		21/22	21/22

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

AEGL 1 **Motion:** Rudyse **Second:** Hornshaw

AEGL 2 **Motion:** Falke **Second:** Benson

AEGL 3 **Motion:** ↓ **Second:** ↓

Approved by Chair: [signature] **DFO:** Paul S. Tobin **Date:** 4/27/00

Appendix J

10 MIN AEGLs CAS # 123-73-9 trans # 4170-30-3

NAC/AEGL Meeting 17: 4/26-28/2000 **Chemical:** CROTONALDEHYDE

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

NAC Member	AEGL 1	AEGL 2	AEGL 3
Loren Koller	Y	→	→
Glenn Leach	A	A	A
Mark A. McClanahan	Y	→	→
John S. Morawetz	Y	→	→
Richard W. Niemeier	Y	→	→
Zarena Post	Y	→	→
George Rodgers	Y	→	→
George Rusch, Chair	Y	→	→
Michelle Schaper Membership Pending	A	A	A
Bob Snyder	Y	→	→
Thomas Sobotka	A	A	A
Kenneth Still	Y	→	→
Judy Strickland Membership pending	Y	→	→
Richard Thomas	A	A	A
Thomas Tuccin/ Doan ardi Hansen	A	A	A
TALLY	22/22	22/22	22/22

PPM, (mg/m³) 10 MIN	30 Min	60 Min	4 Hr	8Hr
AEGL 1 0.19	, ( )	, ( )	, ( )	, ( )
AEGL 2 27	, ( )	, ( )	, ( )	, ( )
AEGL 3 44	, ( )	, ( )	, ( )	, ( )

AEGL 1 **Motion:** Rodgers **Second:** Hinz

AEGL 2 **Motion:** Rodgers **Second:** Hinz

AEGL 3 **Motion:** ↓ **Second:** ↓

Approved by Chair: George M Rusch **DFO:** Paul S. Tobin **Date:** 4/27/00

Appendix K

10 MIN. AEGLS

NAC/AEGL Meeting 17: 4/26-28/2000 **Chemical:** ALLYLAMINE # 107-11-9

NAC Member	AEGL 1	AEGL 2	AEGL 3	NAC Member	AEGL 1	AEGL 2	AEGL 3
George Alexeeff	P	Y	Y	Loren Koller	Y	Y	Y
Steven Barbee	Y	Y	Y	Glenn Leach	A	A	A
Lynn Beasley	Y	Y	Y	Mark A. McClanahan	Y	Y	Y
David Belluck	Y	Y	Y	John S. Morawetz	Y	Y	Y
Robert Benson	P	Y	Y	Richard W. Niemeier	Y	Y	Y
Jonathan Borak	A	A	A	Zarena Post	P	Y	Y
William Bress	A	A	A	George Rodgers	Y	Y	Y
George Cushmac	Y	Y	Y	George Rusch, Chair	Y	Y	Y
Ernest Falke	Y	Y	Y	Michelle Schaper	A	A	A
Larry Gephart	Y	Y	Y	Bob Snyder	Y	Y	Y
John Hinz	P	Y	Y	Thomas Sobotka	A	A	A
Jim Holler	Y	Y	Y	Kenneth Still	Y	Y	Y
Thomas C. Hornshaw	Y	Y	Y	Judy Strickland Membership pending	(Y)	(Y)	(Y)
Nancy Kim	Y	Y	Y	Richard Thomas	A	A	A
MICAYTON	A	A	A	Thomas Tuccin/ Doan ardi Hansen	A	A	A
				TALLY	17/17	21/21	21/21

PPM, (mg/m³) 10 MIN	30 Min	60 Min	4 Hr	8Hr
AEGL 1 0.2 ~~0.83~~	~~0.83~~ 0.2 ,( )	~~0.83~~ ,( )	~~0.2~~ ,( )	~~0.2~~ ,( )
AEGL 2 4.2	4.2 ,( )	2.8 ,( )	1.2 ,( )	0.83 ,( )
AEGL 3 140 ~~145~~	~~40~~ ,( )	18 ,( )	3.5 ,( )	2.3 ,( )

AEGL 1 **Motion:** McClanahan **Second:** ~~Benson~~ Koller

AEGL 2 **Motion:** Koller **Second:** Hinz

AEGL 3 **Motion:** ↓ **Second:** ↓

Approved by Chair: [signature] **DFO:** [signature] **Date:** 4/27/00

Appendix L

10 MIN AEGLs

NAC/AEGL Meeting 17: 4/26-28/2000 **Chemical:** ETHYLENEDIAMINE #107-15-3

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

NAC Member	AEGL 1	AEGL 2	AEGL 3
Loren Koller	P P	Y	Y
Glenn Leach	A A	A	A
Mark A. McClanahan	Y N	Y	Y
John S. Morawetz	N Y	Y	Y
Richard W. Niemeier	Y N	A	A
Zarena Post	N Y	Y	Y
George Rodgers	N Y	Y	Y
George Rusch, Chair	Y P	P	Y
Michelle Schaper	A A	A	A
Bob Snyder	N Y	A	A
Thomas Sobotka	A A	A	A
Kenneth Still	Y P	Y	Y
Judy Strickland Membership pending	P P	Y	Y
Richard Thomas	A	A	A
Thomas Tuccin/ Doan ardi Hansen	A	A	A
TALLY	13/~~20~~ 9*	14/18	17/19

* DOES NOT PASS

PPM, (mg/m³) 10 Min	30 Min	60 Min	4 Hr	8Hr
AEGL 1 (2) NA (1) 2.4	NA 3.4, ( )	NA 3.4, ( )	NA 3.4, ( )	NA 3.4, ( )
AEGL 2 12	12, ( )	9.7, ( )	6.1, ( )	4.8, ( )
AEGL 3 25	25, ( )	20, ( )	13, ( )	10, ( )

AEGL 1 **Motion:** (2) Benson (1) McClanahan **Second:** Snyder Niemeier

AEGL 2 **Motion:** Post **Second:** Rodgers

AEGL 3 **Motion:** ↓ **Second:** ↓

Approved by Chair: [signature] **DFO:** Paul S Tobin **Date:** 4/27/00

Appendix M

10 MIN AEGLs

NAC/AEGL Meeting 17: 4/26-28/2000 **Chemical:** CYCLOHEXYLAMINE # 108-91-8

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

NAC Member	AEGL 1	AEGL 2	AEGL 3
Loren Koller	Y	Y	Y
Glenn Leach	A	A	A
Mark A. McClanahan	N	N	N
John S. Morawetz	Y	Y	Y
Richard W. Niemeier	Y	Y	Y
Zarena Post	Y	Y	Y
George Rodgers	Y	Y	Y
George Rusch, Chair	Y	Y	Y
Michelle Schaper	A	A	A
Bob Snyder	Y	Y	Y
Thomas Sobotka	A	A	A
Kenneth Still	Y	Y	Y
Judy Strickland membership pending	(Y)	(Y)	(Y)
Richard Thomas	A	A	A
Thomas Tuccin/ Doan ardi Hansen	A	A	A
TALLY	18/21	19/21	19/21

PPM, (mg/m³) 10 Min	30 Min	60 Min	4 Hr	8Hr
AEGL 1 1.8	1.8 ,( )	1.8 ,( )	1.8 ,( )	1.8 ,( )
AEGL 2 ~~11~~ 11	11 ,( )	8.6 ,( )	5.4 ,( )	2.7 ,( )
AEGL 3 ~~55~~ 38	38 ,( )	30 ,( )	19 ,( )	9.4 ,( )

AEGL 1 **Motion:** Rodgers **Second:** Hinz

AEGL 2 **Motion:** ↓ **Second:** ↓

AEGL 3 **Motion:** ↓ **Second:** ↓

Approved by Chair: George M. Rusch **DFO:** Paul S. Tobin **Date:** 4/27/00

Appendix N

10 MIN AEGLS
2A TOLUENEDIISOCYANATE #584-84-9
2,6 TOLUENEDIISOCYANATE #91-08-7

NAC/AEGL Meeting 17: 4/26-28/2000 **Chemical:**

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

NAC Member	AEGL 1	AEGL 2	AEGL 3
Loren Koller	Y	→	→
Glenn Leach	A	A	A
Mark A. McClanahan	Y	→	→
John S. Morawetz	Y	→	→
Richard W. Niemeier	Y	→	→
Zarena Post	Y	→	→
George Rodgers	Y	→	→
George Rusch, Chair	Y	→	→
Michelle Schaper	A	A	A
Bob Snyder	Y	→	→
Thomas Sobotka	A	A	A
Kenneth Still	Y	→	→
Judy Strickland MEMBERSHIP PENDING	(Y)	→	→
Richard Thomas	A	A	A
Thomas Tuccin/ Doan ardi Hansen	A	A	A
TALLY	21/21	21/21	21/21

PPM, (mg/m³) 10 Min	30 Min	60 Min	4 Hr	8Hr
AEGL 1 0.02	0.02 ,( )	0.02 ,( )	0.01 ,( )	0.01 ,( )
AEGL 2 0.24	0.17 ,( )	0.083 ,( )	0.021 ,( )	0.021 ,( )
AEGL 3 0.65	0.65 ,( )	0.51 ,( )	0.32 ,( )	0.16 ,( )

AEGL 1 **Motion:** Barbee **Second:** Niemeier

AEGL 2 **Motion:** ↓ **Second:** ↓

AEGL 3 **Motion:** ↓ **Second:** ↓

Approved by Chair: [signature] **DFO:** [signature] **Date:** 4/27/00

Appendix O

10 MIN AEGLS

NAC/AEGL Meeting 17: 4/26-28/2000 **Chemical:** IRON PENTACARBONYL #13463-40-6

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

NAC Member	AEGL 1	AEGL 2	AEGL 3
Loren Koller	Y	Y	Y
Glenn Leach	A	A	A
Mark A. McClanahan	Y	Y	Y
John S. Morawetz	Y	N	Y
Richard W. Niemeier	Y	Y	Y
Zarena Post	Y	Y	Y
George Rodgers	Y	Y	Y
George Rusch, Chair	Y	Y	Y
Michelle Schaper	A	A	A
Bob Snyder	Y	Y	Y
Thomas Sobotka	A	A	A
Kenneth Still	Y	Y	Y
Judy Strickland Membership Pending	(Y)	(Y)	(Y)
Richard Thomas	A	A	A
Thomas Tuccin/ Doan ardi Hansen	A	A	A
TALLY	21/21	19/20	22/22

PPM, (mg/m³) 10 Min	30 Min	60 Min	4 Hr	8Hr
AEGL 1 NR	NR ,( )	NR ,( )	NR ,( )	NR ,( )
AEGL 2 1,2	0,40 ,( )	0,19 ,( )	0,050 ,( )	NA ,( )
AEGL 3 3,5	~~3,5~~ 1,2 ,( )	0,58 ,( )	0,15 ,( )	NA ,( )

AEGL 1 **Motion:** Rodgers **Second:** Belluck

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

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

Approved by Chair: _____ **DFO:** Paul S. Tobin **Date:** 4/27/00

Appendix P

NAC/AEGL Meeting 17: 4/26-28/2000 **Chemical:** NICKEL CARBONYL #13463-39-3 . 10 MIN AEGL

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

NAC Member	AEGL 1	AEGL 2	AEGL 3
Loren Koller	Y	Y	Y
Glenn Leach	A	A	A
Mark A. McClanahan	Y	Y	Y
John S. Morawetz	Y	Y	Y
Richard W. Niemeier	Y	Y	Y
Zarena Post	Y	Y	Y
George Rodgers	Y	Y	Y
George Rusch, Chair	Y	Y	Y
Michelle Schaper	A	A	A
Bob Snyder	Y	Y	Y
Thomas Sobotka	A	A	A
Kenneth Still	Y	Y	Y
Judy Strickland Membership pending	(Y)	(Y)	(Y)
Richard Thomas	A	A	A
Thomas Tuccin/ Doan ardi Hansen	A	A	A
TALLY	22/22	22/22	22/22

PPM, (mg/m³)	30 Min	60 Min	4 Hr	8Hr
AEGL 1 NR	NR ,( )	NR ,( )	NR ,( )	NR ,( )
AEGL 2 0.096	0.042 ,( )	0.021 ,( )	0.005 ,( )	NA ,( )
AEGL 3 0.46	0.32 ,( )	0.16 ,( )	0.04 ,( )	NA ,( )

NR = not recommended because of lack of data
NA = not assigned due to ~~insolubility of compound in air~~ inability to extrapolate 15 min data to 8 hr.

AEGL 1 **Motion:** Rodgers **Second:** Belluck

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

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

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

Appendix Q

10 MIN AEGLs

NAC/AEGL Meeting 17: 4/26-28/2000 **Chemical:** PHOSPHORUS OXYCHLORIDE # 10025873

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

NAC Member	AEGL 1	AEGL 2	AEGL 3
Loren Koller			A
Glenn Leach	A	A	A
Mark A. McClanahan			Y
John S. Morawetz			Y
Richard W. Niemeier			A
Zarena Post			Y
George Rodgers			Y
George Rusch, Chair			Y
Michelle Schaper	A	A	A
Bob Snyder			Y
Thomas Sobotka	A	A	A
Kenneth Still			Y
Judy Strickland Membership pending			Y
Richard Thomas	A	A	A
Thomas Tuccin/ Doan ardi Hansen	A	A	A
TALLY			8/18

PPM, (mg/m^3) 10 Min	30 Min	60 Min	4 Hr	8Hr
AEGL 1	, ( )	, ( )	, ( )	, ( )
AEGL 2	, ( )	, ( )	, ( )	, ( )
AEGL 3 1.1	1.1 , ( )	0.85 , ( )	0.54 , ( )	0.27 , ( )

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

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

AEGL 3 **Motion:** POST **Second:** Belluck

Approved by Chair: _____ **DEO:** _____ **Date:** 4/28/00

Appendix R

10 MIN DATA

NAC/AEGL Meeting 17: 4/26-28/2000 **Chemical:** PHOSPHORUS TRICHLORIDE #7719-12-2

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

NAC Member	AEGL 1	AEGL 2	AEGL 3
Loren Koller			Y
Glenn Leach	A	A	A
Mark A. McClanahan			Y
John S. Morawetz			Y
Richard W. Niemeier			Y
Zarena Post			Y
George Rodgers			Y
George Rusch, Chair			Y
Michelle Schaper	A	A	A
Bob Snyder			Y
Thomas Sobotka	A	A	A
Kenneth Still			Y
Judy Strickland MEMBERSHIP PENDING			(Y)
Richard Thomas	A	A	A
Thomas Tuccin/ Doan ardi Hansen	A	A	A
TALLY			20/20

PPM, (mg/m³) 10 Min	30 Min	60 Min	4 Hr	8Hr
AEGL 1	,( )	,( )	,( )	,( )
AEGL 2	,( )	,( )	,( )	,( )
AEGL 3 1.1 ~~1.6~~	1.1 ,( )	0.88 ,( )	0.56 ,( )	0.28 ,( )

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

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

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

Approved by Chair: [signature] **DFO:** Paul S. Tobin **Date:** 4/28/00

Appendix S 10 MIN. AEGLs

NAC/AEGL Meeting 17: 4/26-28/2000 **Chemical:** HYDROGEN CHLORIDE # 7647-01-0

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

NAC Member	AEGL 1	AEGL 2	AEGL 3
Loren Koller	Y	Y	Y
Glenn Leach	A	A	A
Mark A. McClanahan	Y	Y	Y
John S. Morawetz	Y	Y	N
Richard W. Niemeier	Y	Y	Y
Zarena Post	Y	N	N
George Rodgers	Y	Y	Y
George Rusch, Chair	Y	Y	Y
Michelle Schaper	A	A	A
Bob Snyder	Y	Y	Y
Thomas Sobotka	A	A	A
Kenneth Still	Y	Y	Y
Judy Strickland Membership pending	(Y)	(Y)	(Y)
Richard Thomas	A	A	A
Thomas Tuccin/ Doan ardi Hansen	A	A	A
TALLY	20/20	16/19	18/20

PPM, (mg/m³) 10 Min	30 Min	60 Min	4 Hr	8Hr
AEGL 1 1.8	,( )	,( )	,( )	,( )
AEGL 2 100	,( )	,( )	,( )	,( )
AEGL 3 620	,( )	,( )	,( )	,( )

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

AEGL 2 **Motion:** McClanahan **Second:** Hinz

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

Approved by Chair: _____ **DFO:** Paul S. Tobin **Date:** 4/28/00

Appendix T 10 MIN AEGS

NAC/AEGL Meeting 17: 4/26-28/2000 **Chemical:** METHYLTRICHLORO SILANE #75-79-6

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

NAC Member	AEGL 1	AEGL 2	AEGL 3
Loren Koller	Y		
Glenn Leach	A	A	A
Mark A. McClanahan	Y		
John S. Morawetz	Y	N	N
Richard W. Niemeier	Y		
Zarena Post	Y	N	N
George Rodgers	Y	N	Y
George Rusch, Chair	Y		
Michelle Schaper	A	A	A
Bob Snyder	Y		
Thomas Sobotka	A	A	A
Kenneth Still	Y		
Judy Strickland Membership pending	(Y)		
Richard Thomas	A	A	A
Thomas Tuccin/ Doan ardi Hansen	A	A	A
TALLY	20/20	16/20	18/20

PPM, (mg/m³) 10 Min	30 Min	60 Min	4 Hr	8Hr
AEGL 1 0.60	0.60 ,( )	0.60 ,( )	0.60 ,( )	0.60 ,( )
AEGL 2 37	12 ,( )	6.2 ,( )	1.6 ,( )	0.78 ,( )
AEGL 3 170	56 ,( )	28 ,( )	7.0 ,( )	3.5 ,( )

AEGL 1 **Motion:** Koller **Second:** Niemeier

AEGL 2 **Motion:** ↓ **Second:** ↓

AEGL 3 **Motion:** ↓ **Second:** ↓

Approved by Chair: [signature] **DFO:** [signature] **Date:** 4/28/00

Appendix U

10 MIN AEGLS

NAC/AEGL Meeting 17: 4/26-28/2000 **Chemical:** DIMETHYLDICHLOROSILANE #75-78-5

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

NAC Member	AEGL 1	AEGL 2	AEGL 3
Loren Koller	Y	Y	
Glenn Leach	A	A	A
Mark A. McClanahan	Y	Y	
John S. Morawetz	Y	N	N
Richard W. Niemeier	Y	Y	
Zarena Post	Y	N	N
George Rodgers	Y	N	Y
George Rusch, Chair	Y	Y	
Michelle Schaper	A	A	A
Bob Snyder	Y	Y	
Thomas Sobotka	A	A	A
Kenneth Still	Y	Y	
Judy Strickland (Membership pending)	(X)	(X)	
Richard Thomas	A	A	A
Thomas Tuccin/ Doan ardi Hansen	A	A	A
TALLY	20/20	15/20	18/20

PPM, (mg/m³) 10 Min	30 Min	60 Min	4 Hr	8Hr
AEGL 1 0.9	0.9 ,( )	0.9 ,( )	0.9 ,( )	0.9 ,( )
AEGL 2 78	26 ,( )	13 ,( )	3.3 ,( )	1.6 ,( )
AEGL 3 320	106 ,( )	53 ,( )	13 ,( )	6.6 ,( )

AEGL 1 **Motion:** Benson **Second:** McClanahan

AEGL 2 **Motion:** ↓ **Second:** ↓

AEGL 3 **Motion:** ↓ **Second:** ↓

Approved by Chair: [signature] **DFO:** [signature] **Date:** 4/28/00

Appendix V

10 MIN AEGLs

NAC/AEGL Meeting 17: 4/26-28/2000 **Chemical:** METHYL ISOCYANATE #624-83-9

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

NAC Member	AEGL 1	AEGL 2	AEGL 3
Loren Koller	Y	→	→
Glenn Leach	A	A	A
Mark A. McClanahan	Y	→	→
John S. Morawetz	Y	→	→
Richard W. Niemeier	Y	→	→
Zarena Post	Y	→	→
George Rodgers	Y	→	→
George Rusch, Chair	Y	→	→
Michelle Schaper	A	A	A
Bob Snyder	P	→	→
Thomas Sobotka	A	A	A
Kenneth Still	Y	→	→
Judy Strickland Membership pending	(Y)	→	→
Richard Thomas	A	A	A
Thomas Tuccin/ Doan ardi Hansen	A	A	A
TALLY	20/20	20/20	20/20

PPM, (mg/m³) 10 Min	30 Min	60 Min	4 Hr	8Hr
AEGL 1 * N.A	NA ,( )	NA ,( )	NA ,( )	NA ,( )
AEGL 2 0,40	0,13 ,( )	0,067 ,( )	0,017 ,( )	0,008 ,( )
AEGL 3 1,2	0,40 ,( )	0,20 ,( )	0,05 ,( )	0,025 ,( )

* Not recruited

AEGL 1 **Motion:** Benson **Second:** Koller

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

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

Approved by Chair: _____ **DFO:** _____ **Date:** 4/27/00

Appendix W

NAC/AEGL Meeting 17: 4/26-28/2000 **Chemical:** BROMINE # 7726-95-6

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

NAC Member	AEGL 1	AEGL 2	AEGL 3
Loren Koller	Y	Y	Y
Glenn Leach	A	A	A
Mark A. McClanahan	N	N	N
John S. Morawetz	Y	Y	Y
Richard W. Niemeier	N	Y	Y
Zarena Post	Y	Y	Y
George Rodgers	A	A	Y
George Rusch, Chair	N	Y	Y
Michelle Schaper	A	A	A
Bob Snyder	Y	Y	Y
Thomas Sobotka	A	A	A
Kenneth Still	Y	Y	Y
Judy Strickland MEMBERSHIP PENDING	(P)	(P)	(P)
Richard Thomas	A	A	A
Thomas Tuccin/ Doan ardi Hansen	A	A	A
TALLY	15/20	16/20	18/19

PPM, (mg/m³)	30 Min	60 Min	4 Hr	8Hr
AEGL 1 0.055	0.033 ,( )	0.024 ,( )	0.013 ,( )	0.0095 ,( )
AEGL 2 0.55	0.33 ,( )	0.24 ,( )	0.13 ,( )	0.095 ,( )
AEGL 3 19	12 ,( )	8.5 ,( )	4.5 ,( )	3.2 ,( )

AEGL 1 **Motion:** Benson, Gephart **Second:** Alexeeff

AEGL 2 **Motion:** Alexeeff, Post **Second:** Niemeier

AEGL 3 **Motion:** Alexeeff **Second:** Gephart

Approved by Chair: [signature] **DFO:** Paul S. Tobin **Date:** 4/26/00

Appendix X

NAC/AEGL Meeting 17: 4/26-28/2000 **Chemical:** PHOSPHINE #7803-51-2

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

NAC Member	AEGL 1	AEGL 2	AEGL 3
Loren Koller	Y	N	Y
Glenn Leach	A	A	A
Mark A. McClanahan	Y	Y	Y
John S. Morawetz	Y	Y	N
Richard W. Niemeier	Y	Y	Y
Zarena Post	Y	P	A
George Rodgers	Y	Y	Y
George Rusch, Chair	Y	Y	Y
Michelle Schaper	A	A	A
Bob Snyder	Y	Y	Y
Thomas Sobotka	A	A	A
Kenneth Still	Y	Y	Y
Judy Strickland Membership Pending	(Y)	(Y)	(Y)
Richard Thomas	A	A	A
Thomas Tuccin/ Doan ardi Hansen	A	A	A
TALLY	21/21	17/18	~~19~~ 19/20

PPM, (mg/m³)	30 Min	60 Min	4 Hr	8Hr
AEGL 1 *	, ( )	, ( )	, ( )	, ( )
AEGL 2 0.55	0.38 , ( )	0.30 , ( )	0.19 , ( )	0.13 , ( )
AEGL 3 ~~2.0~~	~~1.4~~ , ( )	~~1.1~~ , ( )	0.59 , ( )	0.45 , ( )

* NOT TO SET AEGL 1 based on lack of data

AEGL 1 **Motion:** Benson **Second:** Belluck

AEGL 2 **Motion:** Barbee **Second:** Niemeier

AEGL 3 **Motion:** Niemeier **Second:** Benson

Approved by Chair: [signature] **DFO:** Paul S. Tobin **Date:** 4/27/00